Tocolytics for delaying preterm birth

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[Intervention Review]

Tocolytics for delaying preterm birth: a network meta-analysis (0924)

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ABSTRACT

Background

Preterm birth is the leading cause of death in newborns and children. Tocolytic drugs aim to delay preterm birth by suppressing uterine contractions to allow time for administration of corticosteroids for fetal lung maturation, magnesium sulphate for neuroprotection, and transport to a facility with appropriate neonatal care facilities. However, there is still uncertainty about their effectiveness and safety.

Objectives

To estimate relative effectiveness and safety profiles for different classes of tocolytic drugs for delaying preterm birth, and provide rankings of the available drugs.

Search methods

We searched Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov (21 April 2021) and reference lists of retrieved studies.

Selection criteria

We included all randomised controlled trials assessing effectiveness or adverse effects of tocolytic drugs for delaying preterm birth. We excluded quasi- and non-randomised trials. We evaluated all studies against predefined criteria to judge their trustworthiness.

Data collection and analysis

At least two review authors independently assessed the trials for inclusion and risk of bias, and extracted data. We performed pairwise and network meta-analyses, to determine the relative effects and rankings of all available tocolytics. We used GRADE to rate the certainty of the network meta-analysis effect estimates for each tocolytic versus placebo or no treatment.

Main results

This network meta-analysis includes 122 trials (13,697 women) involving six tocolytic classes, combinations of tocolytics, and placebo or no treatment. Most trials included women with threatened preterm birth, singleton pregnancy, from 24 to 34 weeks of gestation. We judged 25 (20%) studies to be at low risk of bias. Overall, certainty in the evidence varied.

Relative effects from network meta-analysis suggested that all tocolytics are probably effective in delaying preterm birth compared with placebo or no tocolytic treatment. Betamimetics are possibly effective in delaying preterm birth by 48 hours (risk ratio (RR) 1.12, 95%

confidence interval (CI) 1.05 to 1.20; low-certainty evidence), and 7 days (RR 1.14, 95% CI 1.03 to 1.25; low-certainty evidence). COX inhibitors are possibly effective in delaying preterm birth by 48 hours (RR 1.11, 95% CI 1.01 to 1.23; low-certainty evidence). Calcium channel blockers are possibly effective in delaying preterm birth by 48 hours (RR 1.16, 95% CI 1.07 to 1.24; low-certainty evidence), probably effective in delaying preterm birth by 7 days (RR 1.15, 95% CI 1.04 to 1.27; moderate-certainty evidence), and prolong pregnancy by 5 days (0.1 more to 9.2 more; high-certainty evidence). Magnesium sulphate is probably effective in delaying preterm birth by 48 hours (RR 1.12, 95% CI 1.02 to 1.23; moderate-certainty evidence). Oxytocin receptor antagonists are probably effective in delaying preterm birth by 48 hours (RR 1.13, 95% CI 1.05 to 1.22; moderate-certainty evidence), are effective in delaying preterm birth by 7 days (RR 1.18, 95% CI 1.07 to 1.30; high-certainty evidence), and possibly prolong pregnancy by 10 days (95% CI 2.3 more to 16.7 more). Nitric oxide donors are probably effective in delaying preterm birth by 48 hours (RR 1.17, 95% CI 1.05 to 1.31; moderate-certainty evidence), and 7 days (RR 1.18, 95% CI 1.02 to 1.37; moderate-certainty evidence). Combinations of tocolytics are probably effective in delaying preterm birth by 48 hours (RR 1.17, 95% CI 1.07 to 1.27; moderate-certainty evidence), and 7 days (RR 1.19, 95% CI 1.05 to 1.34; moderate-certainty evidence).

Nitric oxide donors ranked highest for delaying preterm birth by 48 hours and 7 days, and delay in birth (continuous outcome), followed by calcium channel blockers, oxytocin receptor antagonists and combinations of tocolytics.

Betamimetics (RR 14.4, 95% CI 6.11 to 34.1; moderate-certainty evidence), calcium channel blockers (RR 2.96, 95% CI 1.23 to 7.11; moderate-certainty evidence), magnesium sulphate (RR 3.90, 95% CI 1.09 to 13.93; moderate-certainty evidence) and combinations of tocolytics (RR 6.87, 95% CI 2.08 to 22.7; low-certainty evidence) are probably more likely to result in cessation of treatment.

Calcium channel blockers possibly reduce the risk of neurodevelopmental morbidity (RR 0.51, 95% CI 0.30 to 0.85; low-certainty evidence), and respiratory morbidity (RR 0.68, 95% CI 0.53 to 0.88; low-certainty evidence), and result in fewer neonates with birthweight less than 2000 g (RR 0.49, 95% CI 0.28 to 0.87; low-certainty evidence). Nitric oxide donors possibly result in neonates with higher birthweight (mean difference (MD) 425.53 g more, 95% CI 224.32 more to 626.74 more; low-certainty evidence), fewer neonates with birthweight less than 2500 g (RR 0.40, 95% CI 0.24 to 0.69; low-certainty evidence), and more advanced gestational age (MD 1.35 weeks more, 95% CI 0.37 more to 2.32 more; low-certainty evidence). Combinations of tocolytics possibly result in fewer neonates with birthweight less than 2500 g (RR 0.74, 95% CI 0.59 to 0.93; low-certainty evidence).

In terms of maternal adverse effects, betamimetics probably cause dyspnoea (RR 12.09, 95% CI 4.66 to 31.39; moderate-certainty evidence), palpitations (RR 7.39, 95% CI 3.83 to 14.24; moderate-certainty evidence), vomiting (RR 1.91, 95% CI 1.25 to 2.91; moderate-certainty evidence), possibly headache (RR 1.91, 95% CI 1.07 to 3.42; low-certainty evidence) and tachycardia (RR 3.01, 95% CI 1.17 to 7.71; low-certainty evidence) compared with placebo or no treatment. COX inhibitors possibly cause vomiting (RR 2.54, 95% CI 1.18 to 5.48; low-certainty evidence). Calcium channel blockers (RR 2.59, 95% CI 1.39 to 4.83; low-certainty evidence), and nitric oxide donors probably cause headache (RR 4.20, 95% CI 2.13 to 8.25; moderate-certainty evidence).

Authors' conclusions

Compared with placebo or no tocolytic treatment, all tocolytic drug classes that we assessed (betamimetics, calcium channel blockers, magnesium sulphate, oxytocin receptor antagonists, nitric oxide donors) and their combinations were probably or possibly effective in delaying preterm birth for 48 hours, and 7 days. Tocolytic drugs were associated with a range of adverse effects (from minor to potentially severe) compared with placebo or no tocolytic treatment, although betamimetics and combination tocolytics were more likely to result in cessation of treatment. The effects of tocolytic use on neonatal outcomes such as neonatal and perinatal mortality, and on safety outcomes such as maternal and neonatal infection were uncertain.

PLAIN LANGUAGE SUMMARY

Are medicines that delay the start of labour (tocolytics) effective for delaying preterm birth?

Key messages

• All tocolytics (medicines that delay labour) that we assessed (betamimetics, calcium channel blockers, magnesium sulphate, oxytocin receptor antagonists, nitric oxide donors) and their combinations were probably or possibly effective in delaying preterm birth for 48 hours and for 7 days compared with placebo (a dummy treatment) or no tocolytic treatment,

• Tocolytics cause a wide range of unwanted effects (from minor to potentially severe) compared with placebo or no tocolytic treatment. Women taking betamimetics and combinations of tocolytics were more likely to stop taking them as a result of unwanted effects.

• The effects of tocolytics on deaths of babies before and after birth, and on infection in mothers and babies were uncertain.

What is the issue?

Preterm birth is the most common reason why a newborn baby may die, and is the leading cause of death in children under five years of age. Preterm birth (previously called premature birth) is defined as birth of a baby before 37 completed weeks of pregnancy. The earlier the baby is born, the poorer the outcome. Preterm infants are not only at increased risk of death, but also serious illness. They are more likely

to face breathing complications, difficulties with feeding and body temperature regulation. Long-term complications include disability associated with brain function, and lung and gut complications.

Why is this important?

Tocolytics aim to delay preterm birth and allow time for women to receive medicines that can help with baby's breathing and feeding if born preterm, and medicines that lower the chance of the infant having cerebral palsy. Crucially, a short delay in preterm birth can enable women to reach specialist care. The aim of this Cochrane Review was to find out which tocolytic is most effective in delaying preterm birth, and has the fewest unwanted effects. We collected and analysed all studies to answer this question (date of search: 21 April 2021)

What evidence did we find?

We searched for evidence and identified 122 studies of 13,697 women involving six classes of tocolytics (betamimetics, COX inhibitors, calcium channel blockers, magnesium sulphate, oxytocin receptor antagonists, and nitric oxide donors), combinations of tocolytics, and placebo or no tocolytic treatment. Of 122 studies, we judged 25 (20%) to provide the most trustworthy evidence. Overall, the evidence varied widely in quality, and our confidence in our results ranged from very low to high. We compared the different tocolytics against each other as well as against placebo or no treatment.

Delay in birth by 48 hours and 7 days
• Betamimetics may be effective in delaying preterm birth by 48 hours (9853 women), and 7 days (7143 women).
• Calcium channel blockers may be effective in delaying preterm birth by 48 hours, and probably effective in delaying preterm birth by 7 days.
• Magnesium sulphate might be effective in delaying preterm birth by 48 hours.
• Oxytocin receptor antagonists are effective in delaying preterm birth by 7 days, might be effective in delaying birth by 48 hours and possibly result in pregnancy prolongation in average of 10 days (5093 women).
• Nitric oxide donors might be effective in delaying preterm birth by 48 hours, and 7 days.
• COX inhibitors may be effective in delaying preterm birth by 48 hours.
• Combinations of tocolytics - most commonly magnesium sulphate combined with betamimetics - might be effective in delaying preterm birth by 48 hours, and 7 days.
• The most effective tocolytics for delaying preterm birth by 48 hours, and 7 days were the nitric oxide donors, calcium channel blockers, oxytocin receptor antagonists and combinations of tocolytics.

Serious unwanted effects and ending treatment due to unwanted effects
• Tocolytics are associated with a wide range of serious unwanted effects (6983 women) compared with placebo or no treatment.
• Betamimetics and combinations of tocolytics caused the most unwanted effects leading most women to stop treatment.
• Tocolytics are associated with a wide range of treatment effects compared with placebo or no tocolytic treatment for neonatal death at 28 days (8395 babies) and maternal infection (1399 women); so their effects were uncertain.

Summary of findings 1. Delay in birth by 48 hours

Delay in birth by 48 hours

Patient or population: women with signs and symptoms of preterm labour

Settings: hospital setting

Intervention: betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics

Comparison: placebo or no treatment

Outcomes	Direct evidence		Indirect evidence		Network evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.27 (1.11 to 1.45)	⊕⊕⊕⊖ Moderate[a]	1.04 (0.96 to 1.12)	⊕⊕⊖⊖ Low[b]	1.12 (1.05 to 1.20)	⊕⊕⊖⊖ Low[c]	645 per 1000	722 per 1000	77 more per 1000 (from 32 to 129 more)
COX inhibitors	2.02 (0.81 to 5.08	⊕⊖⊖⊖ Very low[d]	1.10 (0.98 to 1.23)	⊕⊖⊖⊖ Very low[e]	1.11 (1.01 to 1.23)	⊕⊕⊖⊖ Low[f]	645 per 1000	716 per 1000	71 more per 1000 (from 6 to 148 more)
Calcium channel blockers	1.87 (1.06 to 3.28)	⊕⊕⊖⊖ Low[g]	1.17 (1.08 to 1.26)	⊕⊕⊖⊖ Low[b]	1.16 (1.07 to 1.24)	⊕⊕⊖⊖ Low[h]	645 per 1000	748 per 1000	103 per 1000 (from 45 to 155 more)
Magnesium sulphate	1.06 (0.88 to 1.29)	⊕⊕⊖⊖ Low[i]	1.14 (1.02 to 1.28)	⊕⊖⊖⊖ Very low[e]	1.12 (1.02 to 1.23)	⊕⊕⊕⊖ Moderate[j]	645 per 1000	722 per 1000	77 more per 1000 (from 13 to 148 more)
Oxytocin receptor antagonists	1.07 (0.91 to 1.27)	⊕⊕⊖⊖ Low[k]	1.17 (1.06 to 1.29)	⊕⊕⊕⊖ Moderate[l]	1.13 (1.05 to 1.22)	⊕⊕⊕⊖ Moderate[m]	645 per 1000	729 per 1000	84 more per 1000 (from 32 to 142 more)

Nitric oxide donors	1.18 (0.76 to 1.84	⊕⊖⊖⊖ Low[n]	1.20 (1.06 to 1.36)	⊕⊕⊕⊖ Moderate[l]	1.17 (1.05 to 1.31)	⊕⊕⊕⊖ Moderate[m]	645 per 1000	755 per 1000	110 per 1000 (from 32 to 200 more)
Combinations of tocolytics	1.05 (0.84 to 1.31)	⊕⊖⊖⊖ Very low[o]	1.18 (1.08 to 1.30)	⊕⊕⊕⊖ Moderate[l]	1.17 (1.07 to 1.27)	⊕⊕⊕⊖ Moderate[m]	645 per 1000	755 per 1000	110 per 1000 (from 45 to 174 more)

*The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Direct evidence downgraded once due to multiple limitations in trial design.
[b]Indirect evidence downgraded twice due to multiple limitations in trial design and suspected publication bias.
[c]Network evidence downgraded twice due to moderate-certainty direct evidence further downgraded once because of lack of coherence between direct and indirect effect estimates.
[d]Direct evidence downgraded three times due to multiple limitations in trial design, severe unexplained statistical heterogeneity, and very serious imprecision.
[e]Indirect evidence downgraded three times due to multiple limitations in trial design, and very serious imprecision.
[f]Network evidence downgraded twice due to very low-certainty direct and indirect evidence; upgraded once because the network estimate is precise.
[g]Direct evidence downgraded twice due to multiple limitations in trial design and severe unexplained statistical heterogeneity.
[h]Network evidence downgraded twice due to low-certainty direct and indirect evidence.
[i]Direct evidence downgraded twice due to multiple limitations in trial design and serious imprecision.
[j]Network evidence downgraded once due to low-certainty direct evidence; upgraded once because the network estimate is precise.
[k]Direct evidence downgraded twice due to severe unexplained statistical heterogeneity and serious imprecision.
[l]Indirect evidence downgraded once due to multiple limitations in trial design.
[m]Network evidence downgraded once due to moderate-certainty indirect evidence.
[n]Direct evidence downgraded twice due to very serious imprecision.
[o]Direct evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.

Summary of findings 2. Delay in birth by 7 days

Delay in birth by 7 days									
Patient or population: women with signs and symptoms of preterm labour									
Settings: hospital setting									
Intervention: betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics									
Comparison: placebo or no treatment									
Outcomes	**Direct evidence**		**Indirect evidence**		**Network evidence**		**Anticipated absolute effects for network estimate**		
	RR (95% CI)	**Certainty**	**RR (95% CI)**	**Certainty**	**RR (95% CI)**	**Certainty**	**Risk with placebo or no treatment**	**Risk with tocolytic agent**	**Risk difference with tocolytic agent**
Betamimetics	1.47 (1.09 to 1.97)	⊕⊕⊕⊖ Moderate[a]	1.07 (0.96 to 1.20)	⊕⊕⊖⊖ Low[b]	1.14 (1.03 to 1.25)	⊕⊕⊖⊖ Low[c]	742 per 1000	846 per 1000	104 more per 1000 (from 22 to 186 more)
COX inhibitors	2.05 (0.41 to 10.33)	⊕⊕⊖⊖ Low[d]	1.01 (0.84 to 1.21)	⊕⊖⊖⊖ Very low[e]	1.04 (0.88 to 1.24)	⊕⊕⊕⊖ Moderate[f]	742 per 1000	772 per 1000	30 more per 1000 (from 89 fewer to 178 more)
Calcium channel blockers	1.25 (0.86 to 1.82)	⊕⊕⊖⊖ Low[g]	1.22 (1.10 to 1.36)	⊕⊕⊕⊖ Moderate[h]	1.15 (1.04 to 1.27)	⊕⊕⊕⊖ Moderate[i]	742 per 1000	853 per 1000	111 per 1000 (from 30 to 200 more)
Magnesium sulphate	0.82 (0.63 to 1.08)	⊕⊖⊖⊖ Very low[j]	0.99 (0.75 to 1.30)	⊕⊖⊖⊖ Very low[e]	0.91 (0.74 to 1.12)	⊕⊖⊖⊖ Very low[k]	742 per 1000	675 per 1000	67 fewer per 1000 (from 193 fewer to 89 more)
Oxytocin receptor antagonists	1.23 (1.11 to 1.37)	⊕⊕⊕⊕ High	1.14 (0.99 to 1.30)	⊕⊕⊖⊖ Low[l]	1.18 (1.07 to 1.30)	⊕⊕⊕⊕ High	742 per 1000	876 per 1000	134 more per 1000 (from 52 to 223 more)
Nitric oxide donors	No estimate possible	Not applicable	1.18	⊕⊕⊕⊖ Moderate[h]	1.18	⊕⊕⊕⊖ Moderate[i]	742 per 1000	876 per 1000	134 per 1000 (from 15 to 275 more)

			(1.02 to 1.37)		(1.02 to 1.37)				
Combinations of tocolytics	0.92 (0.67 to 1.28)	⊕⊖⊖⊖ Very low[j]	1.22 (1.07 to 1.40)	⊕⊕⊕⊖ Moderate[h]	1.19 (1.05 to 1.34)	⊕⊕⊕⊖ Moderate[i]	742 per 1000	883 per 1000	141 per 1000 (from 37 to 252 more)

*The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Direct evidence downgraded once due to multiple limitations in trial design.
[b]Indirect evidence downgraded twice due to multiple limitations in trial design and serious imprecision.
[c]Network evidence downgraded twice due to moderate-certainty direct evidence further downgraded once because of lack of coherence between direct and indirect effect estimates.
[d]Direct evidence downgraded twice due to very serious imprecision.
[e]Indirect evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.
[f]Network evidence downgraded once due to low-certainty direct evidence; upgraded once because the network estimate is precise.
[g]Direct evidence downgraded twice due to multiple limitations in trial design and serious imprecision.
[h]Indirect evidence downgraded once due to multiple limitations in trial design.
[i]Network evidence downgraded once due to moderate certainty indirect evidence.
[j]Direct evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.
[k]Network evidence downgraded three times due to very low-certainty direct and indirect evidence.
[l]Indirect evidence downgraded twice due to multiple limitations in trial design and severe unexplained statistical heterogeneity.

Summary of findings 3. Neonatal death before 28 days

Neonatal death before 28 days
Patient or population: women with signs and symptoms of preterm labour

Settings: hospital setting

Intervention: betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics

Comparison: placebo or no treatment

Outcomes	Direct evidence		Indirect evidence		Network evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.94 (0.56 to 1.59)	⊕⊖⊖⊖ Low[a]	1.46 (0.56 to 3.79)	⊕⊖⊖⊖ Very low[b]	1.01 (0.66 to 1.55)	⊕⊖⊖⊖ Low[c]	66 per 1000	67 per 1000	1 more per 1000 (from 22 fewer to 36 more)
COX inhibitors	0.77 (0.22 to 2.72)	⊕⊖⊖⊖ Low[d]	1.42 (0.53 to 3.81)	⊕⊖⊖⊖ Very low[b]	1.12 (0.51 to 2.45)	⊕⊖⊖⊖ Low[c]	66 per 1000	74 per 1000	8 more per 1000 (from 32 fewer to 96 more)
Calcium channel blockers	5.18 (0.26 to 103.15)	⊕⊖⊖⊖ Very low[e]	0.77 (0.40 to 1.47)	⊕⊕⊖⊖ Low[f]	0.84 (0.44 to 1.57)	⊕⊕⊖⊖ Low[g]	66 per 1000	55 per 1000	11 fewer per 1000 (from 37 fewer to 38 more)
Magnesium sulphate	0.89 (0.15 to 5.09)	⊕⊖⊖⊖ Very low[e]	1.75 (0.61 to 4.99)	⊕⊖⊖⊖ Very low[b]	1.19 (0.55 to 2.58)	⊕⊖⊖⊖ Very low[h]	66 per 1000	79 per 1000	13 more per 1000 (from 30 fewer to 104 more)
Oxytocin receptor antagonists	4.10 (0.88 to 19.13)	⊕⊕⊖⊖ Low[d]	0.60 (0.21 to 1.68)	⊕⊖⊖⊖ Very low[b]	1.08 (0.46 to 2.56)	⊕⊖⊖⊖ Very low[i]	66 per 1000	71 per 1000	5 more per 1000 (from 36 fewer to 103 more)
Nitric oxide donors	0.49 (0.07 to 3.64)	⊕⊕⊖⊖ Low[d]	0.79 (0.15 to 4.29)	⊕⊖⊖⊖ Very low[b]	0.65 (0.18 to 2.36)	⊕⊕⊖⊖ Low[c]	66 per 1000	43 per 1000	23 fewer per 1000 (from 54 fewer to 90 more)
Combinations of tocolytics	Not estimable	Not applicable	0.55 (0.18 to 1.66)	⊕⊖⊖⊖ Very low[b]	0.55 (0.18 to 1.66)	⊕⊖⊖⊖ Very low[j]	66 per 1000	36 per 1000	30 fewer per 1000 (from 54 fewer to 44 more)

*The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.
CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

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[g]Network evidence downgraded twice due to low-certainty indirect evidence.
[h]Network evidence downgraded three times due to very low-certainty direct and indirect evidence.
[i]Network evidence downgraded three times due to low-certainty direct evidence, further downgraded once because of lack of coherence between direct and indirect effect estimates.
[j]Network evidence downgraded three times due to very low-certainty indirect evidence only being available.

Summary of findings 4. Pregnancy prolongation (time from trial entry to birth in days)

Pregnancy prolongation (time from trial entry to birth in days)				
Patient or population: women with signs and symptoms of preterm labour **Settings:** hospital setting **Intervention:** betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics **Comparison:** placebo or no treatment				
Outcomes	**Direct evidence**	**Indirect evidence**	**Network evidence**	**Anticipated absolute effects for network estimate**

	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.86 (−2.24 to 5.95)	⊕⊖⊖⊖ Low[a]	−0.10 (−6.18 to 5.98)	⊕⊕⊖⊖ Moderate[b]	0.83 (−3.12 to 4.78)	⊕⊕⊕⊖ Moderate[c]	20 days more	21 days more	1 day more (from 3 days fewer to 5 days more)
COX inhibitors	−0.30 (−6.32 to 5.72)	⊕⊕⊖⊖ Low[d]	5.45 (−4.35 to 15.24)	⊕⊖⊖⊖ Very low[e]	3.31 (−4.41 to 11.03)	⊕⊕⊖⊖ Low[f]	20 days more	23 days more	3 days more (from 4 days fewer to 11 days more)
Calcium channel blockers	4.71 (0.32 to 9.10)	⊕⊕⊕⊖ Moderate[g]	4.72 (−0.59 to 10.02)	⊕⊕⊖⊖ Low[h]	4.66 (0.13 to 9.19)	⊕⊕⊕⊕ High[i]	20 days more	25 days more	5 days more (from 0 days to 9 days more)
Magnesium sulphate	0.33 (−3.39 to 4.04)	⊕⊖⊖⊖ Very low[j]	0.09 (−8.11 to 8.29)	⊕⊖⊖⊖ Very low[k]	0.34 (−5.01 to 5.69)	⊕⊖⊖⊖ Very low[l]	20 days more	20 days more	0 days (from 5 days fewer to 6 days more)
Oxytocin receptor antagonists	Not estimable	Not applicable	9.54 (2.35 to 16.73)	⊕⊕⊖⊖ Low[h]	9.54 (2.35 to 16.73)	⊕⊕⊖⊖ Low[m]	20 days more	30 days more	10 days more (from 2 days more to 17 days more)
Nitric oxide donors	11.91 (3.53 to 20.28)	⊕⊕⊕⊖ Moderate[g]	3.94 (−6.13 to 14.01)	⊕⊕⊖⊖ Low[h]	7.44 (−0.44 to 15.32)	⊕⊕⊕⊖ Moderate[n]	20 days more	27 days more	7 days more (from 0 days to 15 days more)
Combinations of tocolytics	−6.10 (−13.54 to 1.34)	⊕⊖⊖⊖ Very low[j]	4.30 (−3.56 to 12.16)	⊕⊖⊖⊖ Very low[e]	1.55 (−5.31 to 8.40)	⊕⊖⊖⊖ Very low[l]	20 days more	22 days more	2 days more (from 5 days fewer to 8 days more)

*The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Direct evidence downgraded twice due to multiple limitations in trial design and serious imprecision.
[b]Indirect evidence downgraded once due to multiple limitations in trial design.
[c]Network evidence downgraded once due to moderate-certainty indirect evidence.
[d]Direct evidence downgraded twice due to very serious imprecision.
[e]Indirect evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.
[f]Network evidence downgraded twice due to low-certainty direct evidence.
[g]Direct evidence downgraded once due to serious imprecision.
[h]Indirect evidence downgraded twice due to multiple limitations in trial design and serious imprecision.
[i]Network evidence moderate-certainty direct evidence and upgraded +1 since the network estimate is precise.
[j]Direct evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.
[k]Indirect evidence downgraded three times due to multiple serious limitations in trial design and serious imprecision.
[l]Network evidence downgraded three times due to very low-certainty direct and indirect evidence.
[m]Network evidence downgraded twice due to low-certainty indirect evidence.
[n]Network evidence downgraded once due to moderate-certainty direct evidence.

Summary of findings 5. Serious adverse effects of drugs

Serious adverse effects of drugs

Patient or population: women with signs and symptoms of preterm labour

Settings: hospital setting

Intervention: betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics

Comparison: placebo or no treatment

Outcomes	Direct evidence		Indirect evidence		Network evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent

Betamimetics	We do not present summaries of relative and absolute effects because of high risk of bias, heterogeneous definitions, and serious imprecision.
COX inhibitors	
Calcium channel blockers	
Magnesium sulphate	
Oxytocin receptor antagonists	
Nitric oxide donors	
Combinations of tocolytics	

*The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Summary of findings 6. Maternal infection

Maternal infection				
Patient or population: women with signs and symptoms of preterm labour **Settings:** hospital setting **Intervention:** betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics **Comparison:** placebo or no treatment				
Outcomes	**Direct evidence**	**Indirect evidence**	**Network evidence**	**Anticipated absolute effects for network estimate**

	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.44 (0.82 to 2.51)	⊕⊖⊖⊖ Very low[a]	33.26 (0.02 to 62,648.30)	⊕⊖⊖⊖ Very low[b]	1.52 (0.76 to 3.02)	⊕⊖⊖⊖ Very low[c]	290 per 1000	441 per 1000	151 more per 1000 (from 70 fewer to 586 more)
COX inhibitors	1.46 (0.64 to 3.34)	⊕⊕⊖⊖ Low[d]	0.32 (0.01 to 12.79)	⊕⊖⊖⊖ Very low[b]	1.37 (0.51 to 3.69)	⊕⊕⊖⊖ Low[e]	290 per 1000	397 per 1000	107 more per 1000 (from 142 fewer to 780 more)
Calcium channel blockers	Not estimable	Not applicable	6.74 (0.29 to 155.05)	⊕⊖⊖⊖ Very low[b]	6.74 (0.29 to 155.05)	⊕⊖⊖⊖ Very low[f]	290 per 1000	1000 per 1000	710 more per 1000 (from 206 fewer to 1000 more)
Magnesium sulphate	2.38 (0.24 to 23.84)	⊕⊖⊖⊖ Very low[a]	0.76 (0.06 to 8.84)	⊕⊖⊖⊖ Very low[b]	1.16 (0.24 to 5.60)	⊕⊖⊖⊖ Very low[c]	290 per 1000	336 per 1000	46 more per 1000 (from 220 fewer to 1000 more)
Oxytocin receptor antagonists	Not estimable	Not applicable	1.09 (0.02 to 50.70)	⊕⊖⊖⊖ Very low[b]	1.09 (0.02 to 50.70)	⊕⊖⊖⊖ Very low[f]	290 per 1000	316 per 1000	26 more per 1000 (from 284 fewer to 1000 more)
Nitric oxide donors	Not estimable[g]	Not applicable[g]	Not estimable[g]	Not applicable[g]	Not estimable[g]	Not applicable[g]	Not estimable[g]		
Combinations of tocolytics	Not estimable	Not applicable	1.31 (0.16 to 10.71)	⊕⊖⊖⊖ Very low[b]	1.31 (0.16 to 10.71)	⊕⊖⊖⊖ Very low[f]	290 per 1000	380 per 1000	90 more per 1000 (from 244 fewer to 1000 more)

*The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Direct evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.
[b]Indirect evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.
[c]Network evidence downgraded three times due to very low-certainty direct and indirect evidence.
[d]Direct evidence downgraded twice due to very serious imprecision.
[e]Network evidence downgraded twice due to low-certainty direct evidence.
[f]Network evidence downgraded three times due to very low-certainty indirect evidence.
[g]No studies involving nitric oxide donors for this outcome.

Summary of findings 7. Cessation of treatment due to adverse effects

Cessation of treatment due to adverse effects

Patient or population: women with signs and symptoms of preterm labour

Settings: hospital setting

Intervention: betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics

Comparison: placebo or no treatment

Outcomes	Direct evidence		Indirect evidence		Network evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	9.62 (4.33 to 21.36)	⊕⊕⊕⊖ Moderate[a]	20.49 (6.29 to 66.76)	⊕⊕⊖⊖ Low[b]	14.44 (6.11 to 34.11)	⊕⊕⊕⊖ Moderate[c]	108 per 1000	1000 per 1000	892 more per 1000 (from 552 more to 1000 more)
COX inhibitors	Not estimable	Not applicable	2.34 (0.50 to 10.97)	⊕⊖⊖⊖ Very low[d]	2.34 (0.50 to 10.97)	⊕⊖⊖⊖ Very low[e]	108 per 1000	253 per 1000	145 more per 1000 (from 54 fewer to 1000 more)

Calcium channel blockers	1.13 (0.67 to 1.88)	⊕⊕⊖⊖ Low[f]	4.54 (1.51 to 13.63)	⊕⊕⊕⊖ Moderate[g]	2.96 (1.23 to 7.11)	⊕⊕⊕⊖ Moderate[h]	108 per 1000	320 per 1000	212 more per 1000 (from 25 to 660 more)
Magnesium sulphate	9.82 (1.25 to 77.31)	⊕⊕⊖⊖ Low[i]	2.99 (0.58 to 15.48)	⊕⊖⊖⊖ Very low[d]	3.90 (1.09 to 13.93)	⊕⊕⊕⊖ Moderate[j]	108 per 1000	421 per 1000	313 more per 1000 (from 10 more to 1000 more)
Oxytocin receptor antagonists	4.02 (2.05 to 7.85)	⊕⊕⊕⊕ High	0.63 (0.21 to 1.90)	⊕⊕⊕⊖ Moderate[g]	1.24 (0.46 to 3.35)	⊕⊕⊕⊖ Moderate[k]	108 per 1000	134 per 1000	26 more per 1000 (from 58 fewer to 254 more)
Nitric oxide donors	Not estimable	Not applicable	4.31 (0.90 to 20.67)	⊕⊖⊖⊖ Very low[d]	4.31 (0.90 to 20.67)	⊕⊖⊖⊖ Very low[e]	108 per 1000	465 per 1000	357 more per 1000 (from 11 fewer to 1000 more)
Combinations of tocolytics	Not estimable	Not applicable	6.87 (2.08 to 22.65)	⊕⊕⊖⊖ Low[l]	6.87 (2.08 to 22.65)	⊕⊕⊖⊖ Low[m]	108 per 1000	742 per 1000	634 more per 1000 (from 117 to 1000 more)

*The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Direct evidence downgraded once due to multiple limitations in trial design.
[b]Indirect evidence downgraded twice due to very serious imprecision.
[c]Network evidence downgraded once due to moderate-certainty direct evidence.
[d]Indirect evidence downgraded three times due to multiple limitations in trial design and very serious imprecision.
[e]Network evidence downgraded three times due to very low-certainty indirect evidence.

[f]Direct evidence downgraded twice due to very serious imprecision.
[g]Indirect evidence downgraded once due to multiple limitations in trial design.
[h]Network evidence downgraded once due to moderate-certainty direct evidence, upgraded once because the network estimate is precise, but also downgraded because of lack of coherence between direct and indirect effect estimates.
[i]Direct evidence downgraded once due to multiple limitations in trial design and serious imprecision.
[j]Network evidence downgraded once due to low-certainty direct evidence, upgraded once because the network estimate is precise.
[k]Network evidence downgraded because of lack of coherence between direct and indirect effect estimates.
[l]Indirect evidence downgraded twice due to multiple limitations in trial design and serious imprecision.
[m]Network evidence downgraded twice due to low-certainty indirect evidence.

BACKGROUND

Description of the condition

In 2019, five million children under five years of age died. Almost half of these deaths occurred in the first month of life (UNIGME 2020). Preterm birth is the most important contributing factor for high newborn death rates, and is the leading cause of death in children under five (Liu 2016). Preterm birth (previously called premature birth) is defined as birth before 37 completed weeks of pregnancy. In addition to altering the survival chances of newborns, preterm birth also causes significant morbidity. Preterm infants are at increased risk of short-term complications such as breathing complications and difficulties with feeding and body temperature regulation, and long-term complications including neurodevelopmental, respiratory, and gastrointestinal complications (Escobar 2006; Kinney 2006; Wang 2004). Despite advances in medicine, the number of preterm births appears to be rising in most countries (WHO 2018).

The multifactorial aetiology of preterm birth means that it is difficult to predict and prevent. Several risk factors have been identified, including multiple pregnancy, infection, maternal medical conditions, and previous history of miscarriage and preterm birth (Blondel 2006; Lee 2008). Preterm birth can either be spontaneous (occurring without medical intervention) or iatrogenic (when the pregnancy is interrupted with medical intervention). The cause of spontaneous preterm labour often remains uncertain (Menon 2008). Iatrogenic preterm birth occurs only in cases where the continuation of the pregnancy poses greater risks to the mother or the fetus (or both), and its prevention should focus on preventing contributing conditions such as pre-eclampsia (Kalra 2008; Mukhopadhaya 2007).

Description of the intervention

Tocolytic drugs have been used for delaying preterm birth since the 1950s. Tocolytic drugs aim to delay preterm birth by suppressing uterine contractions. Specifically, they induce smooth muscle relaxation by engaging slightly different mechanisms of action, and as a result each has different adverse effects and different administration challenges. Even within individual drug classes there is significant variation in administration regimens. There are many different types of tocolytic drugs, however most fall within the following tocolytic drug classes.

1. Betamimetics (e.g. ritodrine)
2. Calcium channel blockers (e.g. nifedipine)
3. Magnesium sulphate
4. Oxytocin receptor antagonists (e.g. atosiban)
5. Nitric oxide donors (e.g. glyceryl trinitrate)
6. Cyclo-oxygenase (COX) inhibitors (e.g. indomethacin)
7. Combinations of tocolytics (e.g. betamimetics plus magnesium sulphate)

Betamimetics (e.g. ritodrine, terbutaline, and salbutamol) have been widely used, especially in resource-poor countries. Betamimetics are beta receptor agonists mimicking the actions of both adrenaline - and noradrenalise -, in the heart and lungs, and in smooth muscle tissue. Their use has declined over time due to their adverse effects (NICE 2015). They can cause heart palpitations, tremor, nausea, vomiting, headaches, nervousness, anxiety, chest pain, shortness of breath, and biochemical disturbances such as hyperglycaemia. Rarely, they can cause heart failure and pulmonary oedema (Medicines.org.uk 2020). Betamimetics cross the placenta and cause fetal tachycardia and neonatal hypoglycaemia (Medicines.org.uk 2020). They can be administered orally, subcutaneously, intramuscularly, and intravenously.

Calcium channel blockers (e.g. nifedipine, nicardipine) are used for the treatment of hypertension in pregnancy, and are increasingly also used as tocolytic drugs. Calcium channel blockers are administered orally. They are generally tolerated but are associated with cardiovascular adverse effects, such as headache, hypotension, dyspnoea, pulmonary oedema, and even myocardial infarction (Medicines.org.uk 2020).

Magnesium sulphate is used widely in obstetrics for the prevention and treatment of eclampsia. It is also an established fetal neuroprotective drug, and is recommended for women at risk of imminent preterm birth for the prevention of cerebral palsy in infants and children (WHO 2015). It can also be used as a tocolytic drug as it decreases the frequency of depolarisation of smooth muscle, which in turn inhibits uterine contractions. Magnesium sulphate can be administered intravenously or intramuscularly. In current clinical practice, intramuscular administration regimens are recommended only if intravenous access is not possible. Adverse effects are dose-dependent and include nausea, vomiting, headache, heart palpitations, and, rarely, pulmonary oedema (Medicines.org.uk 2020). Concentrations above the recommended therapeutic range can lead to respiratory depression, respiratory arrest, and cardiac arrest (Crowther 2014).

Oxytocin receptor antagonists (e.g. atosiban) are the only drugs that have been purposefully developed to delay preterm birth. They block oxytocin receptors, and by blocking the action of oxytocin they are able to prevent uterine contractions and relax the uterus. They can only be administered intravenously, and are associated with adverse effects such as nausea, vomiting, headache, chest pain, and hypotension (Medicines.org.uk 2020). Important issues for consideration with oxytocin receptor antagonists are their cost and availability.

Nitric oxide donors (e.g. glyceryl trinitrate, isosorbide dinitrate) have also been used as tocolytic drugs. Nitric oxide is a free radical that induces smooth muscle relaxation, cervical ripening, and vasodilation. The effect of nitric oxide donors on the uterus is fast, which can be of great value in obstetric emergencies. They can be administered intravenously, transdermally or sublingually, and are typically associated with maternal adverse effects related to vasodilation, such as headache, flushing, hypotension and tachycardia (Duckitt 2014). Nitric oxide donors could adversely affect the developing fetus because they induce changes to the uterine blood flow (Duckitt 2014).

Cyclo-oxygenase (COX) inhibitors (e.g. indomethacin) can easily be administered orally or rectally. They have a different adverse effect profile compared with betamimetics (Babay 1998). However, COX inhibitors easily cross the placenta and can interfere with the fetal prostaglandin homeostasis. A meta-analysis published in 2006 found that even short-term use of COX inhibitors in late gestations is associated with a 15-fold increase of premature ductal closure (Koren 2006). Because of these concerns, COX inhibitors are currently contraindicated in the third trimester. In view of this

contraindication, COX inhibitors are largely limited to use in the second trimester because of this effect.

Combinations of tocolytic drugs from different classes (e.g. betamimetics plus magnesium sulphate) have been used together to delay preterm birth. Using tocolytic drugs from different classes suppresses uterine contractions by targeting different pathways in the myometrium. Using a combination of tocolytic drugs could have the benefit of improving the desirable effects. A combination of tocolytic drug classes may mean also that a lower dose of the combination drugs could be used to achieve the desirable effect, resulting in fewer adverse effects.

How the intervention might work

Tocolytics can potentially delay preterm birth by suppressing uterine contractions (Haas 2009). The rationale for tocolysis is that the delay in preterm birth can allow time for administration of corticosteroids for fetal lung maturation, magnesium sulphate for neuroprotection, and time for the pregnant woman to be transported to a facility with appropriate neonatal care facilities.

Why it is important to do this review

With the increasing contribution of neonatal deaths to overall child mortality, it is critical to address the determinants of poor outcomes related to preterm birth to achieve further reductions in infant mortality. Infant mortality and morbidity can be reduced through interventions delivered to the mother before or during pregnancy, and to the infant after birth. The most beneficial set of maternal interventions are those that are aimed at improving outcomes for preterm infants when preterm birth is inevitable (e.g. antenatal corticosteroids, and magnesium sulphate; WHO 2015). The success of these interventions is dependent on appropriate timing. For example, corticosteroids are more beneficial when administered more than 24 hours before birth, but no more than seven days before birth; magnesium sulphate needs to be administered no more than 24 hours prior to birth; and transfer takes time to arrange. Therefore, once a diagnosis of preterm labour is made, prompt action is vital for maximising survival and reducing complications for the infant.

Tocolytics could potentially delay preterm birth, which in turn could enhance the beneficial effects of the interventions mentioned above. However, there is still uncertainty about whether they are effective in improving neonatal health outcomes. Current guidelines indicate inconsistencies; the World Health Organization (WHO) state that tocolytic drugs are not recommended for women at risk of imminent preterm birth for the purpose of improving neonatal outcomes (WHO 2015), while others suggest that tocolytic drugs should be offered. The evidence informing these guidelines was based on low-certainty evidence from several individual Cochrane Reviews containing small- to medium-sized trials (Bain 2013; Crowther 2014; Duckitt 2014; Flenady 2014a; Flenady 2014b; Neilson 2014; Reinebrant 2015; Su 2014).

The comparisons of interest for this review are those of tocolytic drugs versus placebo or no treatment with tocolytics, to determine if tocolytics are effective in delaying preterm birth and improving neonatal outcomes. The comparison of tocolytic drugs with each other is also of interest, for determining which tocolytic drug is the most effective. Where several competing drug options exist, not all of which have been directly compared, a network meta-analysis may allow for more comparisons to be made and a more comprehensive synthesis of relative effects for all available tocolytic drugs (Caldwell 2005; Caldwell 2010). A network meta-analysis, unlike conventional Cochrane Reviews, simultaneously pools all direct and indirect evidence into one single coherent analysis. Indirect evidence is obtained by inferring the relative effectiveness of two competing drugs through a common comparator, even when these two drugs have not been compared directly. A network meta-analysis also calculates the probability for each competing drug to constitute the most effective drug with the fewest adverse effects, thereby allowing ranking of the available tocolytic drugs (Caldwell 2005).

OBJECTIVES

To estimate relative effectiveness and safety profiles for different classes of tocolytic drugs for delaying preterm birth, and provide rankings of the available drugs.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials or cluster-randomised trials comparing tocolytic drugs with other tocolytic drugs, placebo or no treatment were eligible for inclusion. Cross-over trials and quasi-randomised trials were excluded. The cross-over trial design is inappropriate to investigate the effectiveness of tocolytic drugs, and quasi-randomisation rather than true randomisation introduces an elevated risk of bias that we wish to eliminate for the purpose of this review. Randomised trials published only as abstracts were eligible only if sufficient information could be retrieved.

Types of participants

This review included trials involving women with live fetus(es), with signs and symptoms of preterm labour, defined as uterine activity with or without ruptured membranes; or ruptured membranes with or without cervical dilatation or shortening, or biomarkers consistent with a high risk of preterm birth. We considered studies conducted in all settings.

Types of interventions

Trials were eligible if they administered tocolytic drugs of any dosage, route, or regimen for delaying preterm birth, and compared them with another tocolytic drug, placebo, or no treatment. We excluded trials that exclusively compared different dosages, routes or regimens of the same tocolytic drug. Eligible interventions include the tocolytic classes listed below.

1. Betamimetics (ritodrine, terbutaline, nylidrin, fenoterol, isoxsuprine salbutamol)
2. COX inhibitors (indomethacin, rofecoxib, celecoxib)
3. Calcium channel blockers (nifedipine, nicardipine)
4. Magnesium sulphate
5. Oxytocin receptor antagonists (atosiban, retosiban, barusiban)
6. Nitric oxide donors (isosorbide dinitrate, glyceryl trinitrate)
7. Combinations of tocolytics (betamimetics plus magnesium sulphate, betamimetic plus calcium channel blockers, COX

inhibitors plus betamimetics, calcium channel blockers plus oxytocin antagonist receptors)

We grouped all tocolytic drugs from the same class in the same node regardless of dose, regime (bolus +/- maintenance) or route. We addressed the effect of regime (bolus +/- maintenance) through subgroup analyses. We would consider splitting the nodes if we found subgroup effects with a specific dose or route. There is no pre-existing evidence that a specific dose or route is superior or inferior to another one.

Participants in the network could in principle be randomised to any of the tocolytic drugs being compared. We included trials in which adjuvant co-interventions such as progesterone or cervical cerclage (inserting a stitch around the cervix) were administered in combination with tocolytic drugs; we tested the effects of such co-interventions through sensitivity analyses. We have included information about co-interventions aimed at improving maternal and neonatal status antenatally (corticosteroids, antibiotics, magnesium sulphate for neuroprotection, where documented within the included studies) in the Characteristics of included studies.

Types of outcome measures

Outcomes are based on WHO critical outcomes for preterm birth and include both neonatal and maternal outcomes (WHO 2015). Outcome measure time points were as reported in the primary studies.

Primary outcomes

The main (primary) outcomes are as follows. These outcomes feature in the summary of findings tables.

1. Delay in birth by 48 hours
2. Delay in birth by 7 days
3. Neonatal death before 28 days
4. Pregnancy prolongation (time from trial entry to birth)
5. Serious adverse effects of drugs
6. Maternal infection after trial entry
7. Cessation of treatment due to adverse effects

Secondary outcomes

1. Birth prior to 28 weeks of gestation
2. Birth prior to 32weeks of gestation
3. Birth prior to 34 weeks of gestation
4. Birth prior to 37 weeks of gestation
5. Maternal death
6. Pulmonary oedema
7. Dyspnoea
8. Palpitation
9. Headaches
10. Nausea or vomiting
11. Tachycardia
12. Maternal cardiac arrhythmias
13. Maternal hypotension
14. Perinatal mortality
15. Stillbirth
16. Neonatal death before 7 days
17. Neurodevelopmental morbidity
18. Gastrointestinal morbidity
19. Respiratory morbidity
20. Mean birthweight
21. Birthweight less than 2000 g
22. Birthweight less than 2500 g
23. Gestational age at birth
24. Neonatal infection

Search methods for identification of studies

Electronic searches

We searched Cochrane Pregnancy and Childbirth's Trials Register by contacting their Information Specialist (21 April 2021).

Cochrane Pregnancy and Childbirth's Trials Register is a database containing over 27,000 reports of controlled trials in the field of pregnancy and childbirth. It represents over 30 years of searching. For full current search methods used to populate Pregnancy and Childbirth's Trials Register including the detailed search strategies for CENTRAL, MEDLINE, Embase and CINAHL; the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this link.

Briefly, Cochrane Pregnancy and Childbirth's Trials Register is maintained by their Information Specialist and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL), which contains Cochrane's centralised searches of WHO International Clinical Trials Registry Platform (ICTRP);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);
5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Two people screen the search results and review the full text of all relevant trial reports identified through the searching activities described above. Based on the intervention described, they assign each trial report a number that corresponds to a specific Pregnancy and Childbirth review topic (or topics), and it is then added to the Register. The Information Specialist searches the Register for each review using this topic number rather than keywords. This results in a more specific search set that has been fully accounted for in the relevant review sections (Included studies, Excluded studies, Studies awaiting classification or Ongoing studies).

In addition, we searched ClinicalTrials.gov for unpublished, planned and ongoing trial reports (21 April 2021) using the search methods detailed in Appendix 1.

Searching other resources

We retrieved additional relevant references cited in papers identified through the above search strategy and we searched for the full texts of trials initially identified as abstracts. For randomised

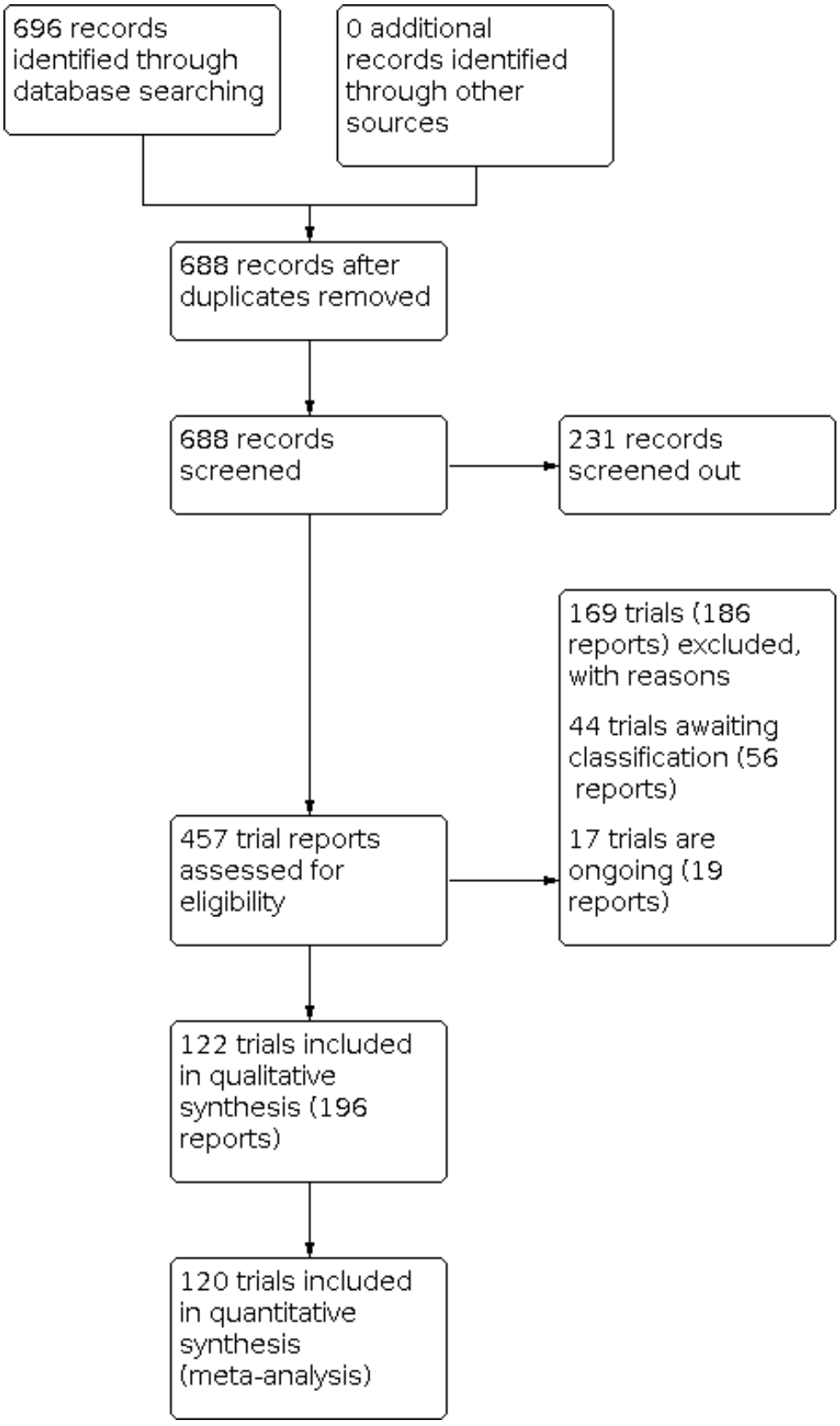
trials published only as abstracts, we sought information from primary authors to investigate whether these studies met our eligibility criteria before including them. Trials that compared at least two of the agents were eligible and we searched for all possible comparisons. We did not apply any language or date restrictions.

Data collection and analysis

Selection of studies

At least two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy (AW, VAH, EJM, ADM, EL). We resolved any disagreement through discussion or, if required, we consulted a third person (KM or IG). We created a flow diagram to present the number of records identified, included and excluded (Liberati 2009; Figure 1).

Figure 1. Study flow diagram

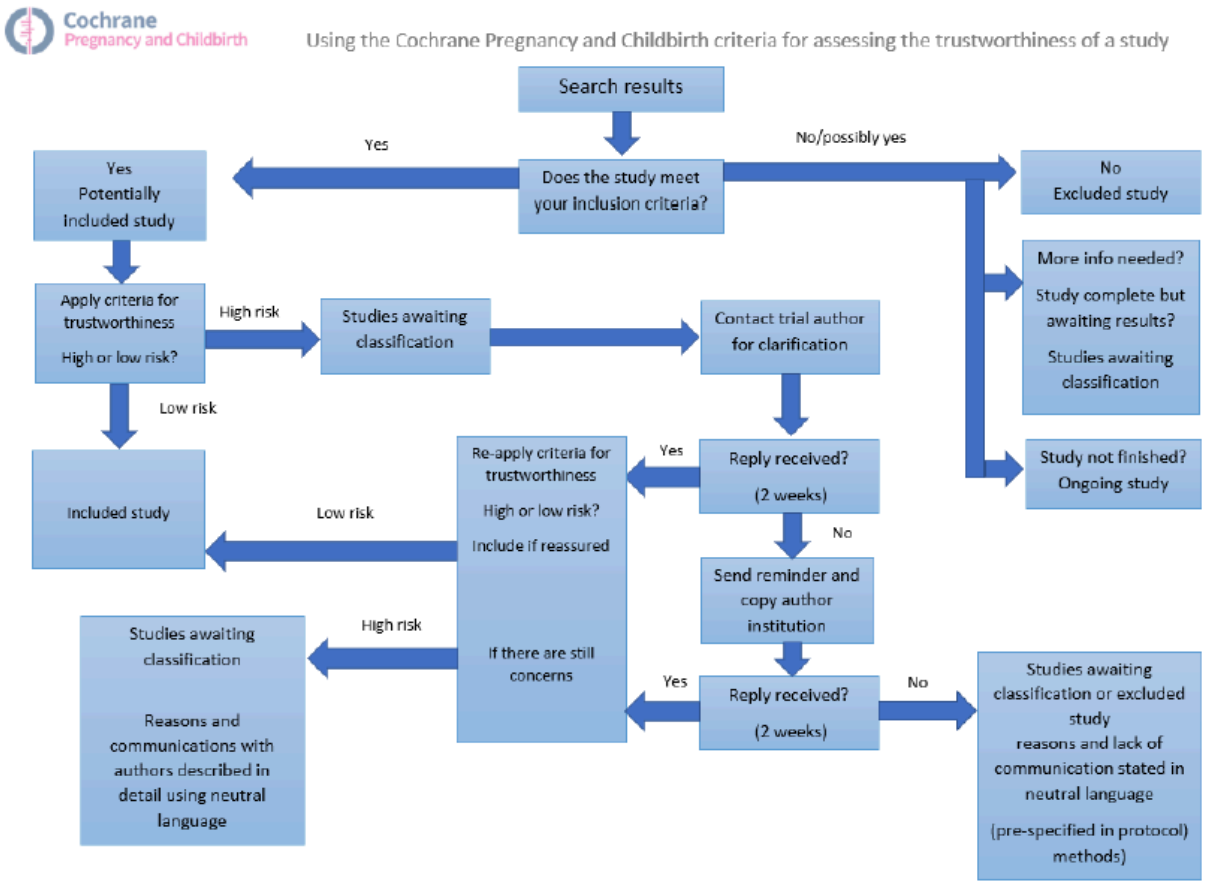


Screening eligible studies for scientific integrity/trustworthiness

Two review authors evaluated all studies that met our inclusion criteria against predefined criteria to select studies that, based on available information, we deemed to be sufficiently trustworthy to be included in the analysis. These criteria are developed by Cochrane Pregnancy and Childbirth (see Appendix 2).

Where a trial is classified as being at 'high risk' for one or more of the predefined criteria, we attempted to contact the trial authors to address any possible lack of information and concerns. If adequate information remained unavailable, we categorised the trial as 'awaiting classification', and described the concerns and communications with the author (or lack thereof) in detail (Characteristics of studies awaiting classification). The process is described fully in Figure 2.

Figure 2. Process for using the Cochrane Pregnancy and Childbirth criteria for assessing the trustworthiness of a study



Data extraction and management

We extracted data from each eligible report using a pre-designed form. For eligible studies, at least two review authors (AW, VAH, EJM, ADM, EL) independently extracted the data using the agreed form. We resolved discrepancies through discussion, or, if required, through consultation with a third person (KM or IG). We entered data into Review Manager 5 (Review Manager 2020), and checked them for accuracy. When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors (AW, VAH, EJM, ADM, EL) independently assessed risk of bias for each trial using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreement by discussion or by involving a third assessor (KM or IG).

We made explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We assessed the likely magnitude and direction of the bias and whether we considered it likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses (see Sensitivity analysis).

Measures of treatment effect

We summarised relative treatment effects for dichotomous outcomes as risk ratios (RR) and for continuous outcomes as mean difference (MD) with 95% confidence intervals (CI). These are summarised in forest plots displaying the results from pairwise, indirect and network (combining direct and indirect) analyses for the comparisons of tocolytic drugs versus placebo or no treatment and the comparisons of tocolytics with other tocolytic drugs.

Unit of analysis issues

Cluster-randomised trials

We planned to include cluster-randomised trials in the analyses along with individually randomised trials. We planned to adjust their sample sizes using the methods described in the *Cochrane Handbook for Systematic Reviews of interventions* (Higgins 2021), using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible), from a similar trial, or from a trial of a similar population. If we had used ICCs from other sources, we planned to report this and to conduct sensitivity analyses to investigate the effect of variation in the ICC. Had we identified both cluster-randomised trials and individually randomised trials, we planned to synthesise the relevant information. In cluster-randomised trials, particular biases to consider include: recruitment bias; baseline imbalance; loss of clusters; incorrect analysis; and comparability with individually randomised trials. We would have considered it reasonable to combine the results from both cluster-randomised trials and individually randomised trials if there was little heterogeneity between the trial designs, and the interaction between the effect of intervention and the choice of randomisation unit was considered to be unlikely. We planned to also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit. We planned to include cluster-randomised trials in the analyses along with individually-randomised trials, but none were found.

Cross-over trials

Cross-over trials were not eligible for inclusion in this review.

Multi-arm trials

We included multi-arm trials and accounted for the correlation between the effect sizes in the network meta-analysis. We treated multi-arm studies as multiple independent comparisons in pairwise meta-analyses.

Dealing with missing data

For included studies, we noted levels of attrition. We explored the impact of including studies with high levels of missing data (> 10%) in the overall assessment of treatment effect by using sensitivity analysis. We imputed missing standard deviations and errors using standard techniques where possible (Deeks 2021). For all outcomes, we performed analyses, as far as possible, on a modified intention-to-treat basis, that is, we attempted to include all participants randomised to each group in the analyses, and we analysed all participants in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

Assessment of clinical and methodological heterogeneity

To evaluate the presence of clinical heterogeneity, we examined trial and trial population characteristics across all eligible trials that compared each pair of interventions. We assessed the presence of clinical heterogeneity within each pairwise comparison by comparing these characteristics.

Assessment of transitivity across treatment comparisons

We assessed the assumption of transitivity by comparing the distribution of potential effect modifiers across the different pairwise comparisons. In this context we expect that the transitivity assumption will hold assuming the following:

1. the common treatment used to compare different tocolytic drugs indirectly is similar when it appears in different trials (e.g. betamimetics are administered in a similar way in betamimetics versus magnesium sulphate trials and in betamimetics versus calcium channel blockers trials);
2. all pairwise comparisons do not differ with respect to the distribution of effect modifiers (e.g. the design and trial characteristics of betamimetics versus magnesium sulphate trials are similar to betamimetics versus calcium channel blockers trials).

We evaluated the assumption of intransitivity epidemiologically by comparing the clinical and methodological characteristics of sets of studies from the various treatment comparisons.

Assessment of statistical heterogeneity and inconsistency

Assumptions when estimating heterogeneity

In standard pairwise meta-analyses we estimated different heterogeneity variances for each pairwise comparison. In the network meta-analysis, we assumed a common estimate for the heterogeneity variance across the different comparisons.

Measures and tests for heterogeneity

We assessed statistically the presence of heterogeneity within each pairwise comparison using the I^2 statistic and its 95% CI that measures the percentage of variability that cannot be attributed to random error (Higgins 2002). We based the assessment of statistical heterogeneity in the entire network on the magnitude of the heterogeneity variance parameter (Tau^2) estimated from the network meta-analysis models. For dichotomous outcomes we compared the magnitude of the heterogeneity variance with the empirical distribution as derived by Turner (Turner 2012). We also estimated a total I^2 statistic value for heterogeneity in the network as described elsewhere (Higgins 2002). We downgraded the certainty of the evidence for inconsistency where I^2 is greater than 60%.

Assessment of statistical inconsistency

We used global and local approaches to evaluate the statistical agreement between the various sources of evidence in a network of interventions (consistency) to complement the evaluation of transitivity. To evaluate the presence of inconsistency locally we used the loop-specific approach. This method evaluates the consistency assumption in each closed loop of the network separately as the difference between direct and indirect estimates for a specific comparison in the loop (inconsistency factor). Then, the magnitude of the inconsistency factors and their 95% CIs can be used to infer the presence of inconsistency in each loop. We assumed a common heterogeneity estimate within each loop. To check the assumption of consistency in the entire network we used the 'design-by-treatment' model as described by Higgins and colleagues (Higgins 2012). This method accounts for different sources of inconsistency that can occur when studies with different designs (two-arm trials versus three-arm trials)

give different results as well as disagreement between direct and indirect evidence. Using this approach we inferred the presence of inconsistency from any source in the entire network based on a Chi^2 test. We performed the design-by-treatment model in STATA using the mvmeta command (StataCorp 2019).

Assessment of reporting biases

We aimed to minimise the potential impact of reporting biases by ensuring a comprehensive search for eligible studies and by being alert to duplication of data. If there were 10 or more studies in any of the direct comparisons, we investigated reporting biases (such as publication bias) using funnel plots to explore the possibility of small-study effects (a tendency for estimates of the intervention effect to be more beneficial in smaller studies) as part of the assessment of the certainty of the direct evidence.

Data synthesis

Methods for direct treatment comparisons

We performed standard pairwise meta-analyses using a random-effects model in Review Manager 5 (Review Manager 2020), for every treatment comparison for all outcomes (DerSimonian 1986). We used a random-effects method for this analysis to mitigate for the high level of heterogeneity observed (DerSimonian 1986). This method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. The standard errors of the trial-specific estimates are therefore adjusted to incorporate a measure of the extent of heterogeneity. This results in wider confidence intervals in the presence of heterogeneity, and corresponding claims of statistical significance are more conservative.

Methods for indirect and network comparisons

We initially generated and assessed the network diagrams to determine if a network meta-analysis was feasible. Then we performed the network meta-analysis on all outcomes within a frequentist framework using multivariate meta-analysis estimated by restricted maximum likelihood. We used Stata statistical software, release 17 (StataCorp, College Station, TX) to carry out all analyses. We used the network suite of Stata commands designed for this purpose (White 2015), and other Stata commands for visualising and reporting results in network meta-analysis (Chaimani 2015).

Relative treatment ranking

We estimated the cumulative probabilities for each tocolytic class being at each possible rank and obtained a treatment hierarchy using the surface under the cumulative ranking curve (SUCRA); the larger the SUCRA the higher its rank among all available agents (Salanti 2011). The probabilities to rank the treatments are estimated under a Bayesian model with flat priors, assuming that the posterior distribution of the parameter estimates is approximated by a normal distribution with mean and variance equal to the frequentist estimates and variance-covariance matrix. Rankings are constructed drawing 1000 samples from their approximate posterior density. For each draw, the linear predictor is evaluated for each trial, and the largest linear predictor is noted (White 2011).

Subgroup analysis and investigation of heterogeneity

For the primary outcomes we had planned to carry out the following prespecified subgroup analyses by using the following effect modifiers.

Population

1. Gestational age at trial entry (fewer than 32 completed weeks versus 32 completed weeks or more)
2. Status of amniotic membranes (women with ruptured membranes versus women with intact membranes)
3. Number of fetuses (singleton versus multiple pregnancy)

Intervention

1. Duration of tocolysis (acute suppression alone versus acute suppression plus long-term maintenance)

Sensitivity analysis

For the primary outcomes we had planned to perform sensitivity analysis for the following.

1. Risk of bias (restricted to studies with low risk of bias only): we planned to rank studies as low risk of bias if they were double-blinded and had allocation concealment with little loss to follow-up (less than 10%). We would consider protocol publication in advance of the results to be an unsuitable criterion for sensitivity analyses, because protocol publication only became widespread in recent years.
2. Co-intervention (we planned to remove trials where participants received co-interventions such as progesterone)
3. Choice of relative effect measure (risk ratio versus odds ratio)
4. Use of fixed-effect versus random-effects model
5. Randomisation unit (cluster versus individual)

In addition to the prespecified sensitivity analysis, we also carried out a post-hoc sensitivity analysis by removing trials published before 1990.

We assessed differences by evaluating the relative effects and assessment of model fit.

Summary of findings and assessment of the certainty of the evidence

The summary of findings tables present evidence comparing all methods with a reference comparator, placebo or no tocolytic treatment. Each table describes key features of the evidence relating to a single outcome. There is a table for each primary outcome in accordance with the GRADE approach. These outcomes are:

1. delay in birth by 48 hours;
2. delay in birth by 7 days;
3. neonatal death before 28 days;
4. pregnancy prolongation (time from trial entry to birth in days);
5. serious adverse effects of drugs;
6. maternal infection; and
7. cessation of treatment due to adverse effects.

We assessed the certainty of the evidence using the GRADE approach as outlined in the GRADE handbook in order to assess the

certainty of the body of evidence relating to each outcome for all comparisons Schünemann 2013).

In order to create summary of findings tables, we used GRADEpro GDT to import data from Review Manager 5 (Review Manager 2020). We used the GRADE working group's approach for rating the certainty of the network meta-analysis effect estimates for all the comparisons and all outcomes (Brignardello-Petersen 2018; Puhan 2014). We appraised the certainty of the direct, indirect, and network evidence sequentially (in this order).

1. First, we assessed the certainty of the direct evidence (where available) for a given outcome, and rated the evidence using the standard GRADE approach based on consideration of: trial design limitations (risk of bias); inconsistency; imprecision; indirectness and publication bias (Schünemann 2021). For the outcomes where network meta-analysis was possible, we display the certainty of the direct evidence in the network diagrams using a colour-coded key (green lines for high-certainty evidence; light green lines for moderate-certainty evidence; orange lines for low-certainty evidence and red lines for very low-certainty evidence).
2. Then we rated the certainty of the indirect evidence for the same given outcomes, based on the lower of the certainty ratings of the two direct arms forming the dominant 'first-order' loop in the network diagram for this outcome.
3. Our final step was to determine the certainty of network evidence based on:
   a. the higher certainty rating of the direct and indirect evidence;
   b. whether the relevant network exhibited 'transitivity', that is, whether all the comparisons contributing data to the estimate were directly consistent with the PICO question;
   c. consideration of coherence between direct and indirect effect estimates; and
   d. precision of the network effect estimate.

At each of these stages, two review authors (AW, AP) independently appraised the certainty ratings for the direct, indirect and network evidence. We resolved disagreements between authors through discussion and consultation with a third review author (IG) where necessary. We rated the certainty of network evidence for each outcome as 'high', 'moderate', 'low' or 'very low' in accordance with the GRADE approach.

1. High certainty: we are very confident that the true effect lies close to that of the effect.
2. Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
3. Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
4. Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

For ease of comparison when interpreting the relative effects of all tocolytic drugs versus placebo or no treatment, the summary of findings tables include the effect estimate and certainty judgements for the direct evidence, the indirect evidence and the network meta-analysis, describing all the findings for a single outcome in each table. We also include the anticipated absolute effects, based on the network effect estimate for each treatment intervention in comparison with placebo or no treatment. The assumed risks in the placebo or no-treatment group are based on weighted means of baseline risks from the studies with placebo or no treatment arms in the network meta-analysis. The corresponding risks for each tocolytic drug (and their 95% CIs) are based on the assumed risk in the placebo or no-treatment group and the relative effect of the individual treatment intervention, when compared with the placebo or no-treatment group (and its 95% CI) as derived from the network meta-analysis.

RESULTS

Description of studies

Results of the search

6The results of the search are summarised in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Liberati 2009; Figure 1). The search of Cochrane Pregnancy and Childbirth's (CPC) Trials Register on 21 April 2021 retrieved in total 696 available records. No further records from additional searches or manual searching of reference lists were obtained. We excluded eight records as duplicates and screened out 231 on title and abstract. We examined the full text of 457 records and included in the network meta-analysis 122 randomised trials (196 reports; Characteristics of included studies). We contacted the authors from 46 references for additional data or clarifications. We were able to obtain additional data or clarifications from trial authors for two randomised trials (Ozhan Baykal 2015; Thornton 2015). We excluded 169 studies (186 reports) (Characteristics of excluded studies), 44 studies (56 reports) could not be classified (Characteristics of studies awaiting classification), and 17 studies (19 reports) were still ongoing (Characteristics of ongoing studies).

Screening eligible studies for trustworthiness

In 457 records identified from the search we judged that 45 trials did not meet our criteria for trustworthiness for the following reasons.

1. Two studies were published only as trial registry entries and we have not been able to confirm with the trial authors that the data were from the final analyses (IRCT2015042621947N1; NCT00486824).
2. We had concerns about the randomisation process in 32 studies, where there was no explanation for substantial imbalances between the numbers allocated to each group (Akhtar 2018; Ali 2013; Al Jawady 2020; Aziz 2018; Badshah 2019; Bina 2012; Chawanpaiboon 2011; Chawanpaiboon 2012; Eftekhari 2012; Esmaeilzadeh 2017; Faisal 2020; Faraji 2013; Ghomian 2015; Hamza 2016; Jamil 2020; Khooshideh 2017; Lotfalizadeh 2010; Madkour 2013; Mesdaghinia 2012; Mirteimoori 2009; Mirzamoradi 2014; Nikbakht 2014; Ozhan Baykal 2015; PriyadarshiniBai 2013; Saadati 2014; Sachan 2012; Shafaie 2014; Shirazi 2015; Toghroli 2020; Xu 2016; Yasmin 2016; Zangooei 2011).
3. Six studies published since 2010 demonstrated no evidence of prospective registration (Caliskan 2015; Dhawle 2013; Nankali 2014; Nauman 2020; Songthamwat 2018; Tabassum 2016).
4. We were unable to obtain translations for four studies (Kim 2001; Lee 2004; Song 2002a; Song 2002b)

In all cases we made every effort to contact the authors and either identified no contact details at all or the authors did not respond to our queries (see Studies awaiting classification).

Included studies

This review included 122 randomised trials, published between 1966 and 2021, involving 13,697 women. All trials were individually randomised; there were no cluster-randomised trials. Most trials were two-arm trials and we also included three, three-arm trials. For the purposes of the network meta-analysis, we combined multi-arm trials that included arms with the same intervention. Most trials were reported in English (88%, 107/122); we obtained 16 translations (Amorim 2009; Aramayo 1990; Asgharnia 2002; Cabar 2008; Francioli 1988; Janky 1990; Kara 2009; Kose 1995; Matsuda 1993; Nonnenmacher 2009; Sakamoto 1985; Szulc 2000; Tohoku 1984; Wang 2000; Zhang 2002; Zhu 1996).

The trials were conducted across 39 countries (including high-, middle- and low-income countries). The median size of the trials was 80 participants (interquartile range (IQR) 50 to 120). Most were single-centre trials (66%, 81/122); 41 were multi-centre trials (34%, 41/122).

The dates in which the trials were conducted varied, with the earliest being conducted in 1965 (Adam 1966). Similar numbers of included trials were conducted across the 1980s, 1990s and 2000s. Fewer trials were conducted from 2010 onwards. Most trials did not report any conflicts of interests. Thirteen reported receiving support from the pharmaceutical industry (de Heus 2009; European Atosiban Study 2001; French and Australian Atosiban Investigators 2001; Goodwin 1994; Goodwin 1996; Leake 1983; Lees 1999; Romero 2000; Saade 2021; Shim 2006; Spellacy 1979; Thornton 2009; Thornton 2015). Many studies did not report the source of funding.

Typically studies recruited women from 24 weeks to 34 weeks of gestation (range from 20 to 36 weeks of gestation). Most studies (71%, 87/122) recruited women with intact membranes, seven studies (6%, 7/122) recruited women with ruptured membranes, 28 studies (23%) recruited a mixed population or did not clearly specify the population. Half of the studies recruited women with a singleton pregnancy (50%, 61/122), no studies recruited women with multiple pregnancies, and 61 studies (50%) recruited a mixed population or did not specify the population. Sixty-seven studies (55%) administered tocolysis to suppress contractions in the acute phase of preterm labour, whereas 49 studies (40%) maintained tocolysis for more than 48 hours and, in the majority of cases, throughout the pregnancy. Six studies (5%) did not specify the duration of tocolysis. The majority of studies excluded women in advanced preterm labour, recruiting women less than 4 cm dilated.

Of the 122 included studies, 120 (98%) contributed data to the analysis, while two studies did not report any outcomes of interest to this review (de Heus 2009; Parsons 1987).

The 122 trials (247 trial arms), used the following agents, either as intervention or comparison:

1. betamimetics, 74 trial arms (30%);
2. COX inhibitors, 13 trial arms (5%);
3. calcium channel blockers, 44 trial arms (18%);
4. magnesium sulphate, 21 trial arms (9%);
5. oxytocin receptor antagonists, 20 trial arms (8%);
6. nitric oxide donors, 13 trial arms (5%);
7. combinations of tocolytics, 23 trial arms (9%);
8. placebo or no treatment, 39 trial arms (16%).

Excluded studies

We excluded 169 studies (for details see Characteristics of excluded studies). The most common reasons for exclusion were that studies compared acute-phase tocolysis with a maintenance dose of tocolysis (Alavi 2015a; Bivins 1993; Brown 1981; Carr 1999; Guinn 1998; Gummerus 1985; How 1994; Matijevic 2006; Newton 1991; Parilla 1993; Ricci 1990; Sanchez Ramos 1997; Sayin 2004; Wenstrom 1997) or they compared doses or routes of the same tocolytic drugs (Cabero 1988; Chhabra 1998; Holleboom 1996; Kawagoe 2011; Kullander 1985; Motazedian 2010; Parry 2014; Rezk 2015; Rios Anez 2001; Ryden 1977; Spatling 1989; Stika 2002; Zygmunt 2003), or were quasi-randomised studies or not randomised (Calder 1985; Dunstan Boone 1990; Kurki 1991a; Leake 1980b; Maitra 2007; Malik 2007; Singh 2011; Sirohiwal 2001).

Risk of bias in included studies

We present summaries of the risk of bias of the included studies for each of the domains that we assessed across all studies (Figure 3), and for each included trial (Figure 4).

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

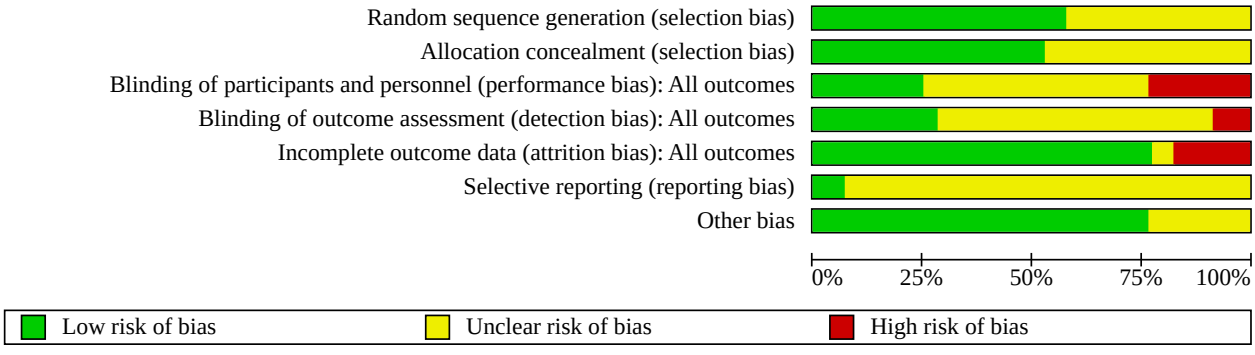


Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

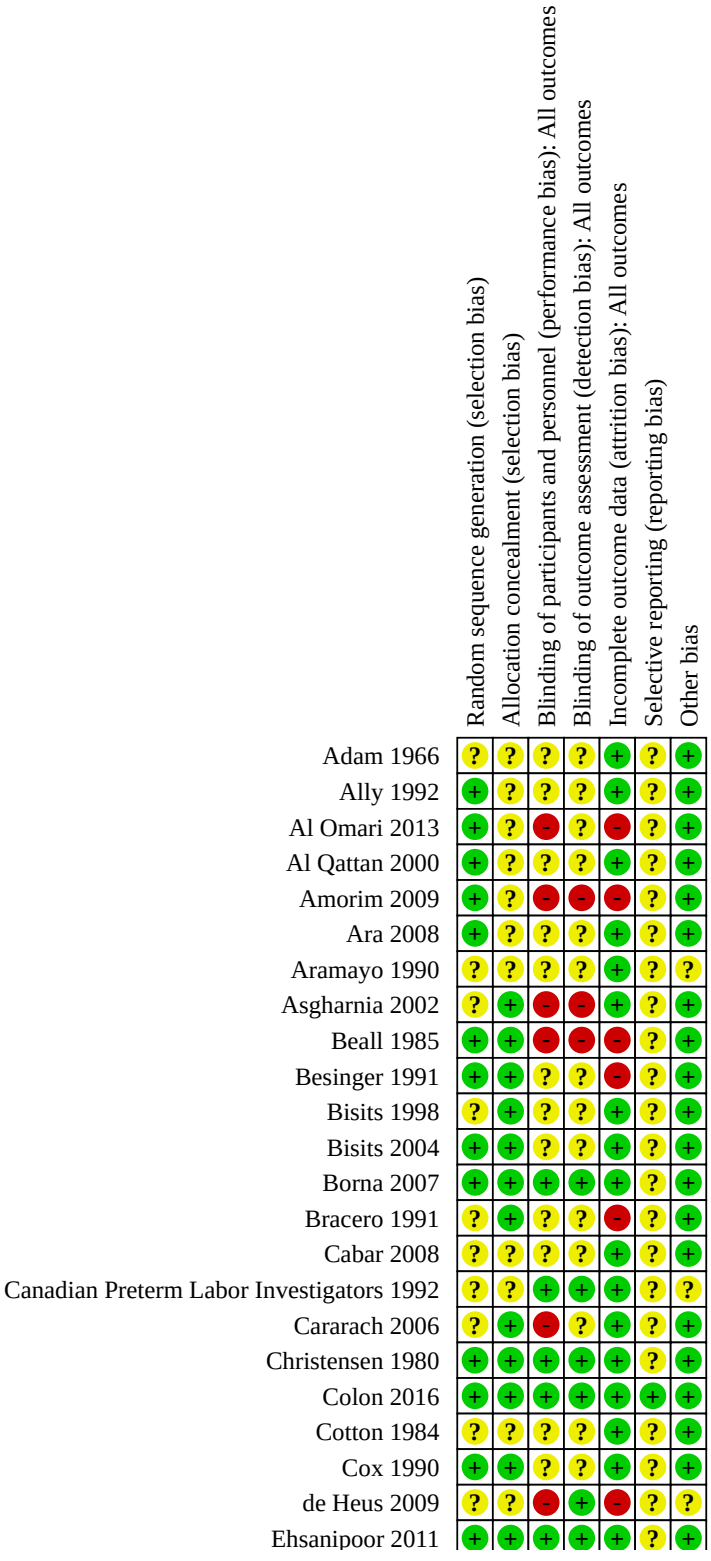
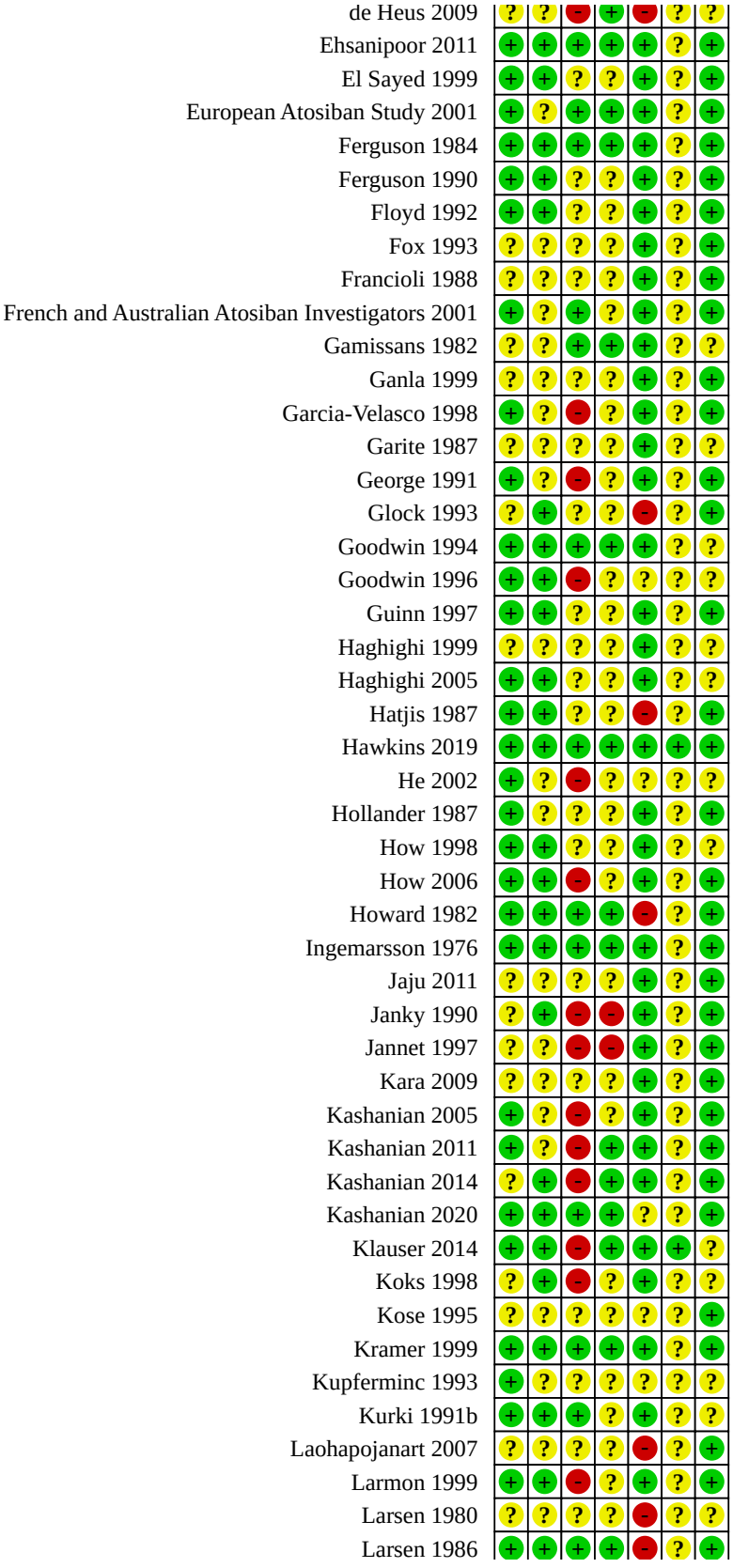


Figure 4. (Continued)



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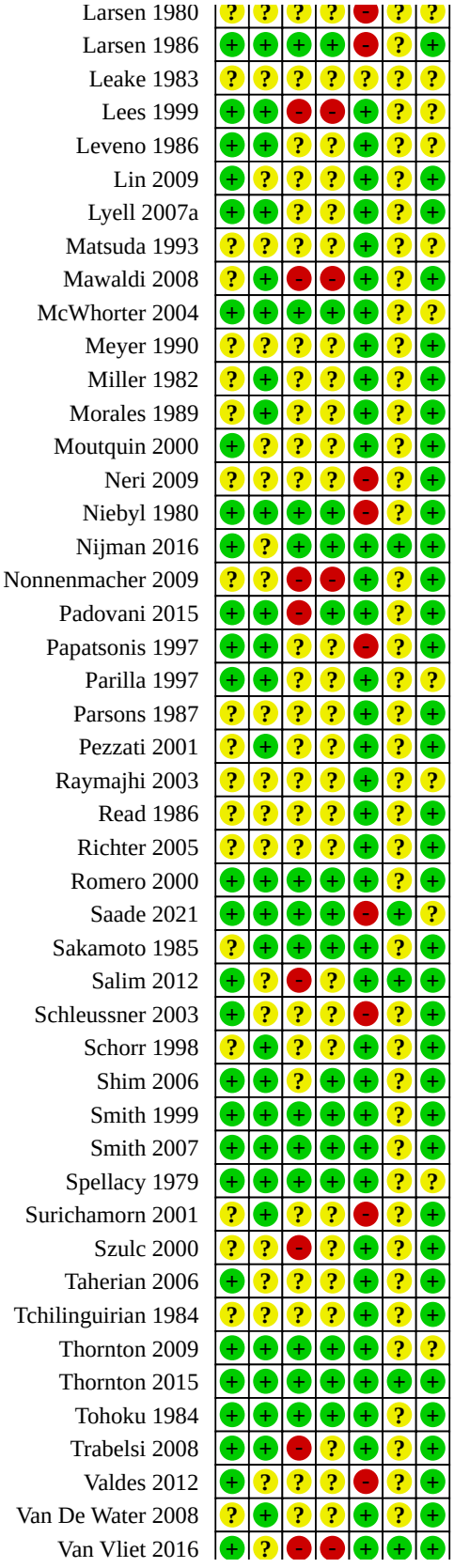

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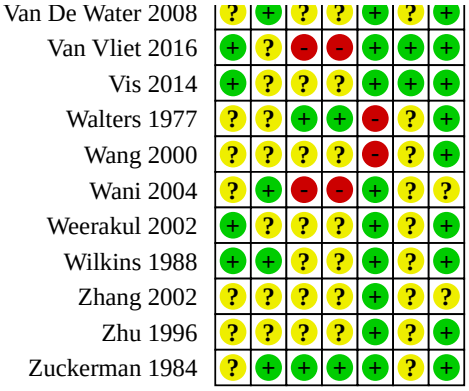


Allocation

Seventy-one of 122 trials (58%) used adequate sequence generation and we judged these trials to be at low risk of bias. Fifty-one of 122 trials (42%) did not clearly state the description of sequence generation and hence they were at unclear risk of bias. Sixty-four of 122 trials (52%) gave a clear description of adequate allocation concealment. However, in 58 of 122 trials (48%) the description of allocation concealment was inadequate and so these trials were at unclear risk of bias. Many of the trials with inadequate information about sequence generation or allocation concealment were abstracts or other forms of short communications, which had limited word counts. Most of the trials that had an inadequate description of random sequence generation also gave inadequate information regarding allocation concealment.

Blinding

Only 31 of 122 trials (25%) blinded participants and personnel and hence we judged them to be at low risk of bias. Sixty-three of 122 trials (52%) gave unclear information regarding blinding of participants and personnel and we therefore judged them to be at unclear risk of bias. The remaining 28 trials (23%) were unblinded to either participants or personnel, or both, and therefore at high risk of bias. In the majority of these unblinded trials, the nature of the intervention and comparator, for example intravenous betamimetics versus oral calcium channel blockers, meant blinding was more difficult to achieve. Seventy-seven (63%) trials inadequately described blinding of the outcome assessor of the primary outcomes, meaning we judged them to be at unclear risk of bias. In 10 of 122 trials (8%) the outcome assessor was unblinded meaning these were at high risk of bias. Only 35 of 122 trials (29%) clearly stated that the outcome assessor was blinded, meaning these trials were at low risk of bias.

Incomplete outcome data

Ninety-five of 122 trials (78%) had minimal missing outcome data (less than 10%) and were balanced in numbers across intervention groups with similar reasons for missing data across groups. They were therefore at low risk of attrition bias. We judged 21 of 122 trials (17%) to be at high risk of attrition bias due to losing more than 10% of their participant population to follow-up. We judged six of 122 trials (5%) to be at unclear risk of attrition bias as they did not provide enough information to assess whether or not their handling of incomplete data was appropriate.

Selective reporting

Only nine of 122 trials (7%) prespecified all outcomes in publicly available trial protocols and we judged them to be at low risk of reporting bias. We were unable to identify a published protocol for most trials (113 of 122 trials; 93%), and we judged the risk of reporting bias to be unclear.

Other potential sources of bias

We detected no other potential sources of bias in 94 of 122 trials (77%) and so we judged them to be at low risk of bias. We judged 28 of 122 trials (23%) to be at unclear risk of bias. The majority of comparisons contained fewer than 10 studies, therefore investigation of publication bias was not valid. The only comparison that we downgraded for publication bias was calcium channel blockers versus betamimetics for delay in birth by 48 hours.

Effects of interventions

See: **Summary of findings 1** Delay in birth by 48 hours; **Summary of findings 2** Delay in birth by 7 days; **Summary of findings 3** Neonatal death before 28 days; **Summary of findings 4** Pregnancy prolongation (time from trial entry to birth in days); **Summary of findings 5** Serious adverse effects of drugs; **Summary of findings 6** Maternal infection; **Summary of findings 7** Cessation of treatment due to adverse effects

See summary of findings tables for the comparisons of tocolytics with placebo or no treatment.

1. Summary of findings 1 Delay in birth by 48 hours
2. Summary of findings 2 Delay in birth by 7 days
3. Summary of findings 3 Neonatal death before 28 days
4. Summary of findings 4 Pregnancy prolongation
5. Summary of findings 5 Serious adverse effects of drugs
6. Summary of findings 6 Maternal infection
7. Summary of findings 7 Cessation of treatment due to adverse effects

Please note that all of the analyses presented in the Data and analyses relate to the 'direct evidence' and we used them to grade the evidence, as described in our methods. We do not describe direct evidence where network evidence is available. The following section presents the results as reported in all of the figures. The figures present the results as network diagrams, forest plots with pairwise, indirect and network (combining direct and indirect) effect estimates, and cumulative rankograms for all the outcomes with available data. The figures present the results for different tocolytics in comparison to placebo or no treatment. The certainty of the evidence (grading of the results) considers the heterogeneity and inconsistency for all outcomes, and all of the tocolytic comparisons stated in the results.

Primary outcomes

1. Delay in birth by 48 hours

Network evidence

The network diagram for delay in birth by 48 hours is presented in Figure 5. Relative effects from the network meta-analysis of 86 trials (9853 women) suggested that all tocolytics are probably effective in delaying preterm birth when compared with placebo or no treatment (Figure 6). Moderate-certainty evidence suggests that magnesium sulphate (RR 1.12, 95% CI 1.02 to 1.23), oxytocin receptor antagonists (RR 1.13, 95% CI 1.05 to 1.22), nitric oxide donors (RR 1.17, 95% CI 1.05 to 1.31), and combinations of tocolytics (the most common combination was magnesium sulphate with betamimetics; RR 1.17, 95% CI 1.07 to 1.27) are probably effective in delaying preterm birth by 48 hours. Meanwhile, low-certainty evidence suggests that betamimetics (RR 1.12, 95% CI 1.05 to 1.20), COX inhibitors (1.11, 95% CI 1.01 to 1.23), and calcium channel blockers (RR 1.16, 95% CI 1.07 to 1.24), are possibly effective in delaying preterm birth by 48 hours compared with placebo or no treatment.

Figure 5. Network diagram for delay in birth by 48 hours. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison

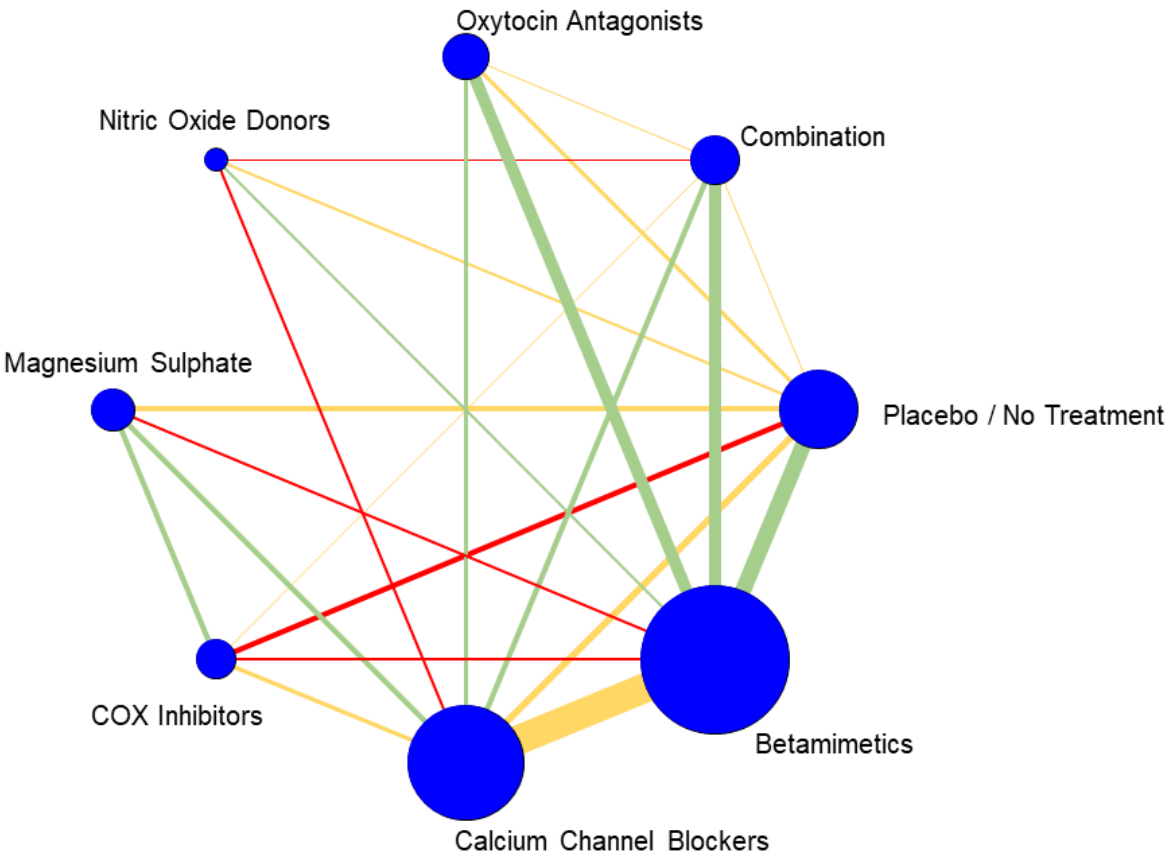
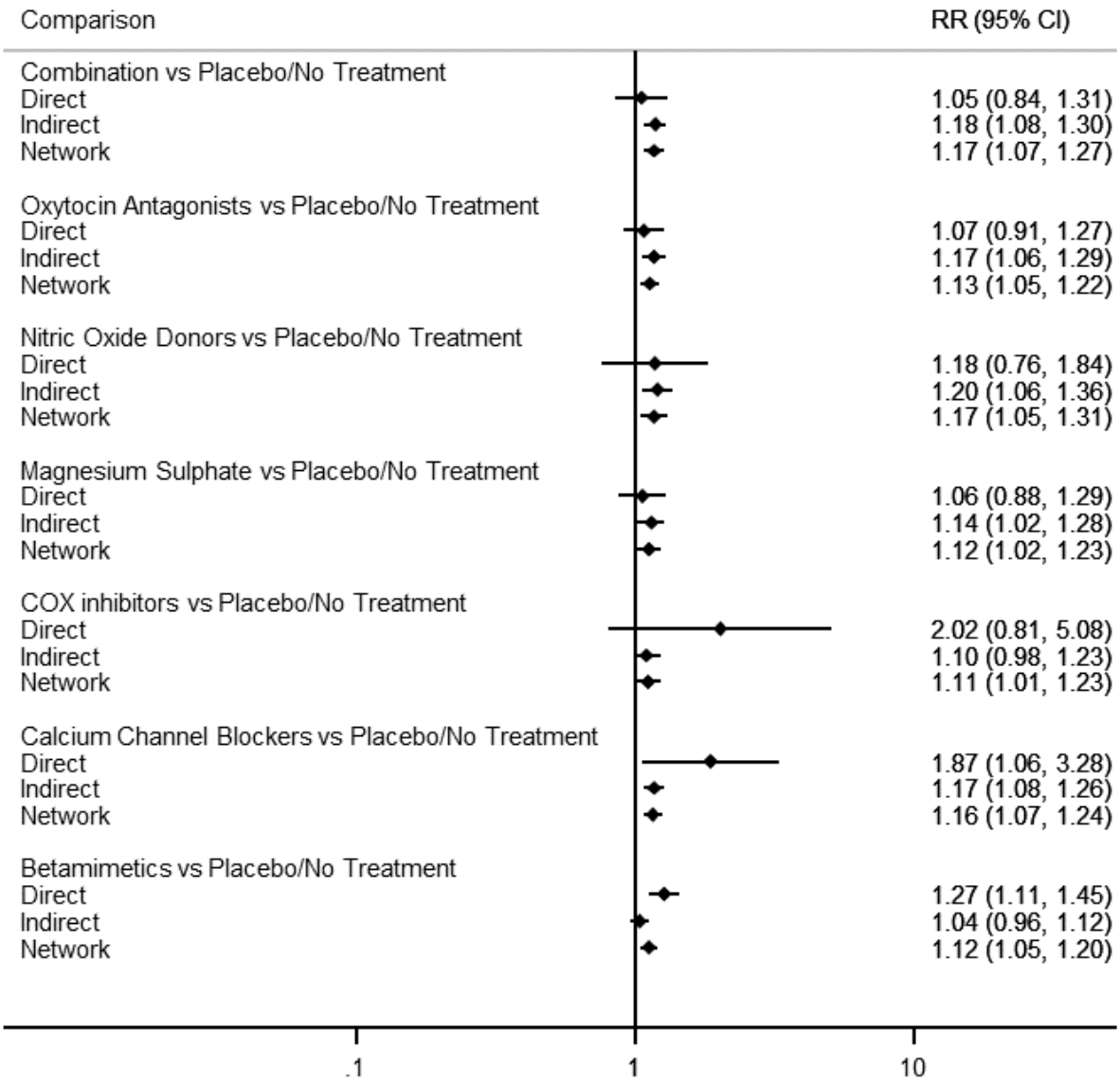


Figure 6. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for delay in birth by 48 hours.

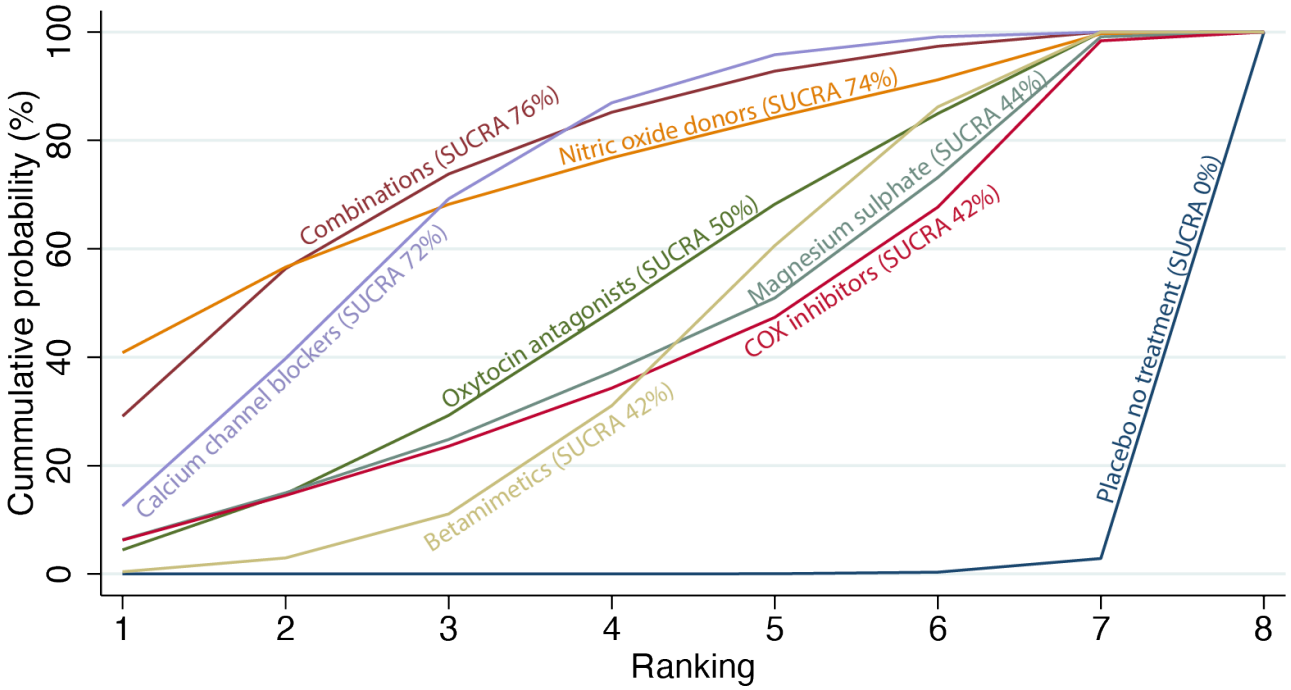


Based on these results, about 645 per 1000 women with placebo or no treatment would have a delay in preterm birth by 48 hours compared with 722 with betamimetics or magnesium sulphate, 716 with COX inhibitors, 748 with calcium channel blockers, 729 with oxytocin receptor antagonists, and 755 with nitric oxide donors or combinations of tocolytics (Summary of findings 1).

Tocolytic ranking

The cumulative probabilities for each agent being at each possible rank for delaying birth by 48 hours are shown in Figure 7. Treatment hierarchies are presented with the surface under the cumulative ranking curve (SUCRA); the larger the SUCRA the higher its rank among all available agents. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, and so on. A SUCRA of 100% means the tocolytic drug is the best and a SUCRA of 0% means the drug is the worst. The tocolytics ranked highest for delaying preterm birth by 48 hours are the combinations of tocolytics (SUCRA 76%), nitric oxide donors (SUCRA 74%), and calcium channel blockers (SUCRA 72%), followed by oxytocin receptor antagonists (SUCRA 50%), magnesium sulphate (SUCRA 44%), COX inhibitors (SUCRA 42%) and betamimetics (SUCRA 42%) with placebo or no treatment being ranked the lowest (SUCRA 0%).

Figure 7. Cumulative rankograms comparing each of the tocolytic drugs for delay in birth by 48 hours. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x-axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



2. Delay in birth by 7 days

Network evidence

The network diagram for the outcome of delay in birth by 7 days is presented in Figure 8. Relative effects from the network meta-analysis of 60 trials (7143 women) suggested that oxytocin receptor antagonists (RR 1.18, 95% CI 1.07 to 1.30; high-certainty evidence) are effective in delaying birth by 7 days compared with placebo or no treatment (Figure 9). Calcium channel blockers (RR 1.15, 95% CI 1.04 to 1.27; moderate-certainty evidence), nitric oxide donors (RR 1.18, 95% CI 1.02 to 1.37; moderate-certainty evidence), and combinations of tocolytics (RR 1.19, 95% CI 1.05 to 1.34; moderate-certainty evidence) are probably effective, while betamimetics (RR 1.14, 95% CI 1.03 to 1.25; low-certainty evidence) are possibly effective in delaying birth by 7 days compared with placebo or no treatment. There is moderate-certainty evidence that COX inhibitors probably make little to no difference to this outcome compared with placebo or no treatment. The effects of magnesium sulphate were unclear because the certainty of the evidence was very low.

Figure 8. Network diagram for delay in birth by 7 days. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

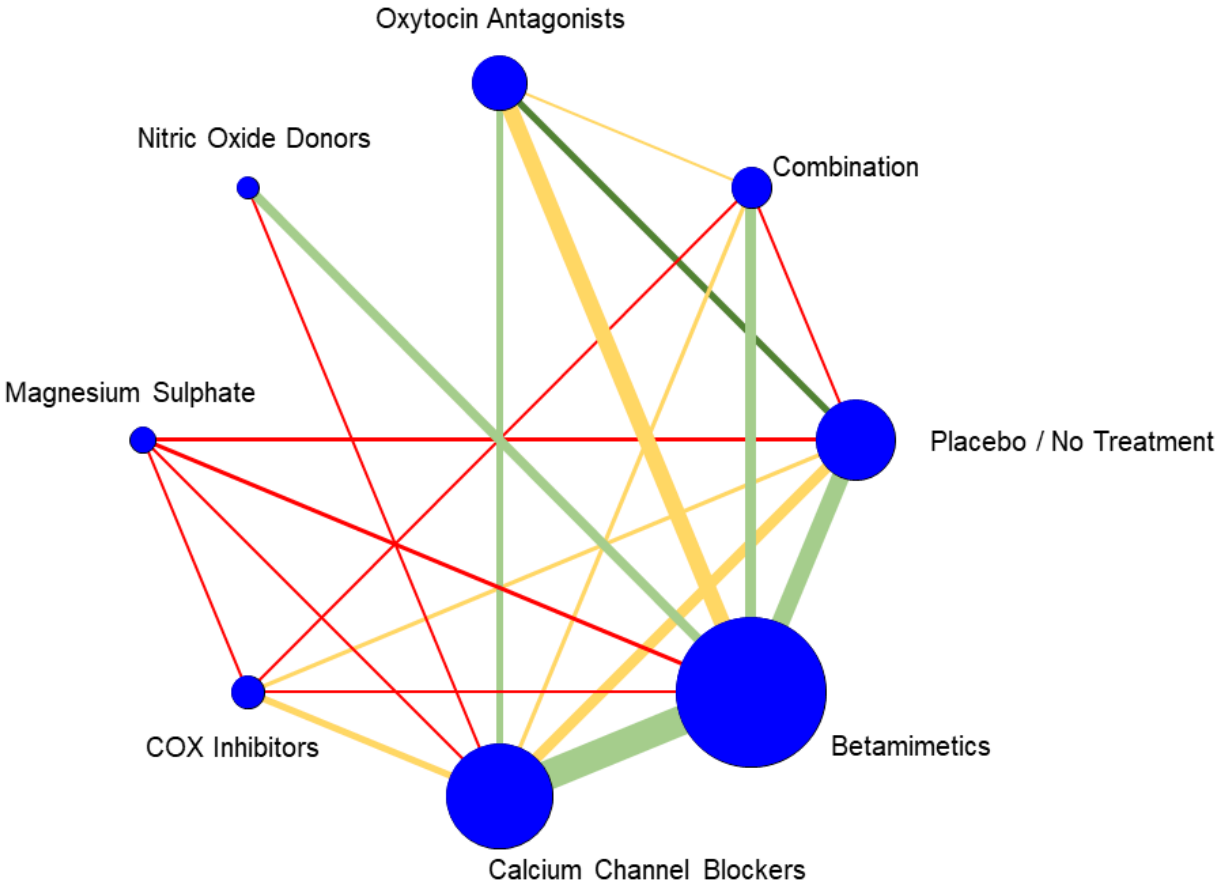
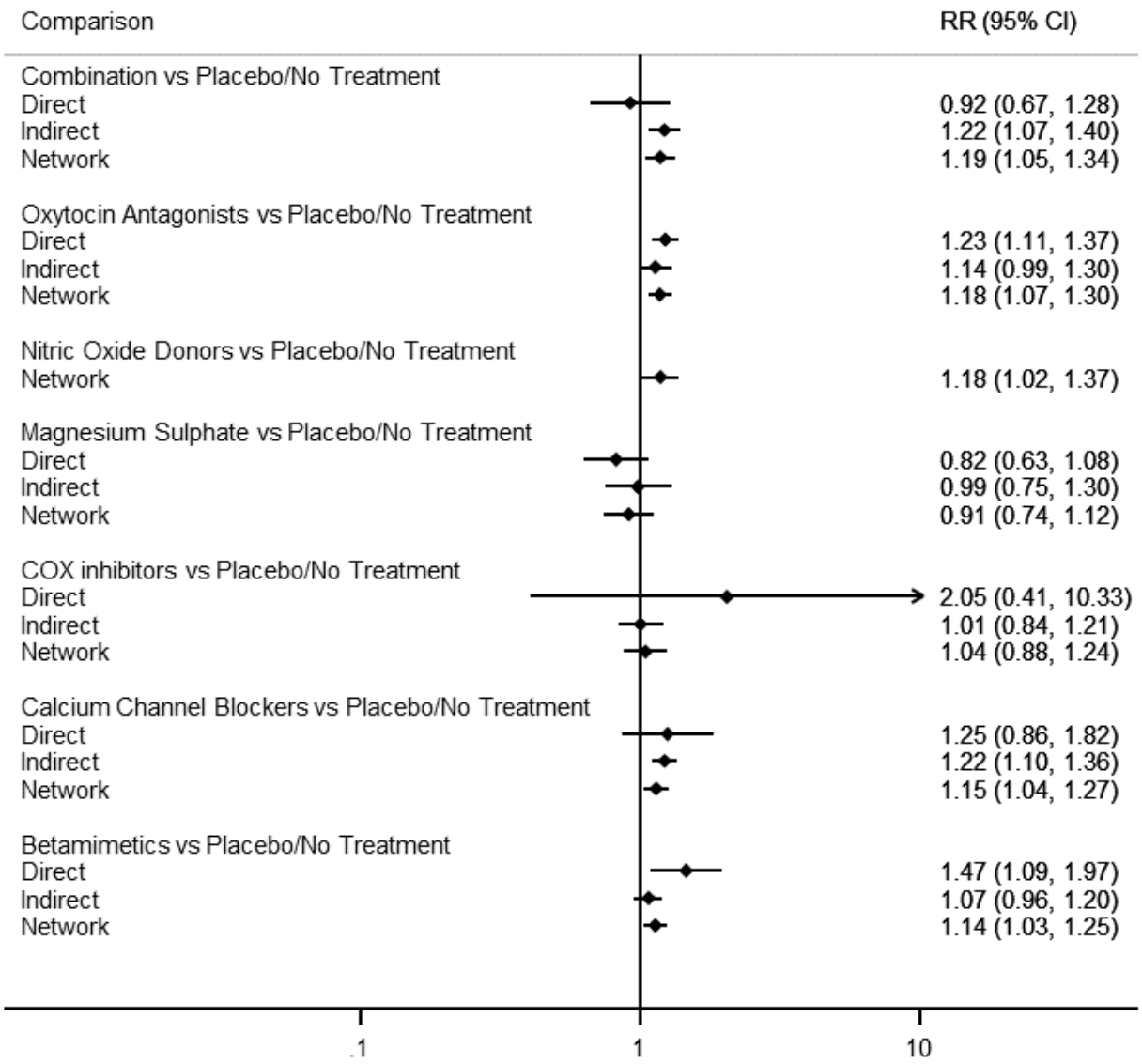


Figure 9. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for delay in birth by 7 days.



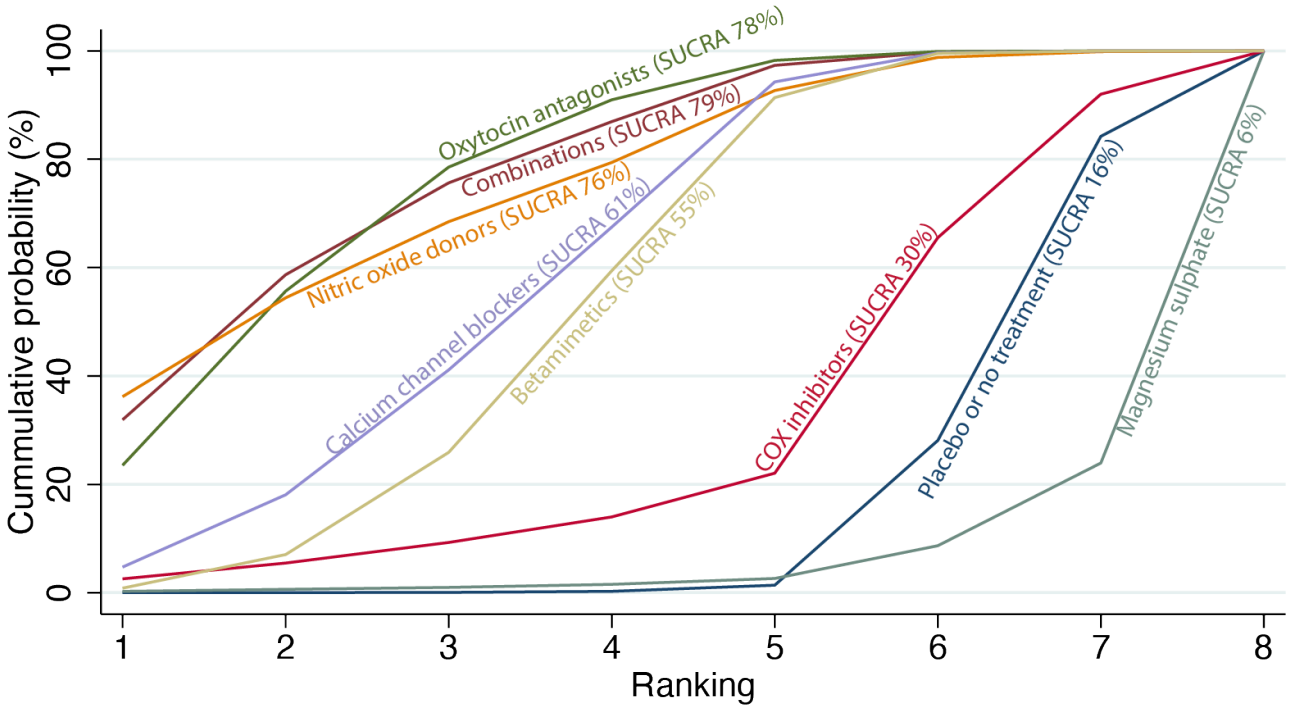
Based on these results, about 742 per 1000 women with placebo or no treatment would experience a delay in preterm birth by 7 days compared with 846 with betamimetics, 772 with COX inhibitors, 853 with calcium channel blockers, 675 with magnesium sulphate, 876 with oxytocin receptor antagonists and nitric oxide donors, and 883 with combinations of tocolytics

(Summary of findings 2).

Tocolytic ranking*

The cumulative probabilities for each agent being at each possible rank for delaying birth by 7 days are shown in Figure 10. The highest ranked tocolytics for delaying preterm birth by 7 days are the combinations of tocolytics (SUCRA 79%), oxytocin receptor antagonists (78%), and nitric oxide donors (SUCRA 76%), followed by the calcium channel blockers (SUCRA 61%) and betamimetics (SUCRA 55%). COX inhibitors (SUCRA 30%), placebo or no treatment (SUCRA 16%), and magnesium sulphate (SUCRA 6%) ranked the lowest.

Figure 10. Cumulative rankograms comparing each of the tocolytic drugs for delay in birth by 7 days. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



3. Neonatal death before 28 days

Network evidence

The network diagram for the outcome of neonatal death before 28 days is presented in Figure 11. Relative effects from the network meta-analysis of 73 trials (8395 babies) suggested that all tocolytics are associated with a wide range of effects for neonatal death before 28 days when compared with placebo or no treatment as there were few neonatal deaths (Figure 12; Summary of findings 3).

Figure 11. Network diagram for neonatal death before 28 days. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

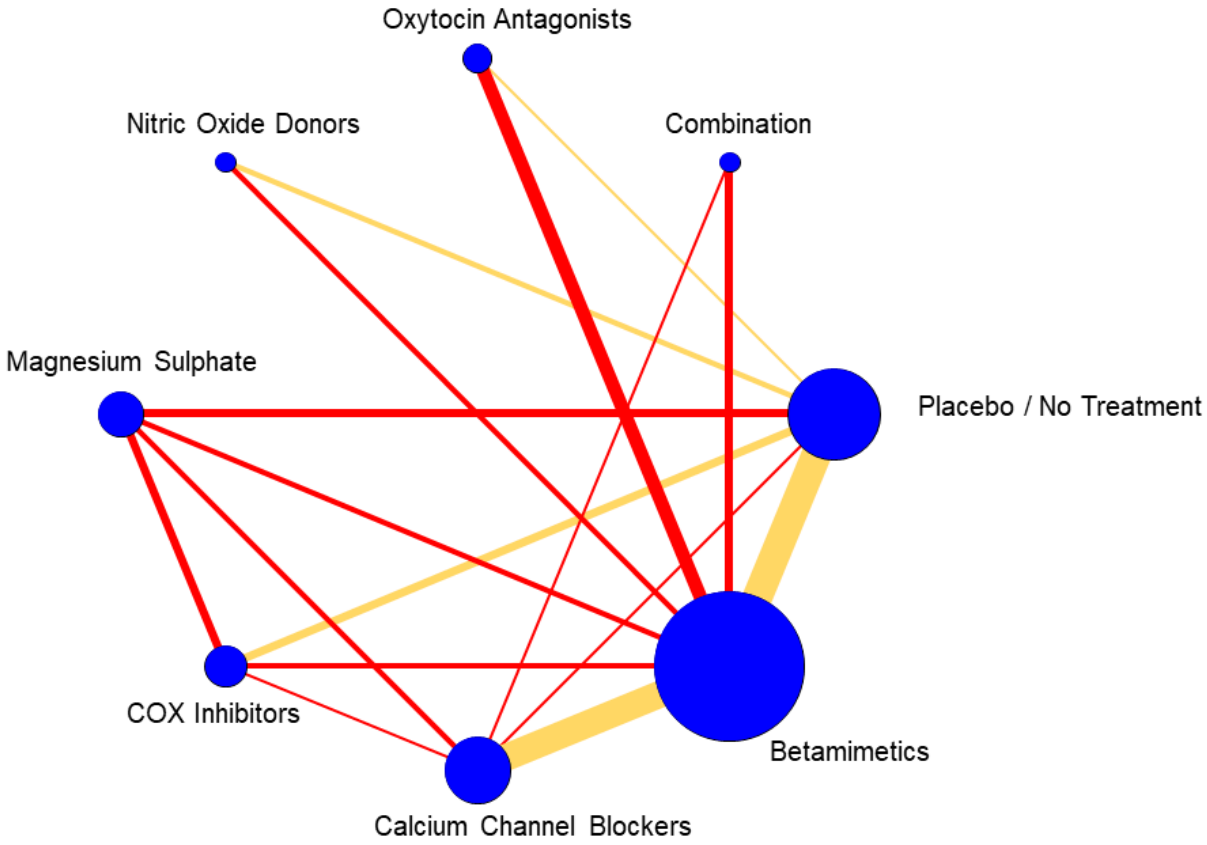
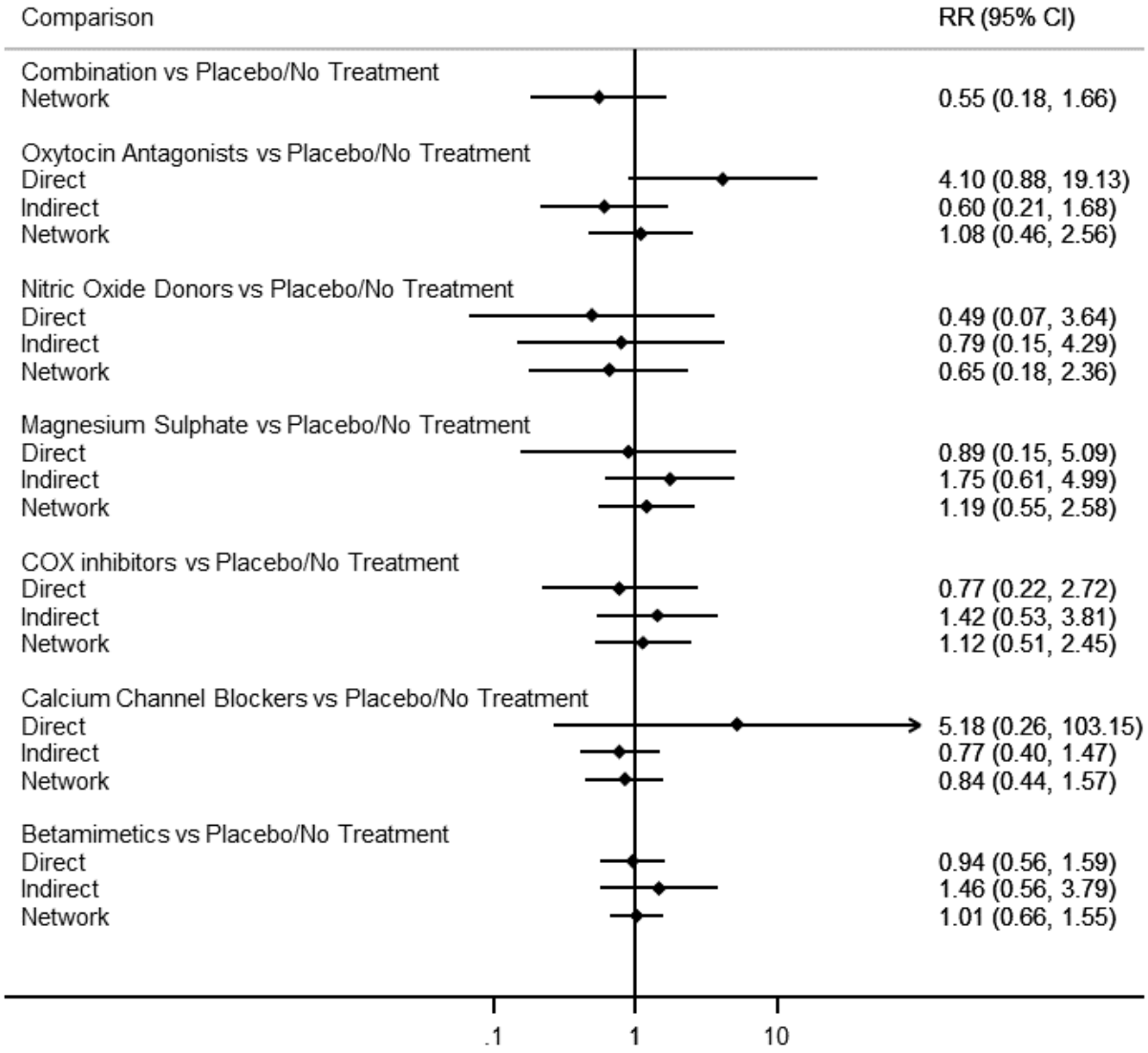


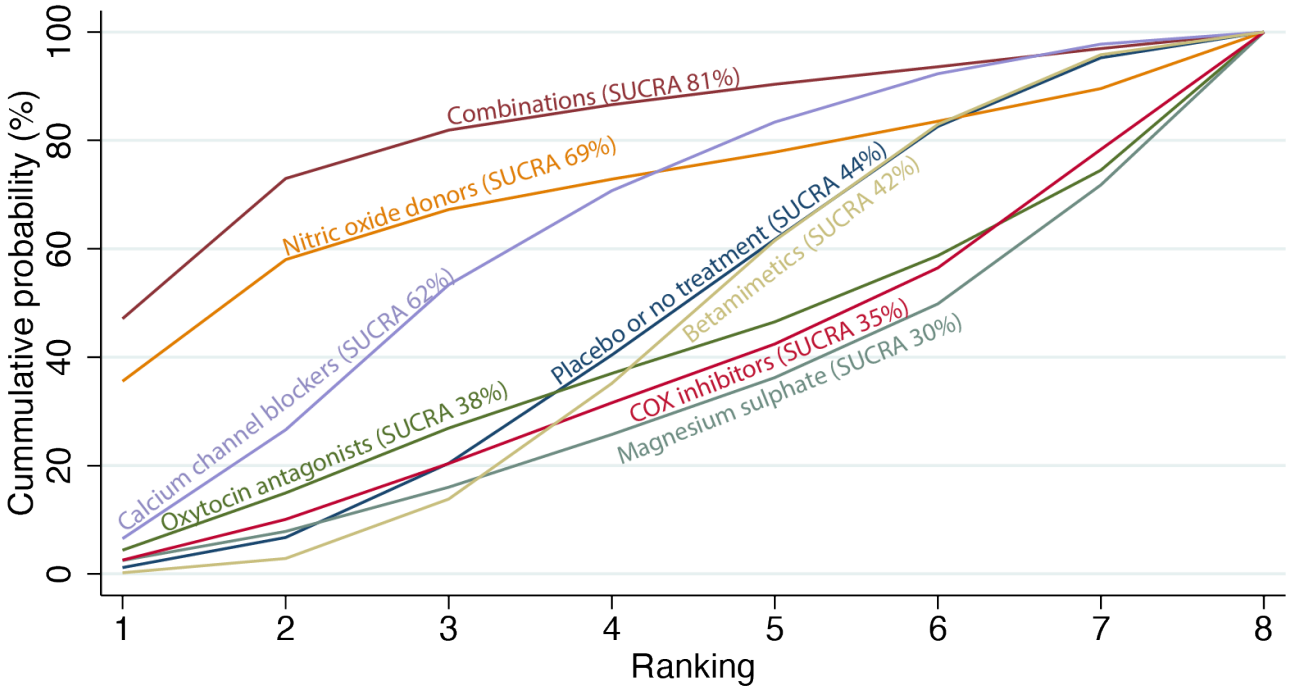
Figure 12. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for neonatal death before 28 days.



Tocolytic ranking

The cumulative probabilities for each agent being at each possible rank for neonatal death before 28 days are shown in Figure 13. The ranking for tocolytics was not clear for this outcome due to few events.

Figure 13. Cumulative rankograms comparing each of the tocolytic drugs for neonatal death before 28 days. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



4. Pregnancy prolongation (time from trial entry to birth in days)

Network evidence

The network diagram for pregnancy prolongation as a continuous outcome is presented in Figure 14. Network meta-analysis of 47 trials (5093 women) suggested that tocolytics except calcium channel blockers and oxytocin antagonists make little to no difference to pregnancy prolongation from trial entry to birth in days as a continuous outcome when compared with placebo or no treatment (Figure 15). When compared with placebo or no treatment, calcium channel blockers result in an average pregnancy prolongation of 4.66 days (95% CI 0.13 more to 9.19 more; high-certainty evidence; Summary of findings 4). Low-certainty evidence suggests that oxytocin antagonists also possibly result in an average pregnancy prolongation of 9.54 days (95% CI 2.35 more to 16.73 more; Summary of findings 4) compared with placebo or no treatment. There is probably little or no difference between betamimetics (MD 0.83 days more, 95% CI 3.12 fewer to 4.78 more; moderate-certainty evidence), nitric oxide donors (MD 7.44 days more, 95% CI 0.44 fewer to 15.32 more; moderate-certainty evidence), and possibly for COX inhibitors (MD 3.31 days more, 95% CI 4.41 fewer to 11.03 more; low-certainty evidence) compared with placebo or no treatment. The effects of magnesium sulphate and combinations of tocolytics were unclear because the certainty of the evidence was very low.

Figure 14. Network diagram for pregnancy prolongation (time from trial entry to birth). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

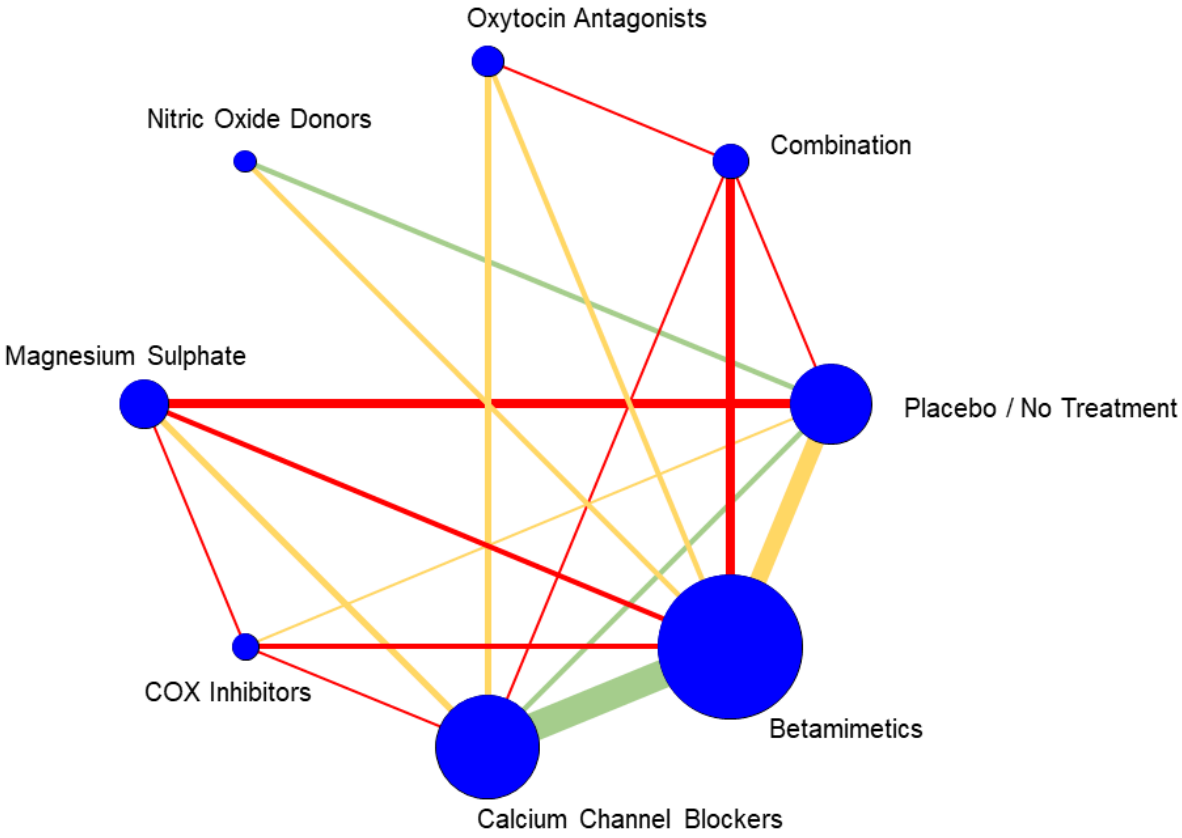
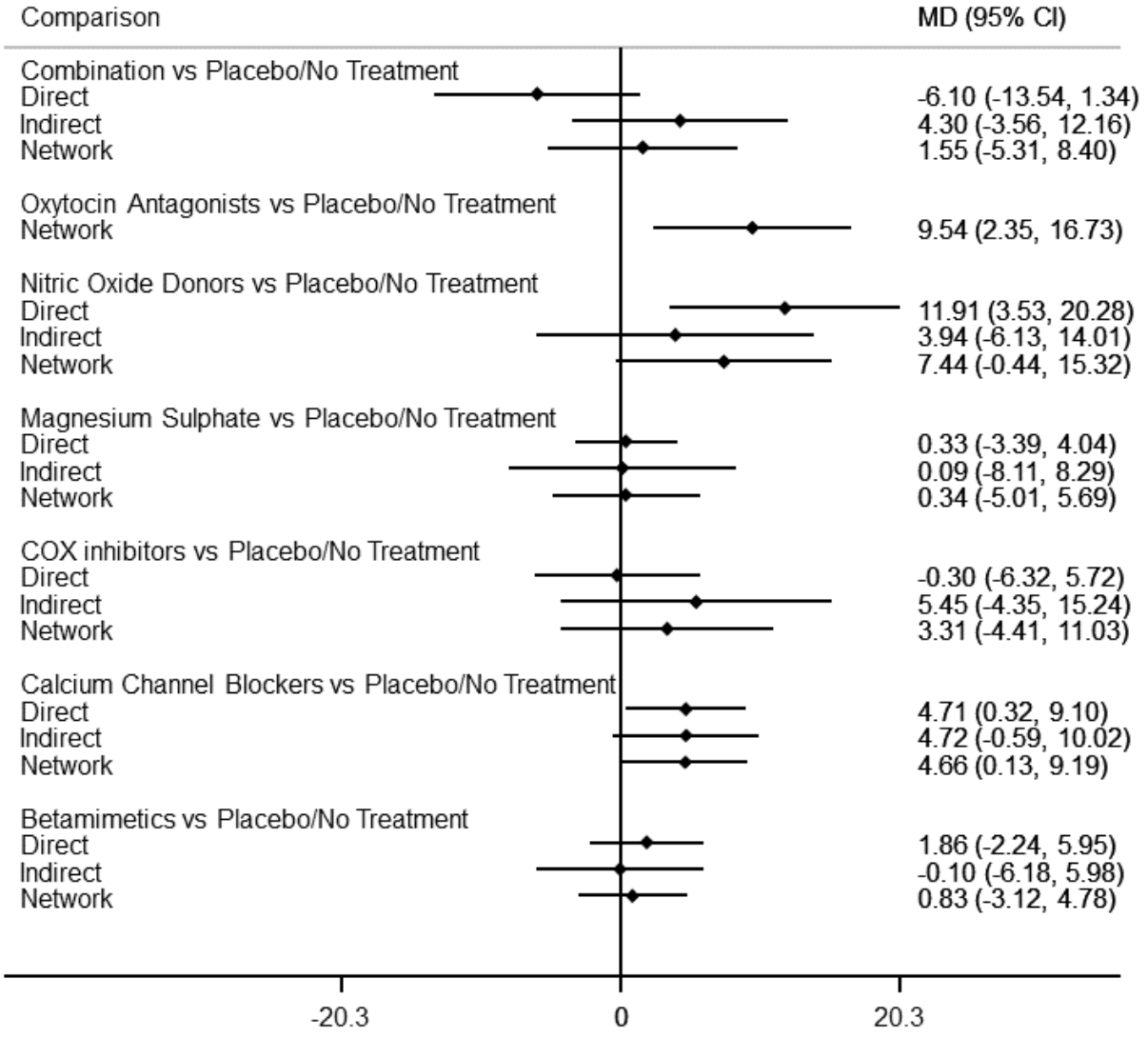


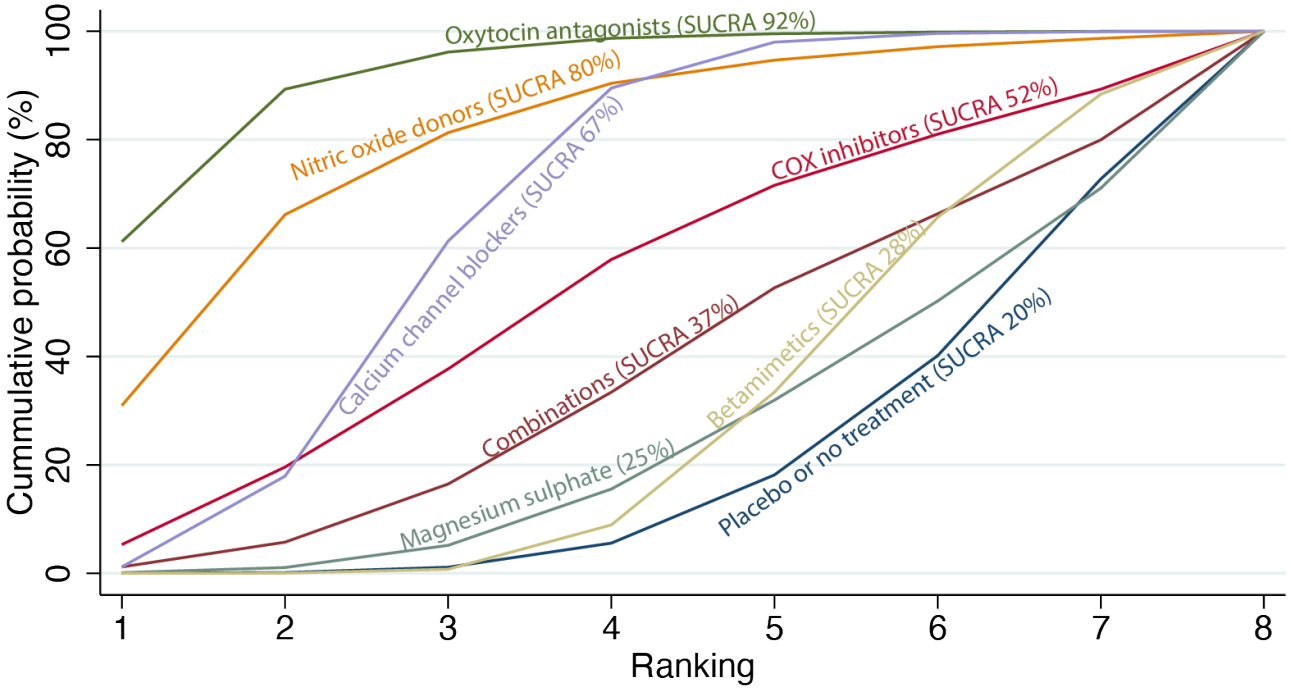
Figure 15. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for pregnancy prolongation (time from trial entry to birth).



Tocolytic ranking

Figure 16 shows the cumulative probabilities for each agent being at each possible rank for pregnancy prolongation as a continuous outcome. The highest ranked tocolytics were oxytocin receptor antagonists (SUCRA 92%) and lowest ranked were the betamimetics (SUCRA 28%), magnesium sulphate (SUCRA 25%) and placebo or no treatment (SUCRA 20%).

Figure 16. Cumulative rankograms comparing each of the tocolytic drugs for pregnancy prolongation (time from trial entry to birth). Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



5. Serious adverse effects of drugs

Network evidence

The network diagram for serious (maternal) adverse effects of drugs is presented in Figure 17. Relative effects from the network meta-analysis of 62 trials (6983 women) suggested that all tocolytics are associated with a wide range of effects for serious adverse effects when compared with placebo or no treatment as there were only few events (Figure 18; Summary of findings 5).

Figure 17. Network diagram for serious adverse effects of the drugs. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

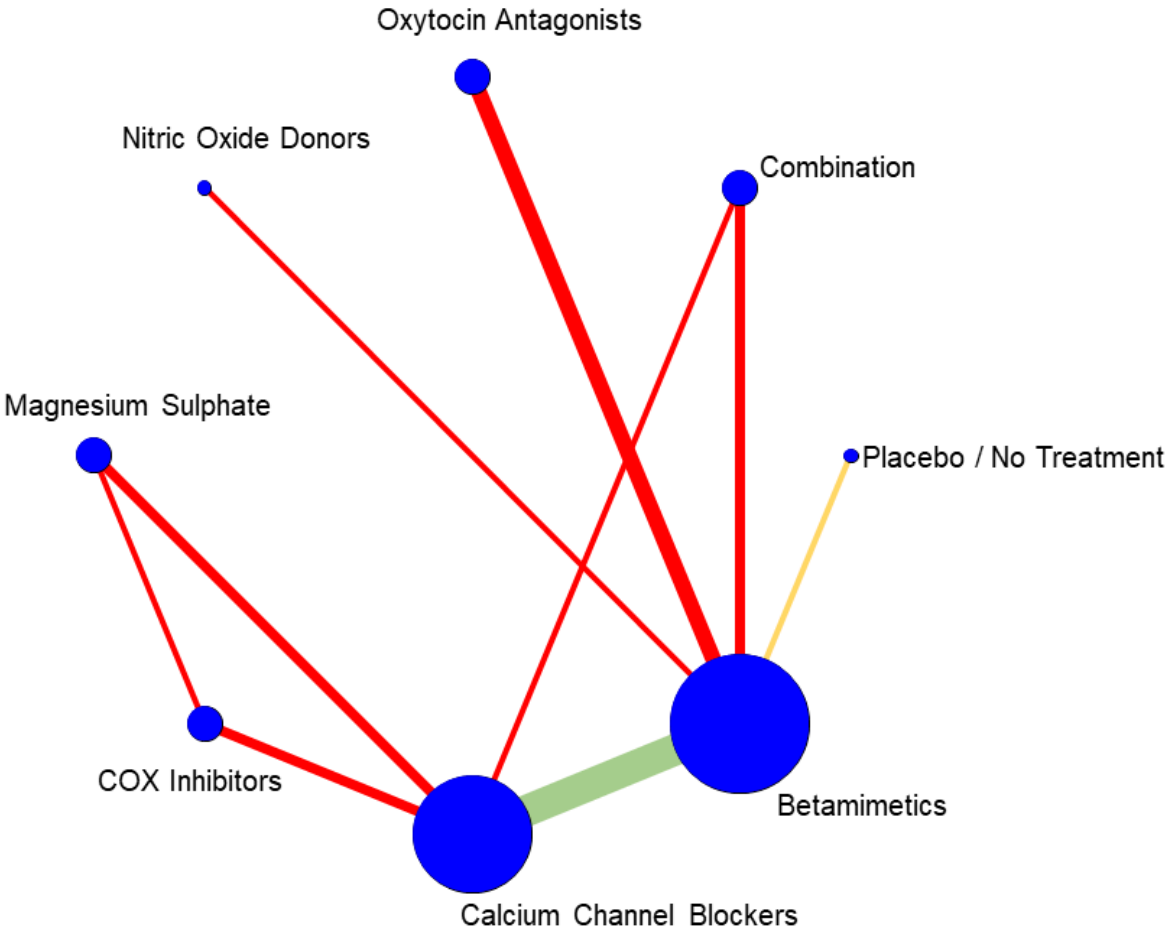
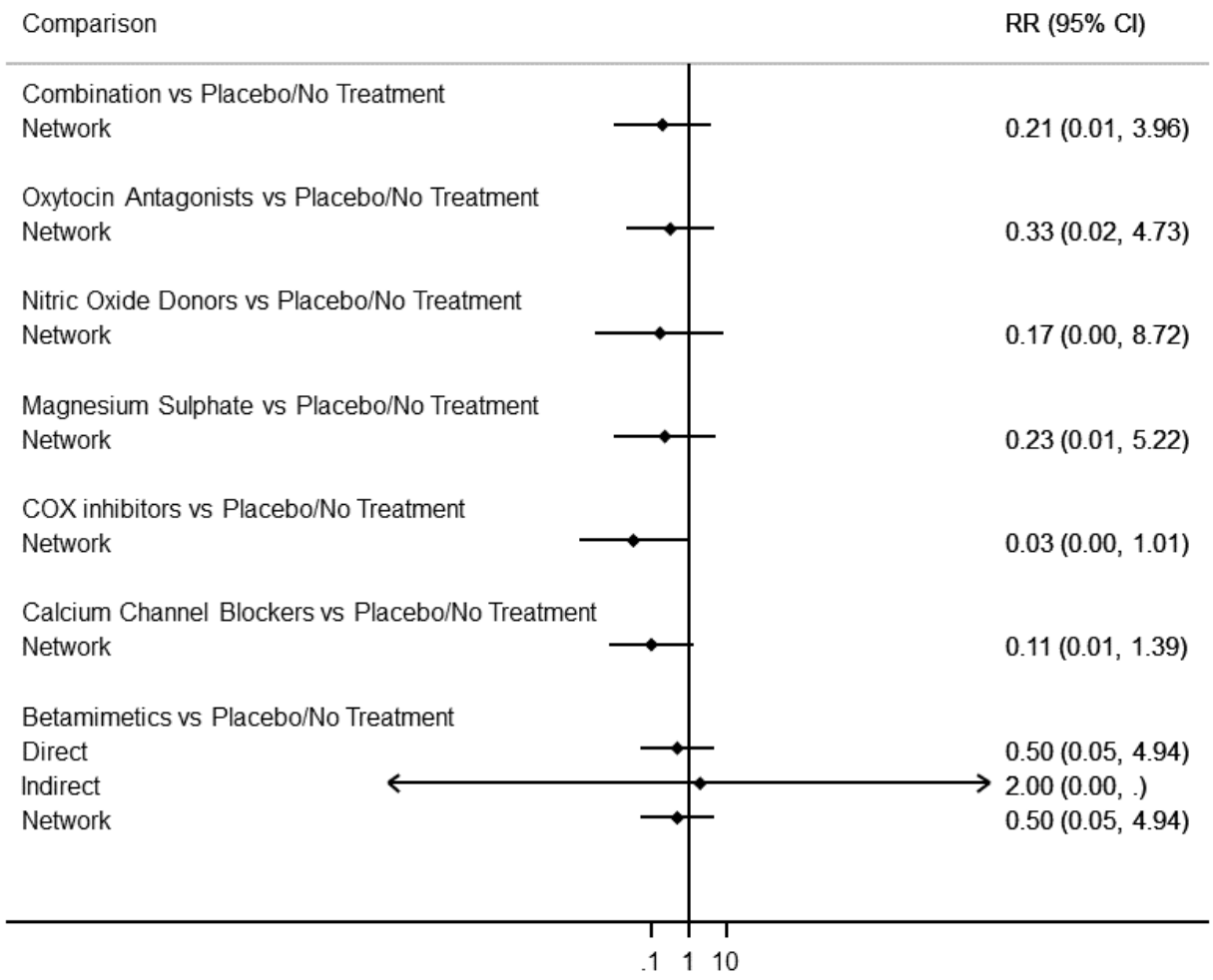


Figure 18. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for serious adverse effects of the drugs.

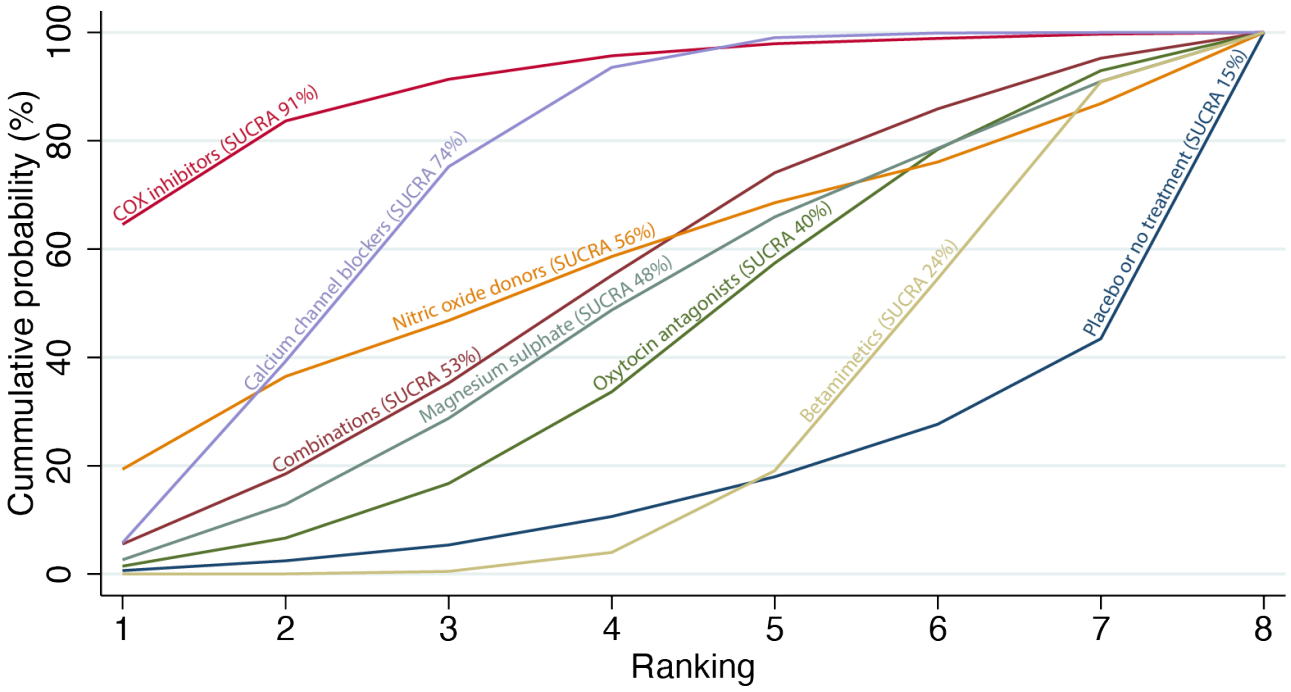


Tocolytic ranking*

The cumulative probabilities for each tocolytic being at each possible rank for serious adverse events are shown in Figure 19.

The ranking for tocolytics was not clear for this outcome due to few events.

Figure 19. Cumulative rankograms comparing each of the tocolytic drugs for serious adverse effects of the drugs. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



6. Maternal infection after trial entry

Network evidence

The network diagram for maternal infection is presented in Figure 20. Relative effects from the network meta-analysis of 13 trials (1399 women) suggested that tocolytics are associated with a wide range of effects when compared with placebo or no treatment as there were only few events (Figure 21, Summary of findings 6).

Figure 20. Network diagram for maternal infection. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

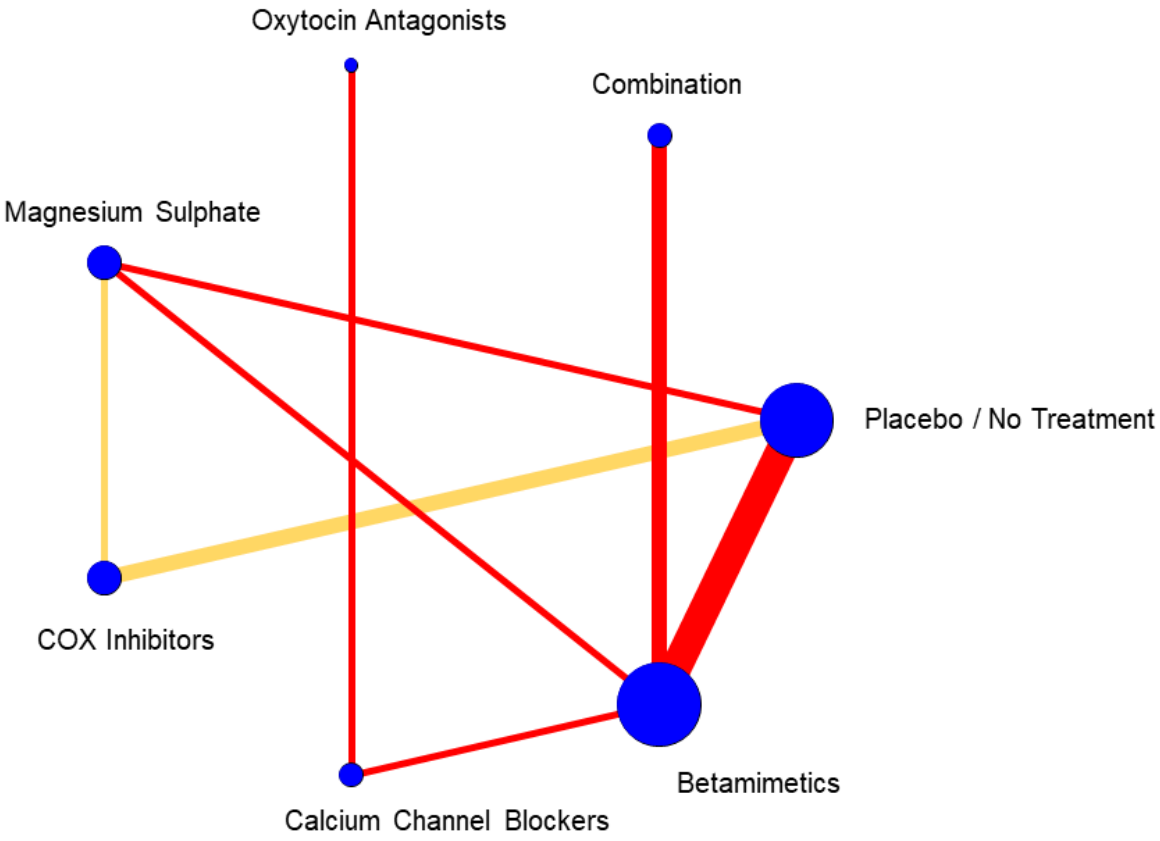
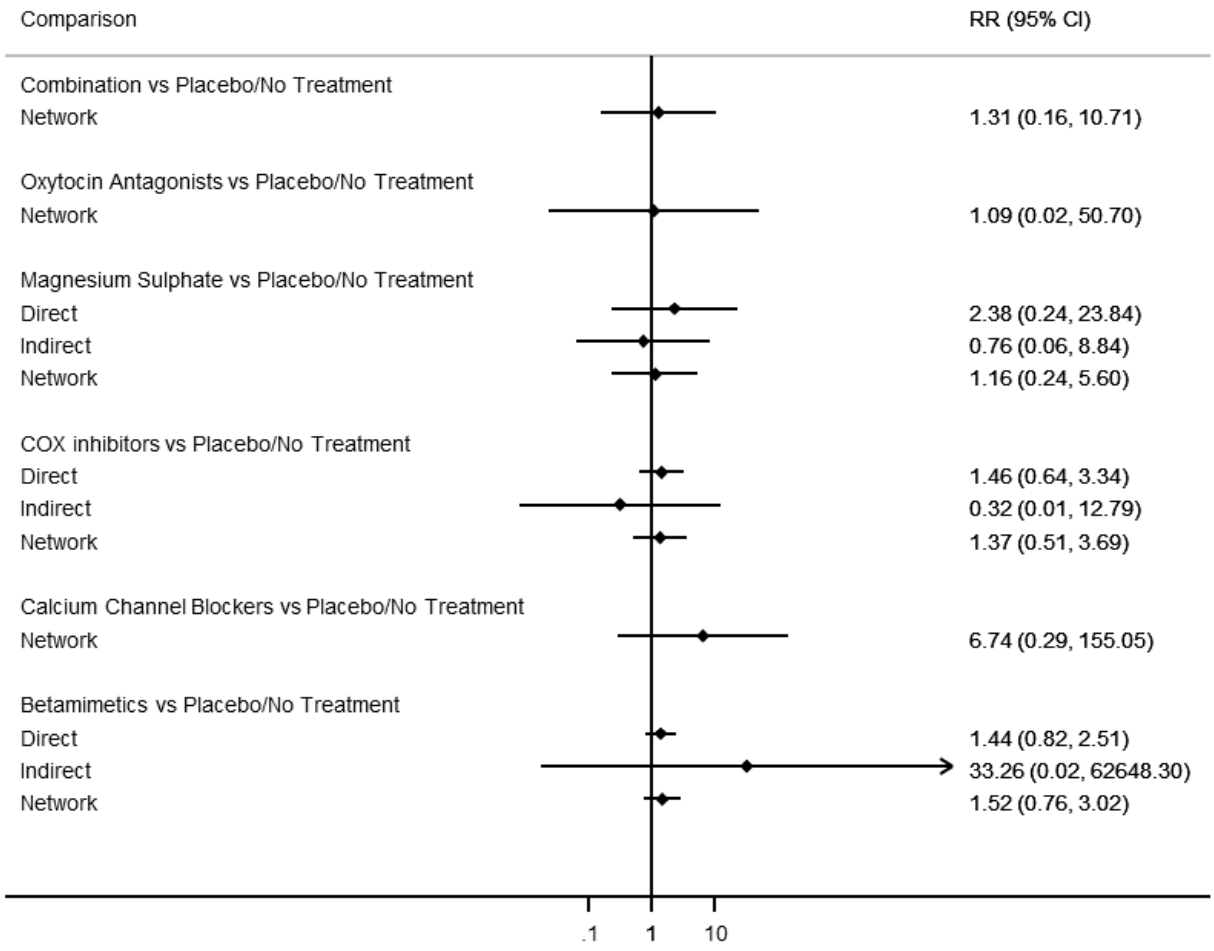


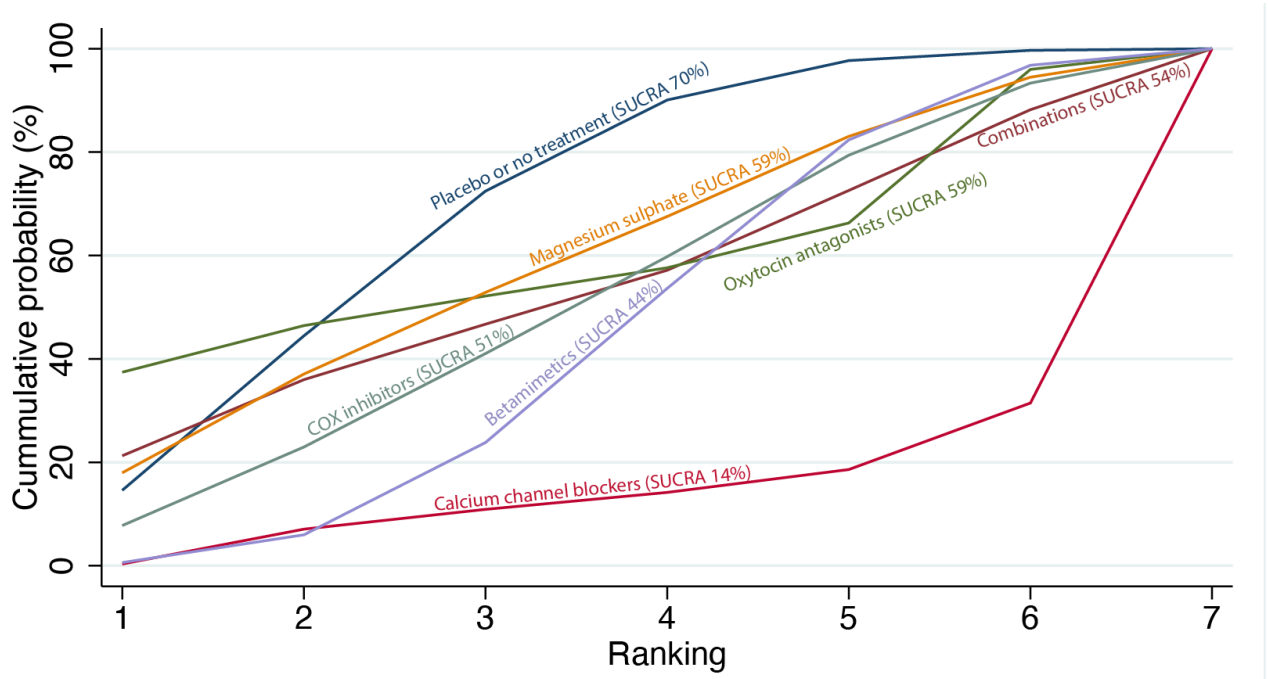
Figure 21. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for maternal infection.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for maternal infection are shown in Figure 22. The ranking for tocolytics was not clear for this outcome due to few events.

Figure 22. Cumulative rankograms comparing each of the tocolytic drugs for maternal infection. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



7. Cessation of treatment due to adverse effects

Network evidence

The network diagram for cessation of treatment due to adverse effects is presented in Figure 23. Relative effects from the network meta-analysis of 68 trials (8122 women) suggested that several tocolytics are more likely to result in cessation of treatment due to adverse effects when compared with placebo or no treatment (Figure 24). When compared with placebo or no treatment, moderate-certainty evidence suggests that betamimetics (RR 14.44, 95% CI 6.11 to 34.11), calcium channel blockers (RR 2.96 (95% CI 1.23 to 7.11), and magnesium sulphate (RR 3.90 (95% CI 1.09 to 13.93) probably result to more frequent cessation of treatment due to adverse effects. The combinations of tocolytics possibly also result in more frequent cessation due to adverse effects (RR 6.87, 95% CI 2.08 to 22.65; low-certainty evidence). Oxytocin receptor antagonists are associated with a wide range of effects (RR 1.24, 95% CI 0.46 to 3.35; moderate-certainty evidence) compared with placebo or no treatment. The effects of COX inhibitors, and nitric oxide donors were unclear because the certainty of the evidence was very low (Summary of findings 7).

Figure 23. Network diagram for cessation of treatment due to adverse effects. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

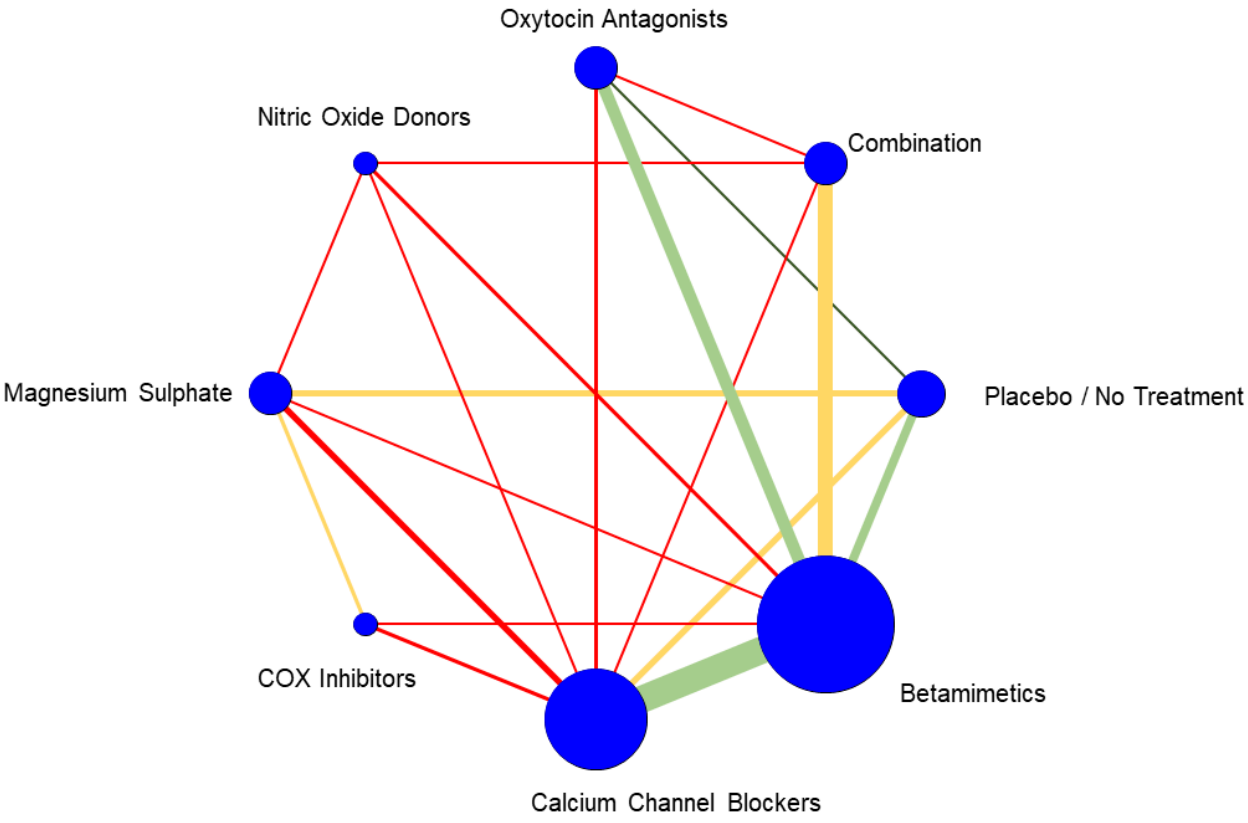
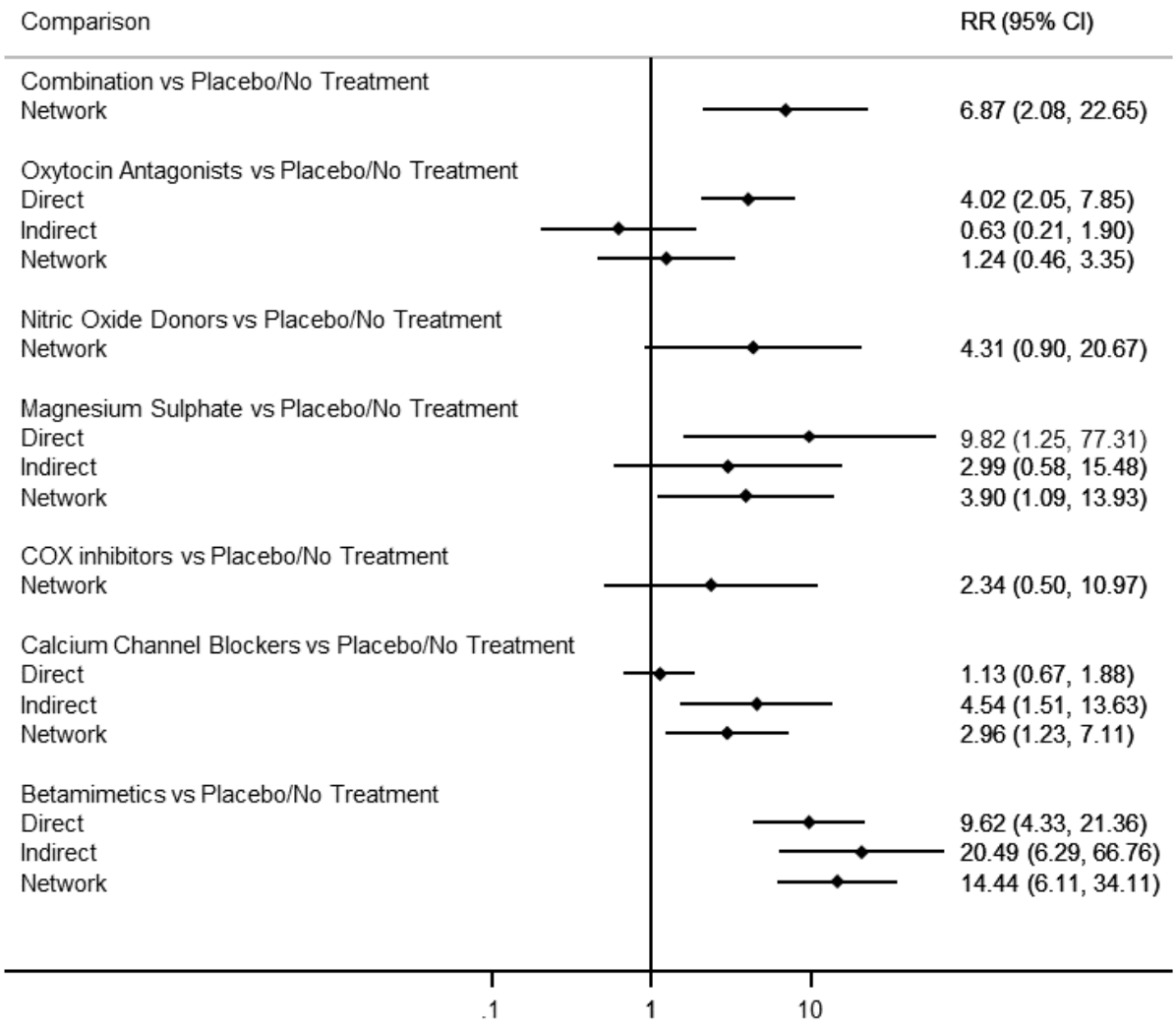


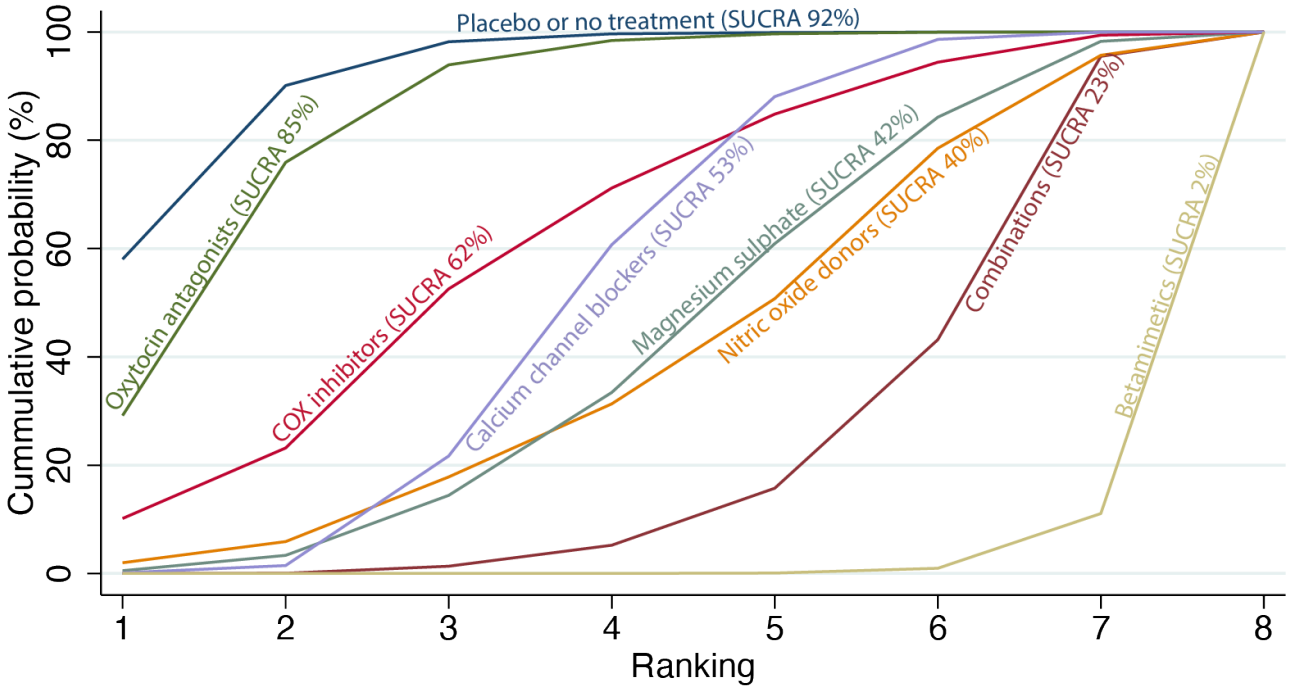
Figure 24. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for cessation of treatment due to adverse effects.



Tocolytic ranking

The cumulative probabilities for each agent being at each possible rank for this outcome are shown in Figure 25. The lowest ranked tocolytics for this outcome were betamimetics (SUCRA 2%) and combinations of tocolytics (SUCRA 23%). Highest ranked were oxytocin receptor antagonists (SUCRA 85%) and placebo or no treatment (SUCRA 92%).

Figure 25. Cumulative rankograms comparing each of the tocolytic drugs for cessation of treatment due to adverse effects. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



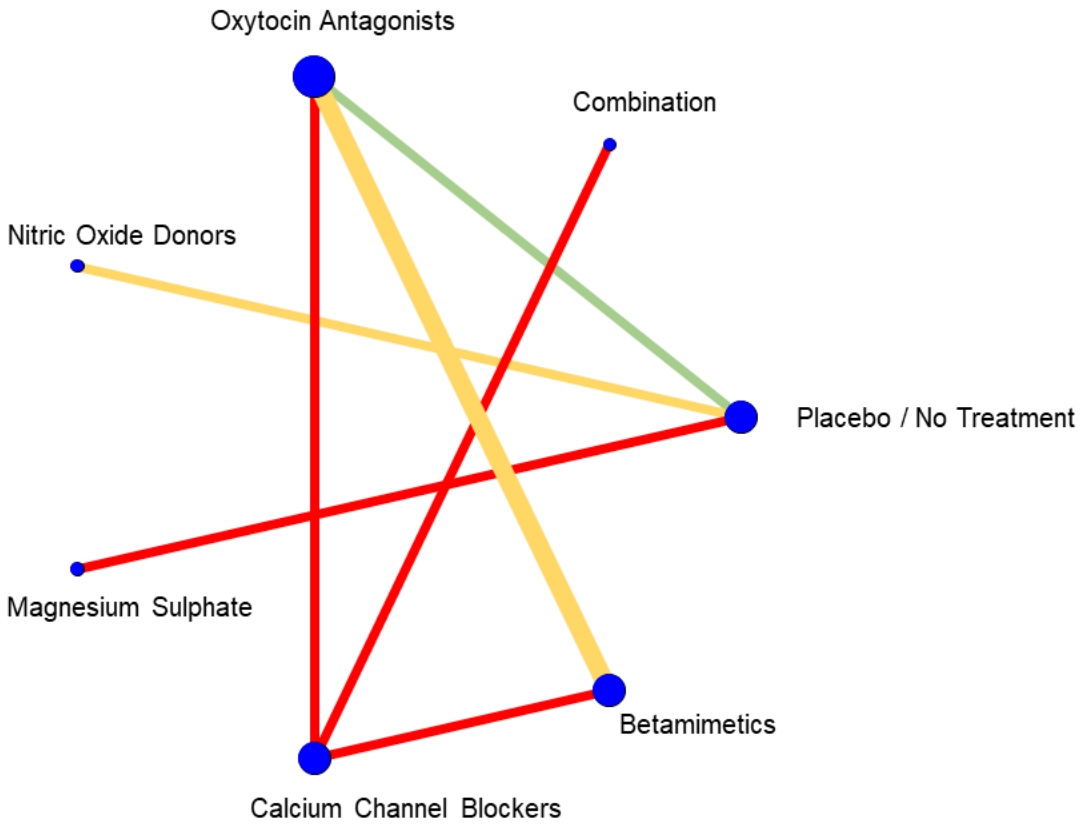
Secondary outcomes

8. Birth before 28 weeks of gestation

Network evidence

The network diagram for birth before 28 weeks of gestation is presented in Figure 26. Due to the small number of trials (8 trials) reporting this outcome, network meta-analysis was not possible, and so were unable to produce network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis (Data and analyses). One trial (501 women) suggests that oxytocin receptor antagonists probably result in fewer births before 28 weeks of gestation compared with placebo or no treatment (RR 3.11, 95% CI 1.02 to 9.51; moderate-certainty evidence; Analysis 5.8; Appendix 3). One trial (153 women) for nitric oxide donors (RR 0.50, 95% CI 0.23 to 1.09; low-certainty evidence; Analysis 6.8) suggests that they are associated with a wide range of effects compared with placebo or no treatment. The evidence for magnesium sulphate is of very low certainty for this outcome. There is no direct evidence comparing betamimetics, COX inhibitors, calcium channel blockers or combinations of tocolytics to placebo or no treatment (Appendix 3).

Figure 26. Network diagram for birth before 28 weeks of gestation. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.



9. Birth before 32 weeks of gestation

Network evidence

The network diagram for birth before 32 weeks of gestation is presented in Figure 27. Relative effects from the network meta-analysis of 11 trials (1954 women) suggested that tocolytics are associated with a wide range of effects for this outcome when compared with placebo or no treatment as there were insufficient studies contributing to this analysis (Figure 28; Appendix 3).

Figure 27. Network diagram for birth before 32 weeks of gestation. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

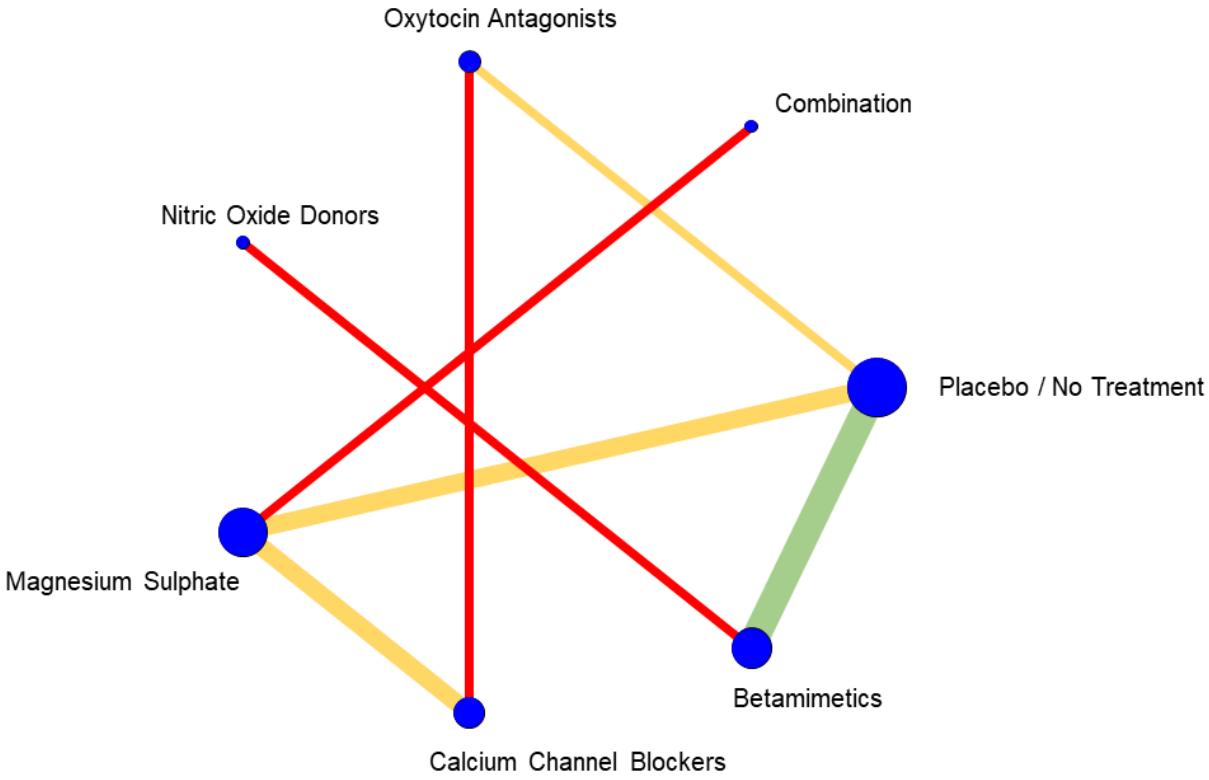
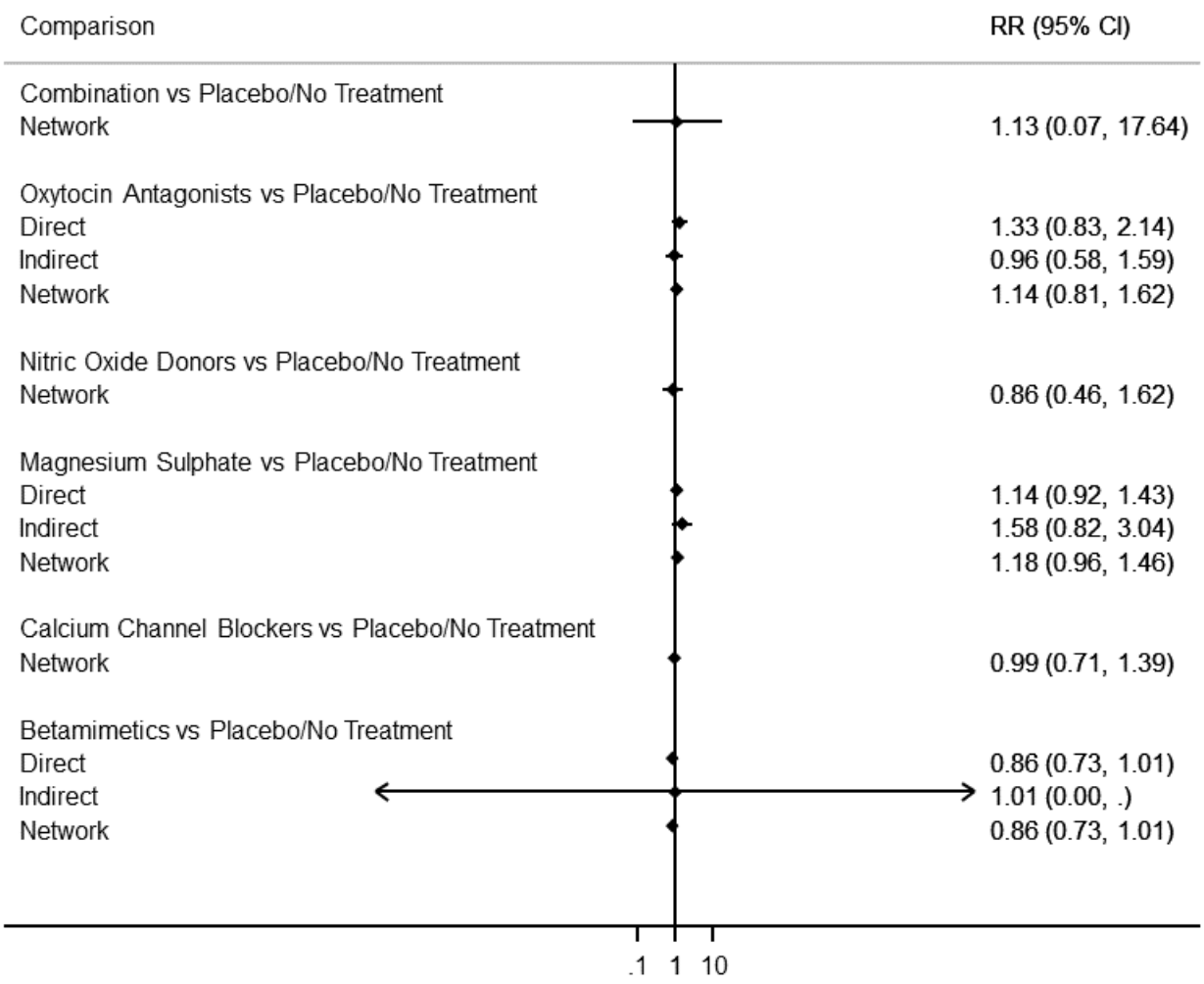


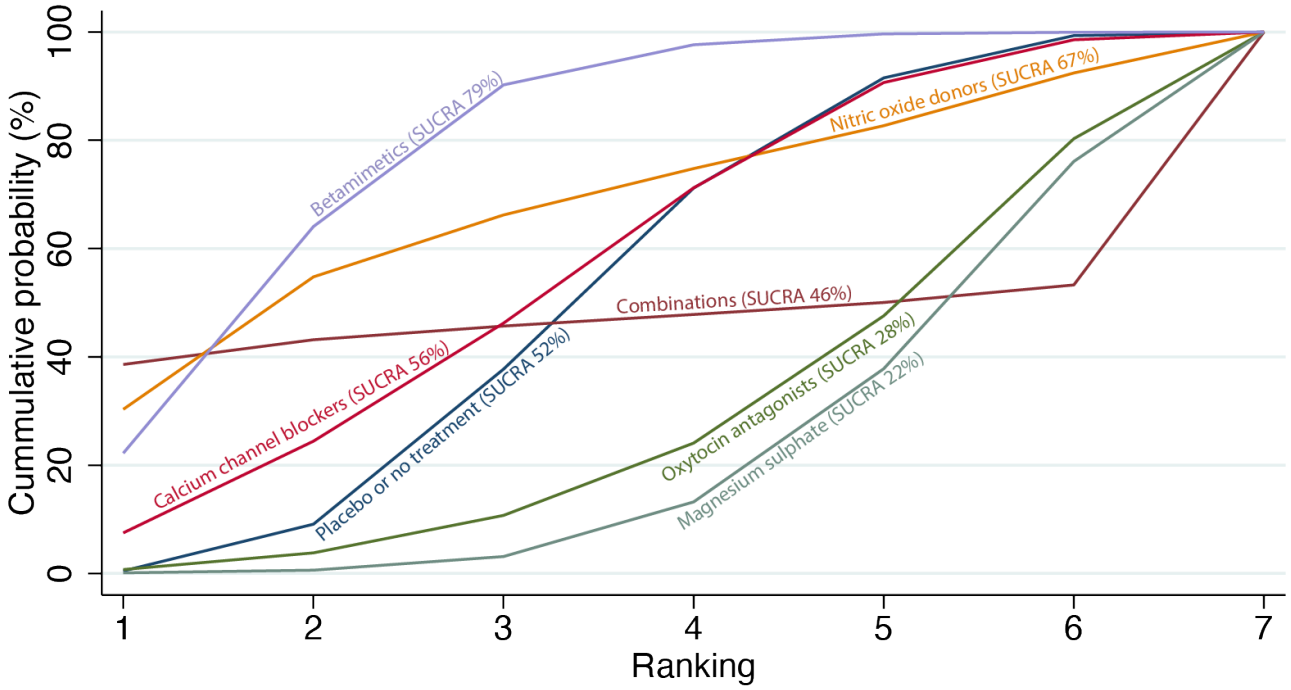
Figure 28. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for birth before 32 weeks of gestation.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for birth before 32 weeks of gestation are shown in Figure 29. The ranking for tocolytics was not clear for this outcome due to few studies in this analysis.

Figure 29. Cumulative rankograms comparing each of the tocolytic drugs for birth before 32 weeks of gestation. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



10. Birth before 34 weeks of gestation

Network evidence

The network diagram for birth before 34 weeks of gestation is presented in Figure 30. Relative effects from the network meta-analysis of 19 trials (2265 women) suggested that nitric oxide donors are associated with a wide range of effects for this outcome (RR 0.86, 95% CI 0.59 to 1.27; low-certainty evidence) when compared with placebo or no treatment (Figure 31; Appendix 3). The comparisons of the other tocolytics with placebo or no treatment are of very low certainty, hence the effects remain uncertain.

Figure 30. Network diagram for birth before 34 weeks of gestation. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

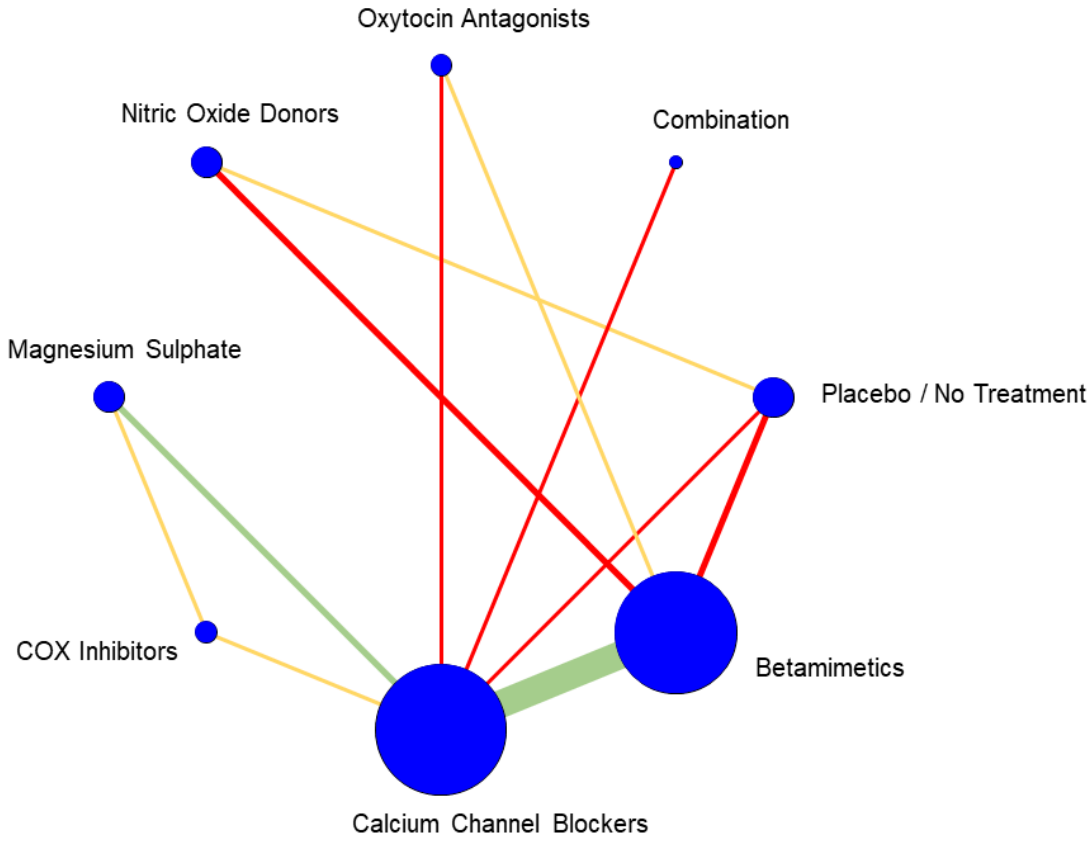
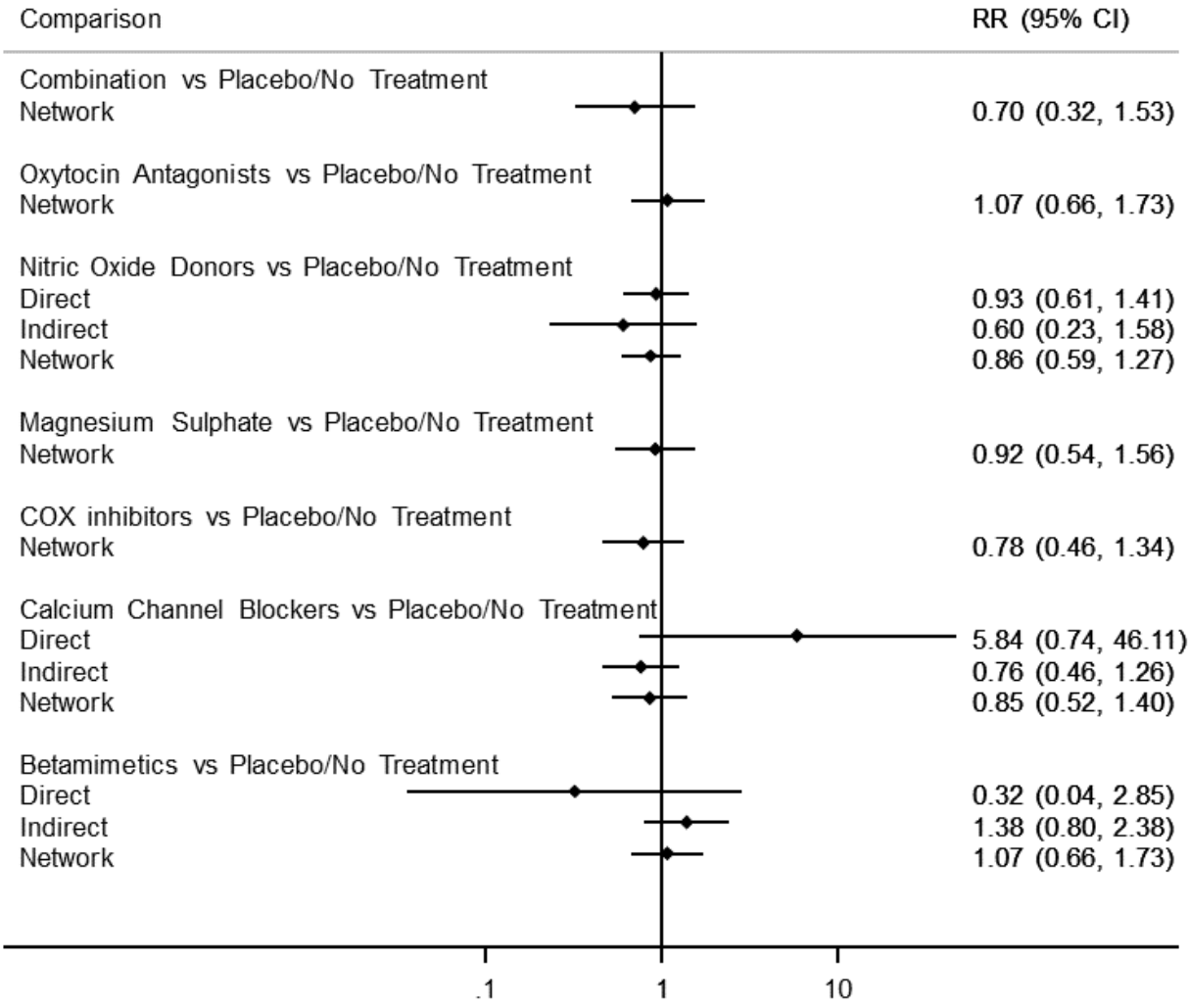


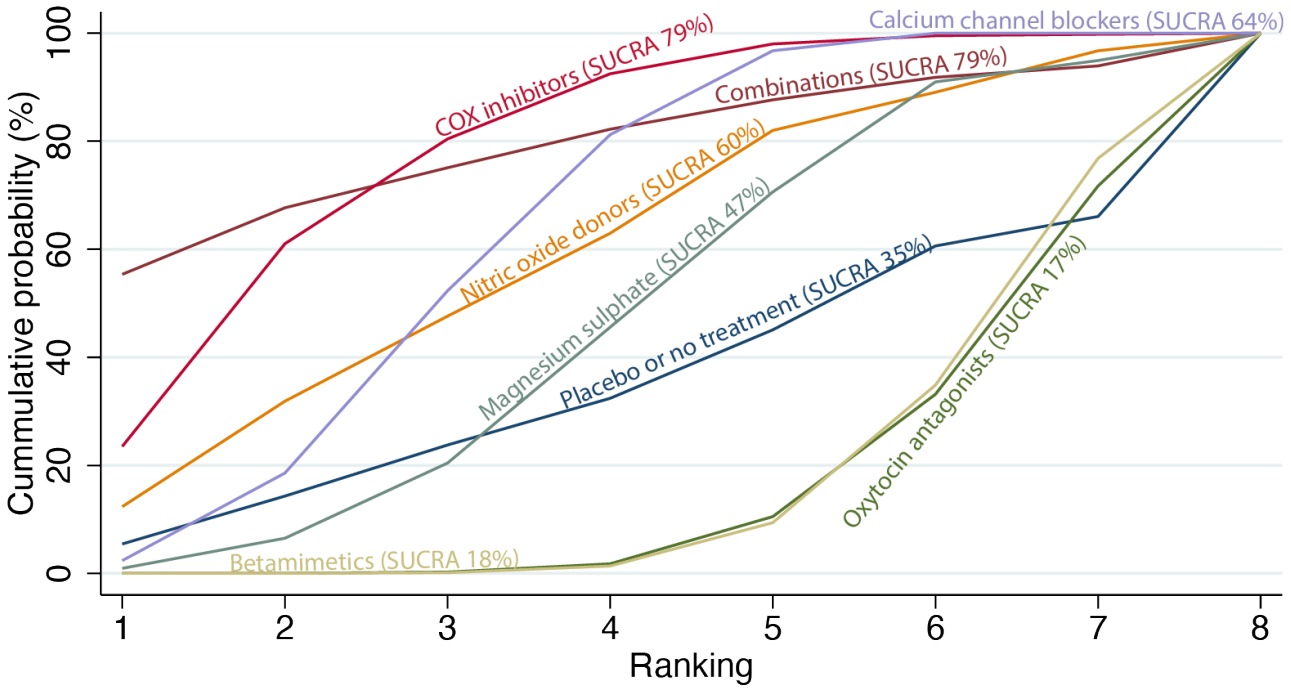
Figure 31. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for birth before 34 weeks of gestation.



Tocolytic ranking*

The cumulative probabilities for each tocolytic being at each possible rank for birth before 34 weeks of gestation are shown in Figure 32. The ranking for tocolytics was not clear for this outcome because of the low number of studies in this analysis.

Figure 32. Cumulative rankograms comparing each of the tocolytic drugs for birth before 34 weeks of gestation. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



11. Birth before 37 weeks of gestation

Network evidence

The network diagram for birth before 37 weeks of gestation is presented in Figure 33. Relative effects from the network meta-analysis of 51 trials (6104 women) suggested that betamimetics (RR 0.97, 95% CI 0.83 to 1.13; low-certainty evidence), calcium channel blockers (RR 0.91, 95% CI 0.78 to 1.07; low-certainty evidence), oxytocin receptor antagonists (1.10, 95% CI 0.89 to 1.36; moderate-certainty evidence), and nitric oxide donors (RR 0.77, 95% CI 0.59 to 1.00; low-certainty evidence) are associated with a wide range of effects for this outcome when compared with placebo or no treatment (Figure 34; Appendix 3). The comparisons of COX inhibitors, magnesium sulphate and combinations of tocolytics compared with placebo or no treatment are of very low certainty, hence the effects remain uncertain.

Figure 33. Network diagram for birth before 37 weeks of gestation. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

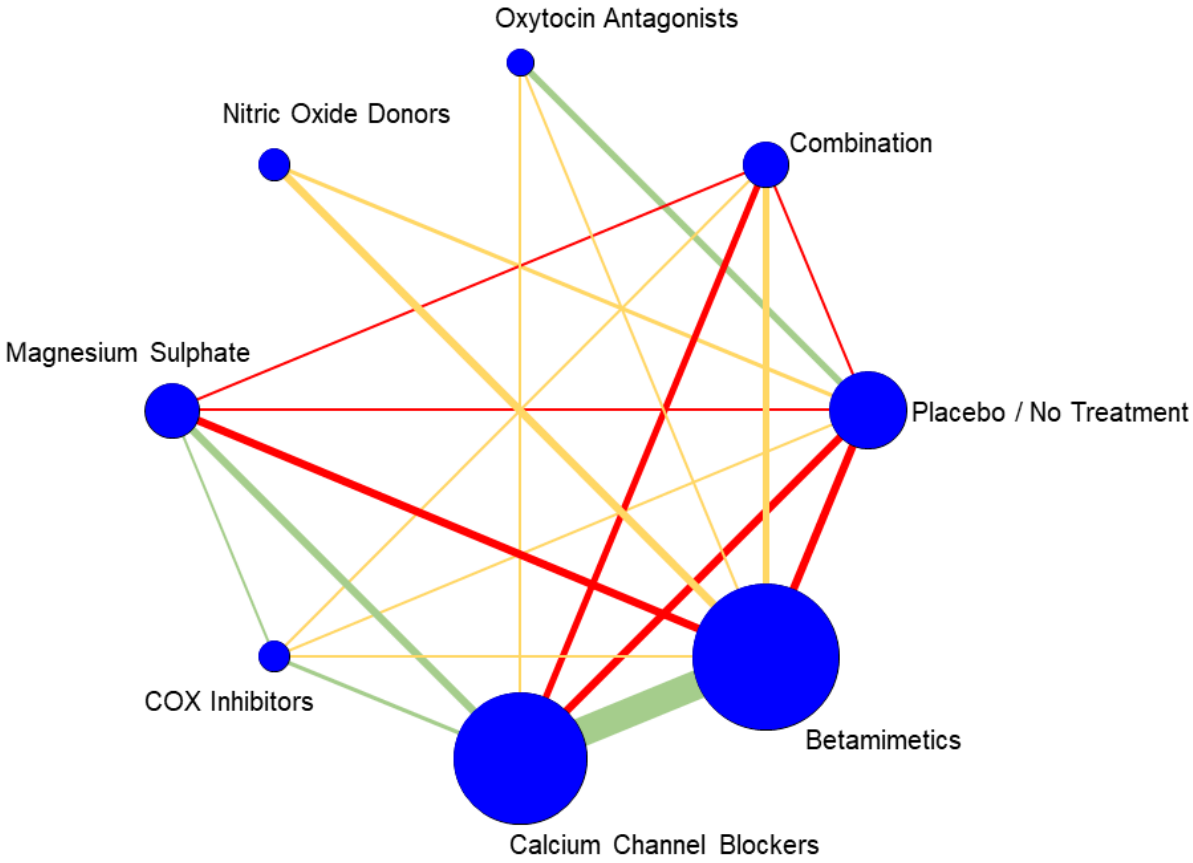
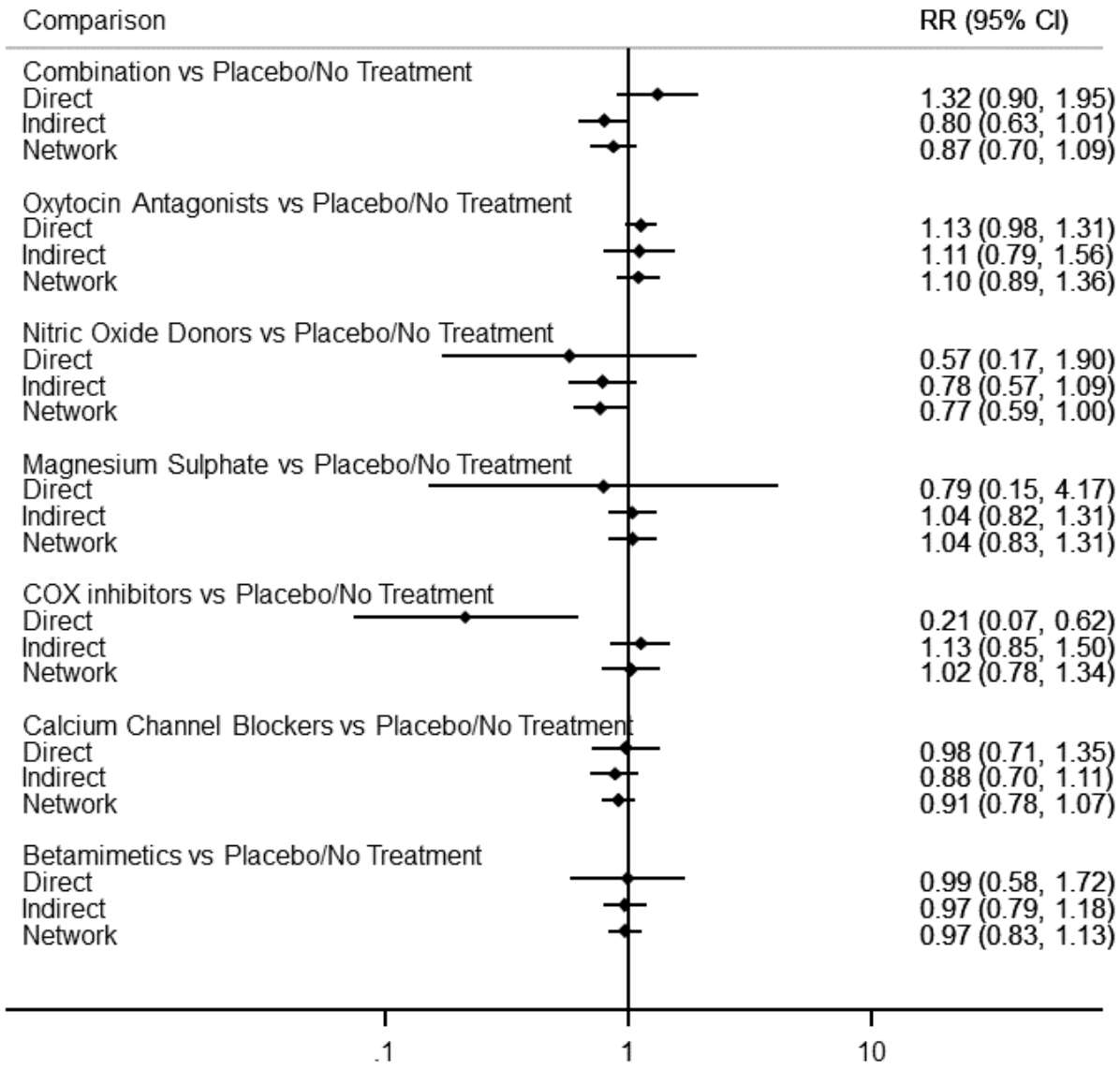


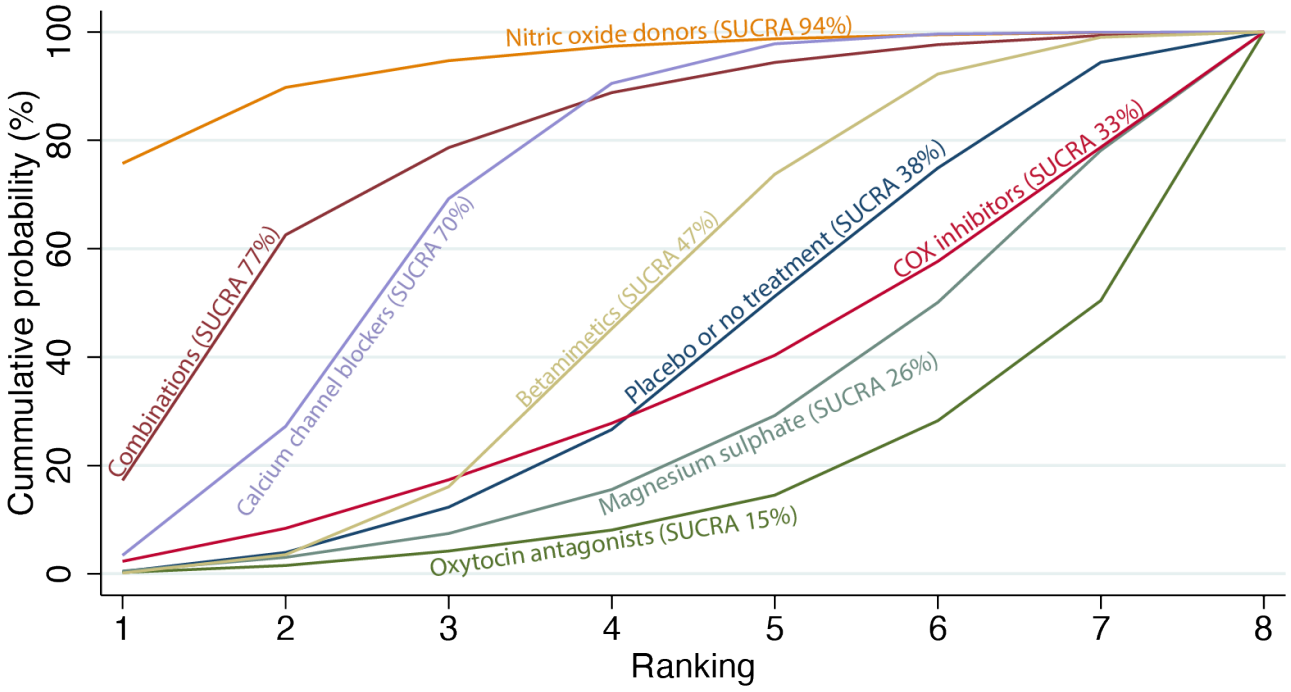
Figure 34. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for birth before 37 weeks of gestation.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for birth before 37 weeks of gestation are shown in Figure 35. The highest ranked tocolytics for birth before 37 weeks of gestation are the nitric oxide donors (SUCRA 94%), combinations of tocolytics (SUCRA 77%), and calcium channel blockers (SUCRA 70%).

Figure 35. Cumulative rankograms comparing each of the tocolytic drugs for birth before 37 weeks of gestation. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



12. Maternal death

Network evidence

There were no maternal deaths in 13 studies (2631 women) that reported this outcome and relative effects for the tocolytics compared with placebo or no treatment were not estimable.

13. Pulmonary oedema

Network evidence

The network diagram for pulmonary oedema as a serious adverse effect from tocolysis is presented in Figure 36. Relative effects from the network meta-analysis of 32 trials (4344 women) found that evidence for all comparisons of tocolytics with placebo was of very low certainty, so their effects remain uncertain (Figure 37; Appendix 3).

Figure 36. Network diagram for pulmonary oedema. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

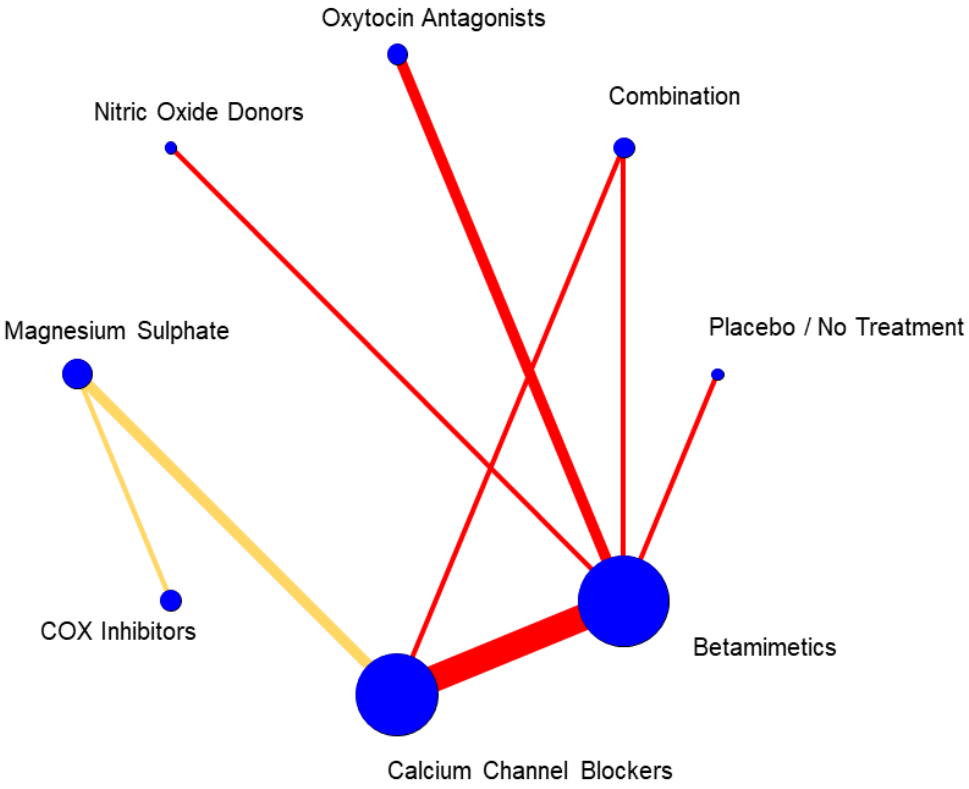
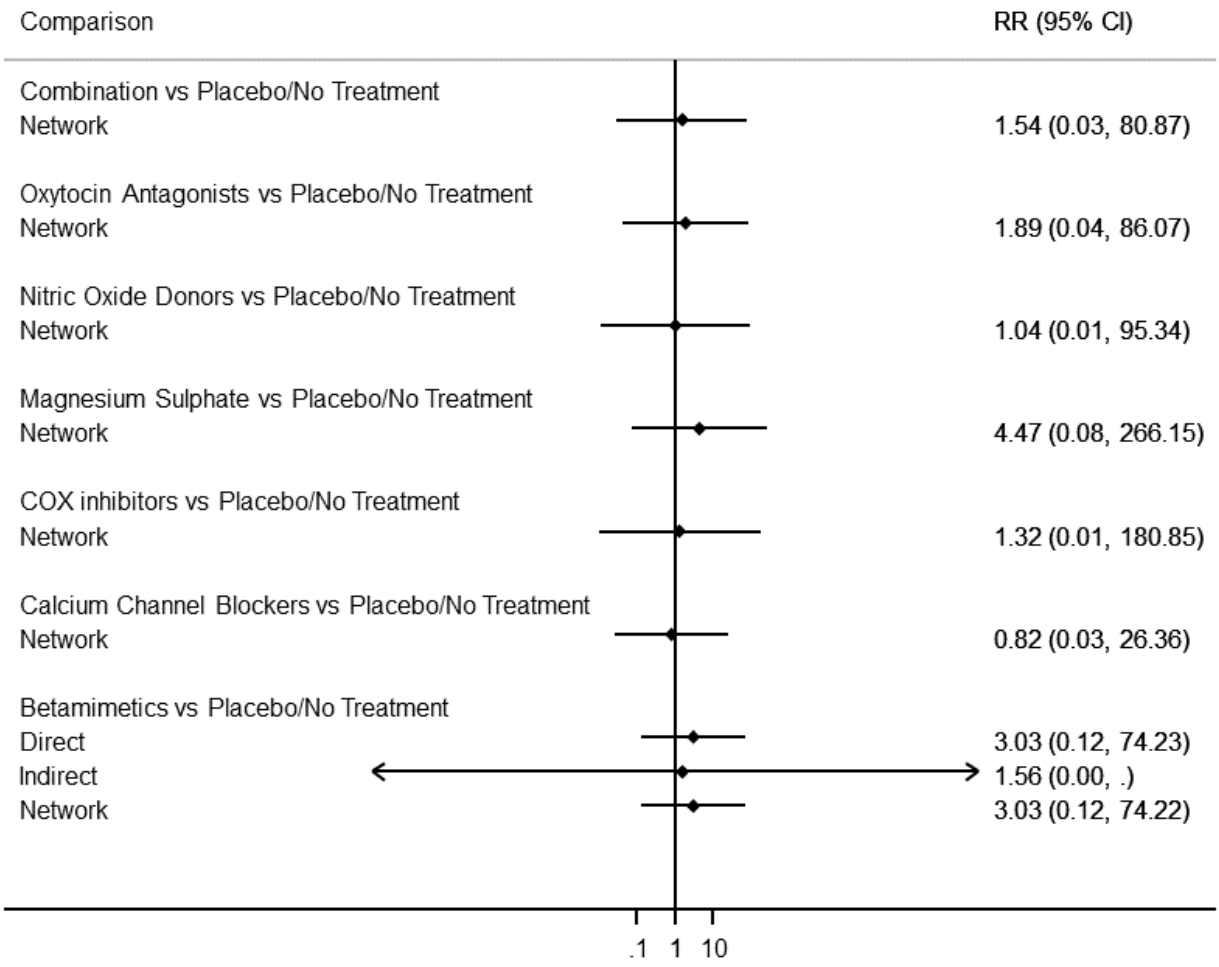


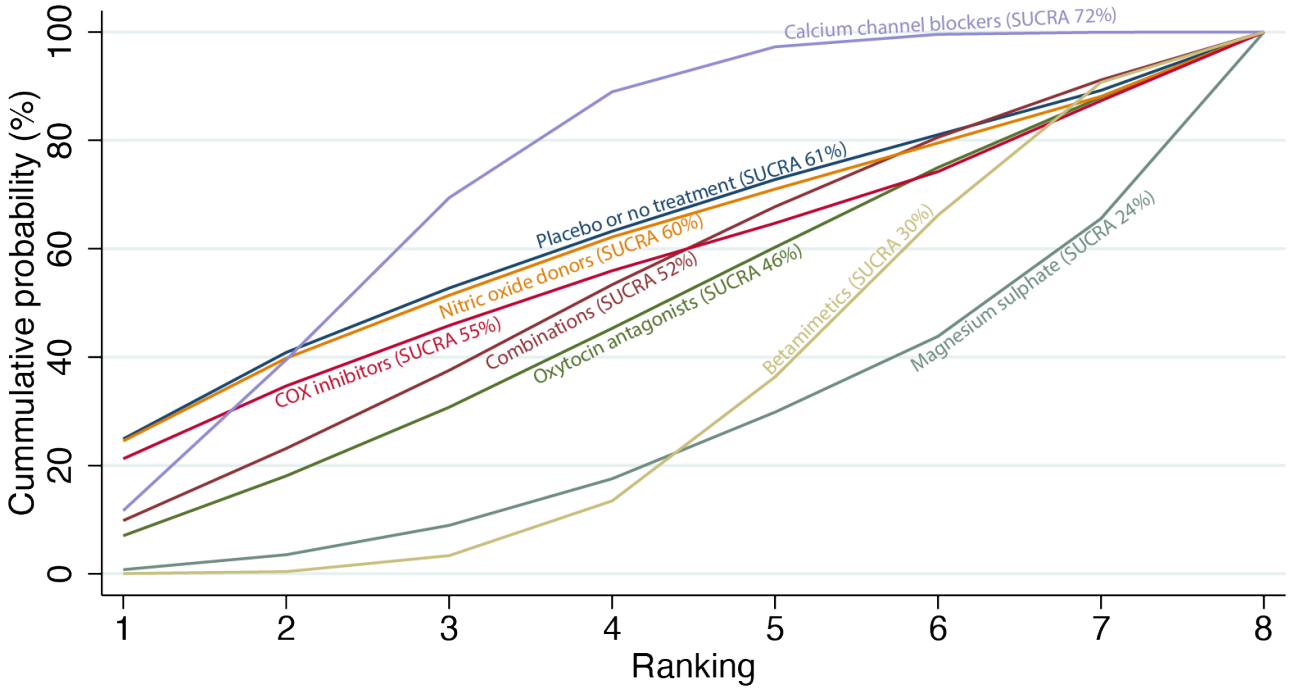
Figure 37. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for pulmonary oedema.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for pulmonary oedema are shown in Figure 38. The ranking for tocolytics was not clear for this outcome because of the low number of events in this analysis.

Figure 38. Cumulative rankograms comparing each of the tocolytic drugs for pulmonary oedema. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



14. Dyspnoea

Network evidence

The network diagram for dyspnoea from tocolysis is presented in Figure 39. Relative effects from the network meta-analysis of 24 trials (3357 women) suggested that betamimetics (RR 12.09, 95% CI 4.66 to 31.39; moderate-certainty evidence) probably cause dyspnoea; the other tocolytics are associated with a wide range of effects when compared with placebo or no treatment (Figure 40; Appendix 3).

Figure 39. Network diagram for dyspnoea. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

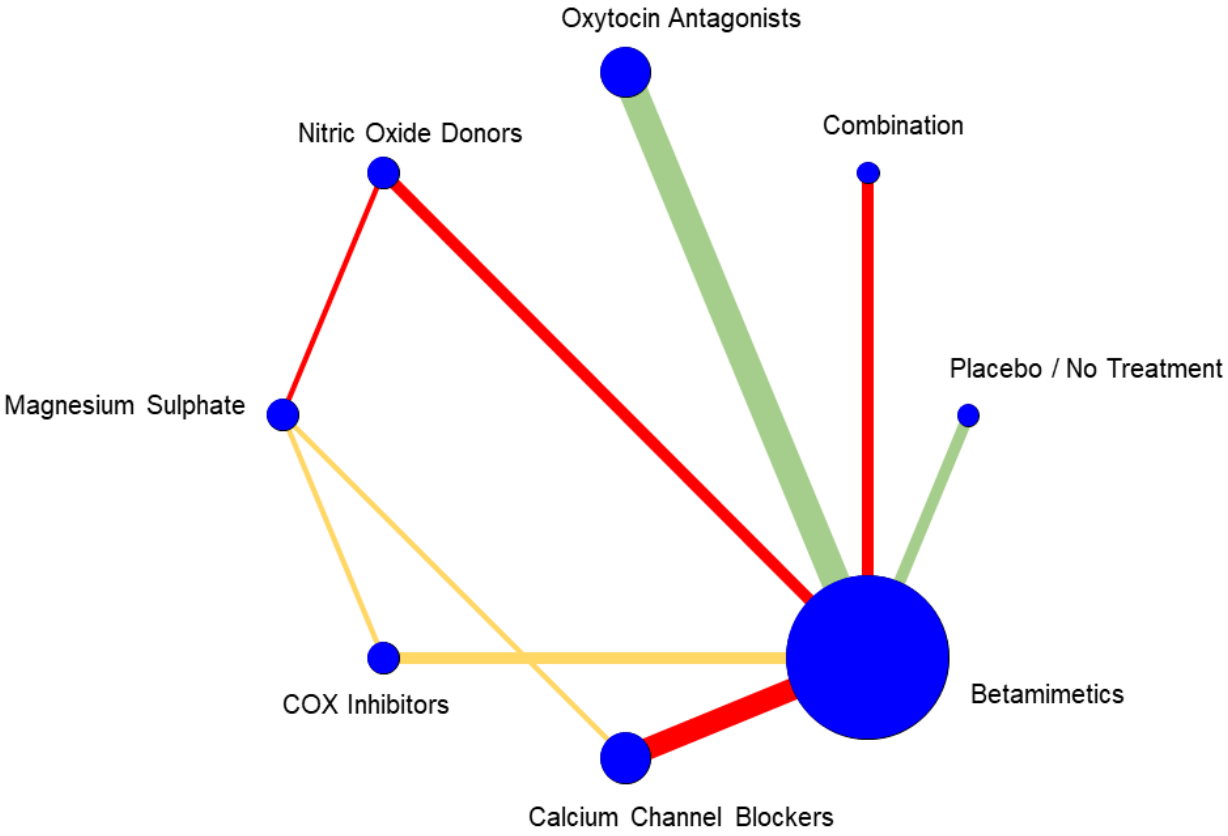
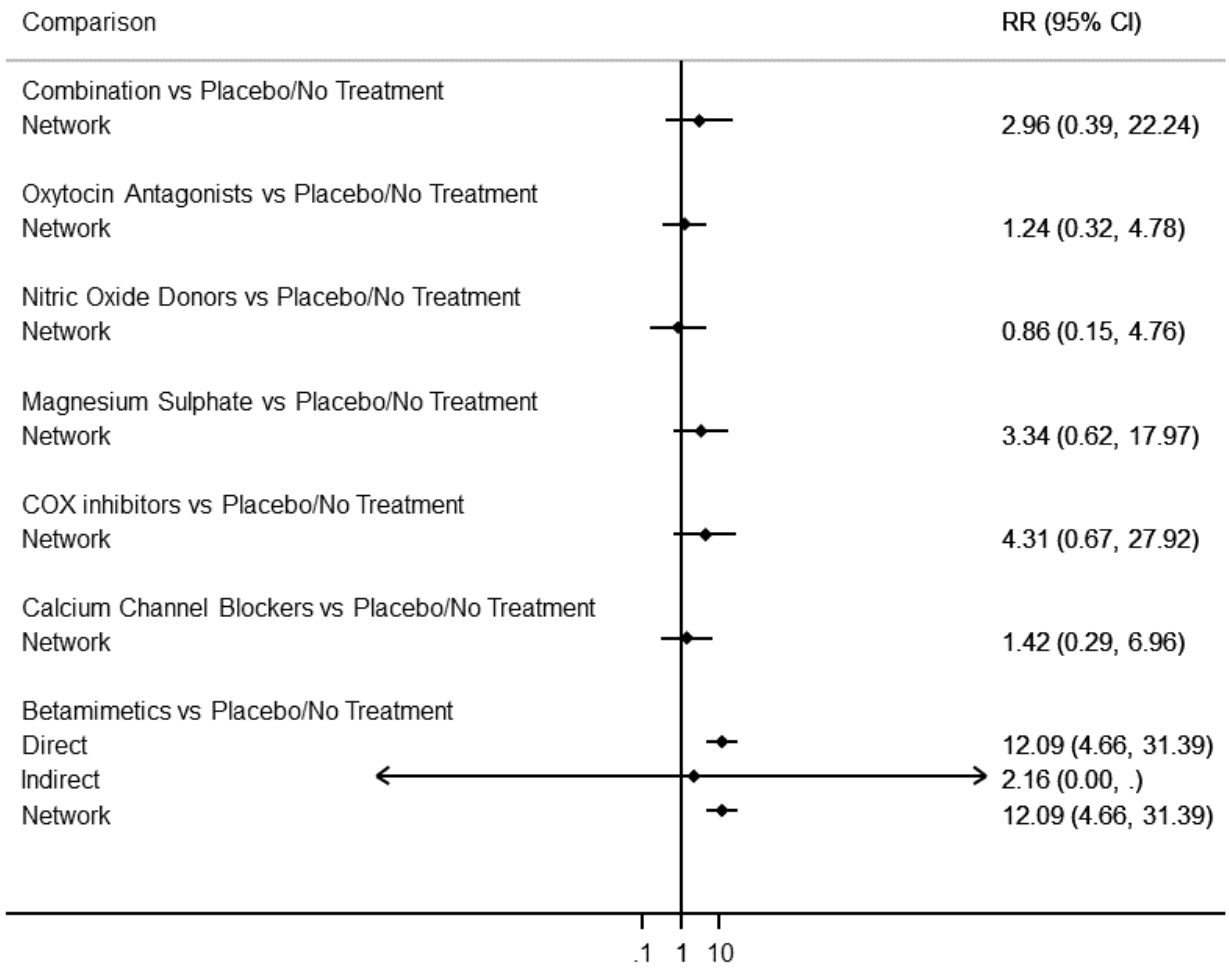


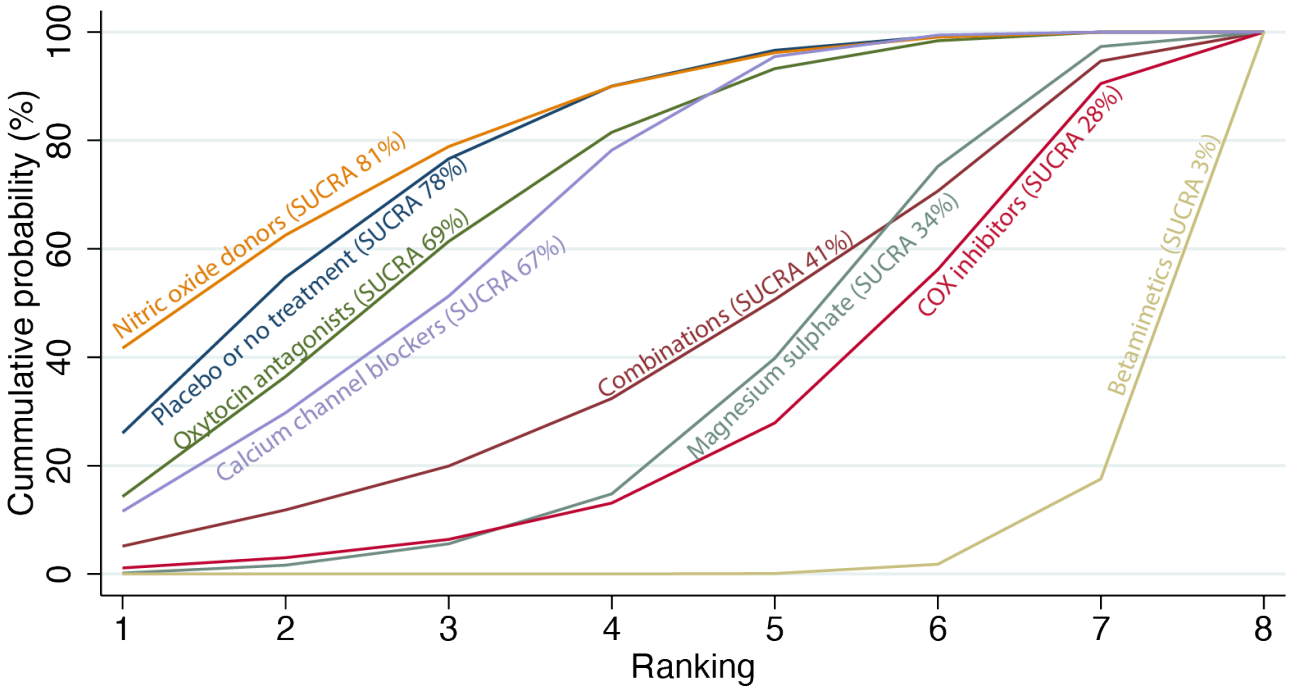
Figure 40. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for dyspnoea.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for dyspnoea are shown in Figure 41. The lowest ranked tocolytics for this outcome were betamimetics (SUCRA 3%). Highest ranked were the nitric oxide donors (SUCRA 81%) and placebo or no treatment (SUCRA 78%).

Figure 41. Cumulative rankograms comparing each of the tocolytic drugs for dyspnoea. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



15. Palpitations

Network evidence

The network diagram for palpitations from tocolysis is presented in Figure 42. Relative effects from the network meta-analysis of 35 trials (4229 women) suggested that betamimetics (RR 7.39, 95% CI 3.83 to 14.24; moderate-certainty evidence) probably cause palpitations, meanwhile the other tocolytics are associated with a wide range of effects when compared with placebo or no treatment (Figure 43; Appendix 3).

Figure 42. Network diagram for palpitations. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

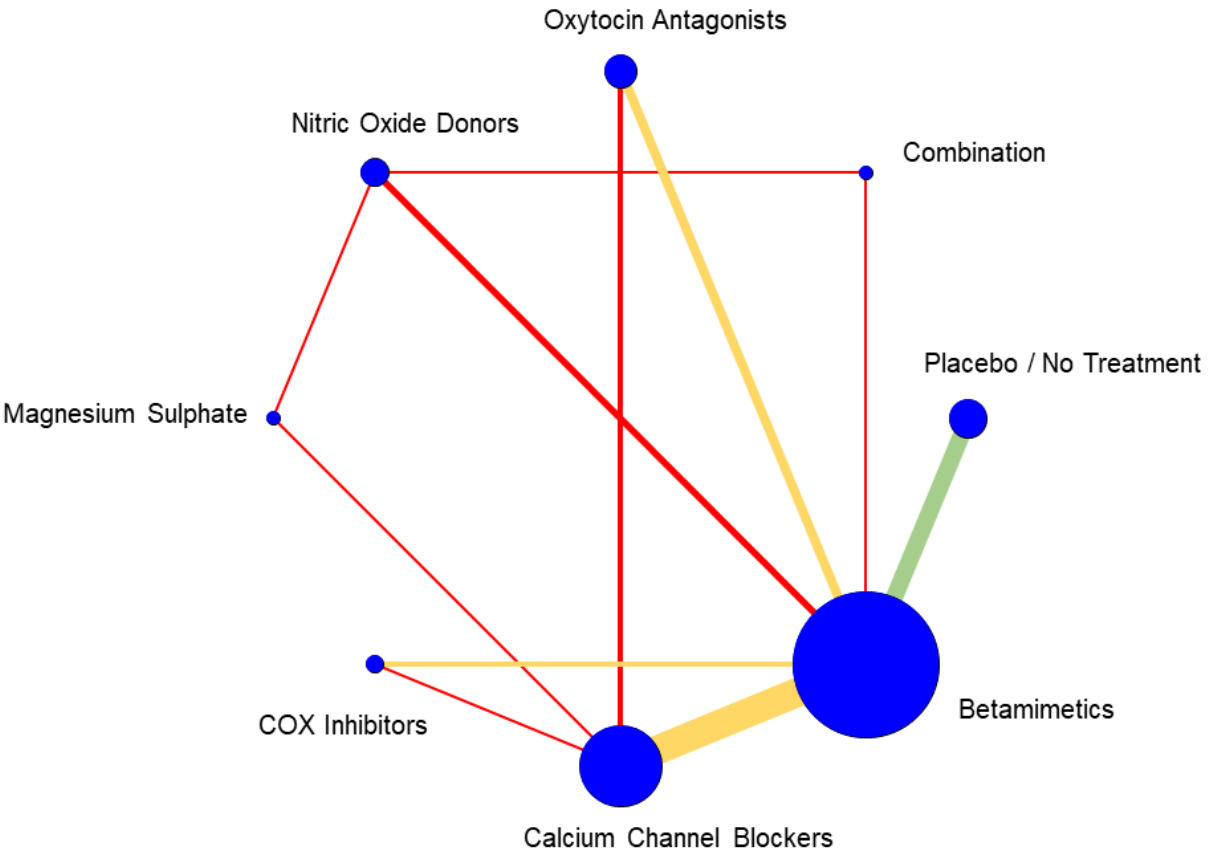
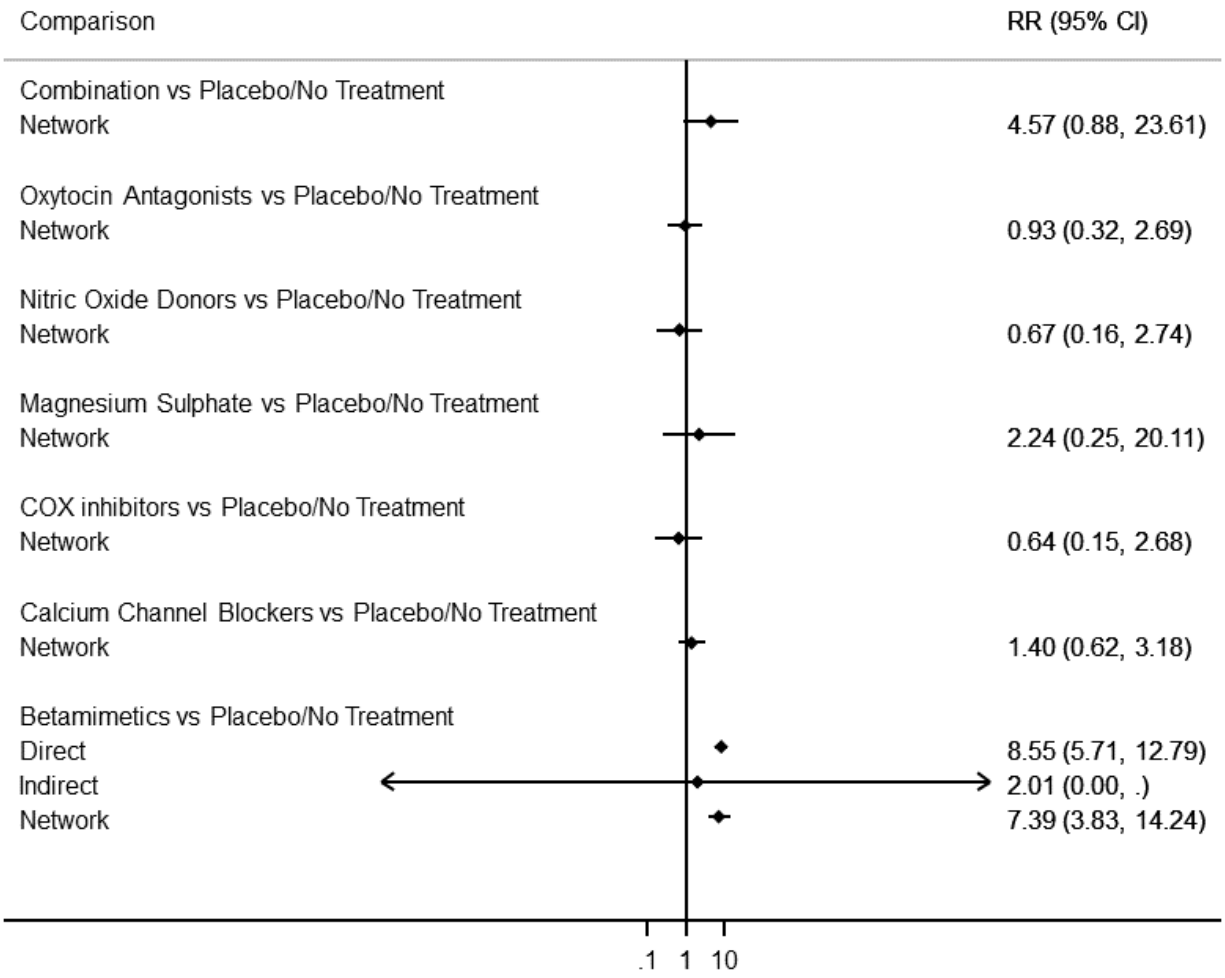


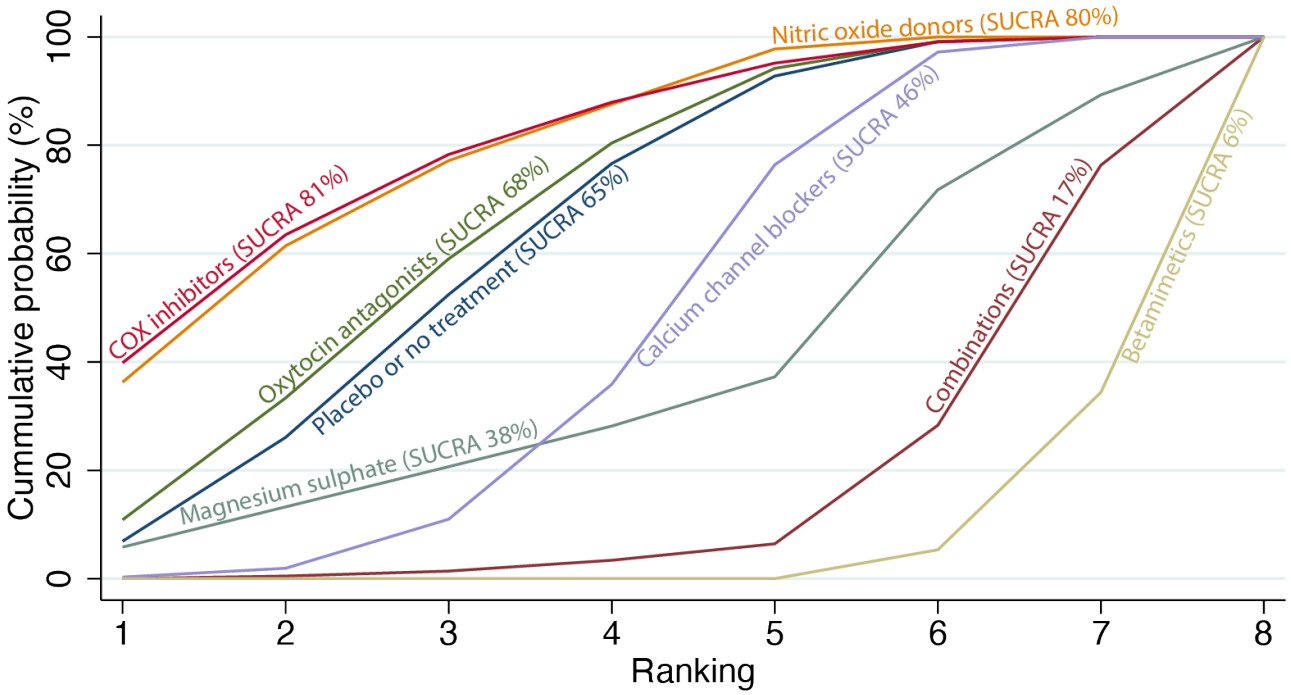
Figure 43. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for palpitations.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for palpitations are shown in Figure 44. The lowest ranked tocolytics for this outcome were betamimetics (SUCRA 6%) and combinations of tocolytics (SUCRA 17%). Highest ranked were the COX inhibitors (SUCRA 81%) and nitric oxide donors (SUCRA 80%), oxytocin receptor antagonists (SUCRA 68%) and placebo or no treatment (SUCRA 65%).

Figure 44. Cumulative rankograms comparing each of the tocolytic drugs for palpitations. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



16. Headaches

Network evidence

The network diagram for headaches from tocolysis is presented in Figure 45. Relative effects from the network meta-analysis of 55 trials (6132 women) suggested that nitric oxide donors (RR 4.20, 95% CI 2.13 to 8.25; moderate-certainty evidence) probably cause headache. There is low-certainty evidence that betamimetics (RR 1.91, 95% CI 1.07 to 3.42) and calcium channel blockers (RR 2.59, 95% CI 1.39 to 4.83) could possibly cause headache as well. COX inhibitors, magnesium sulphate, and oxytocin receptor antagonists are associated with a wide range of effects for this outcome compared with placebo or no treatment. The evidence for the combinations of tocolytics are of very low certainty, hence the effects remain uncertain (Figure 46; Appendix 3).

Figure 45. Network diagram for headache. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

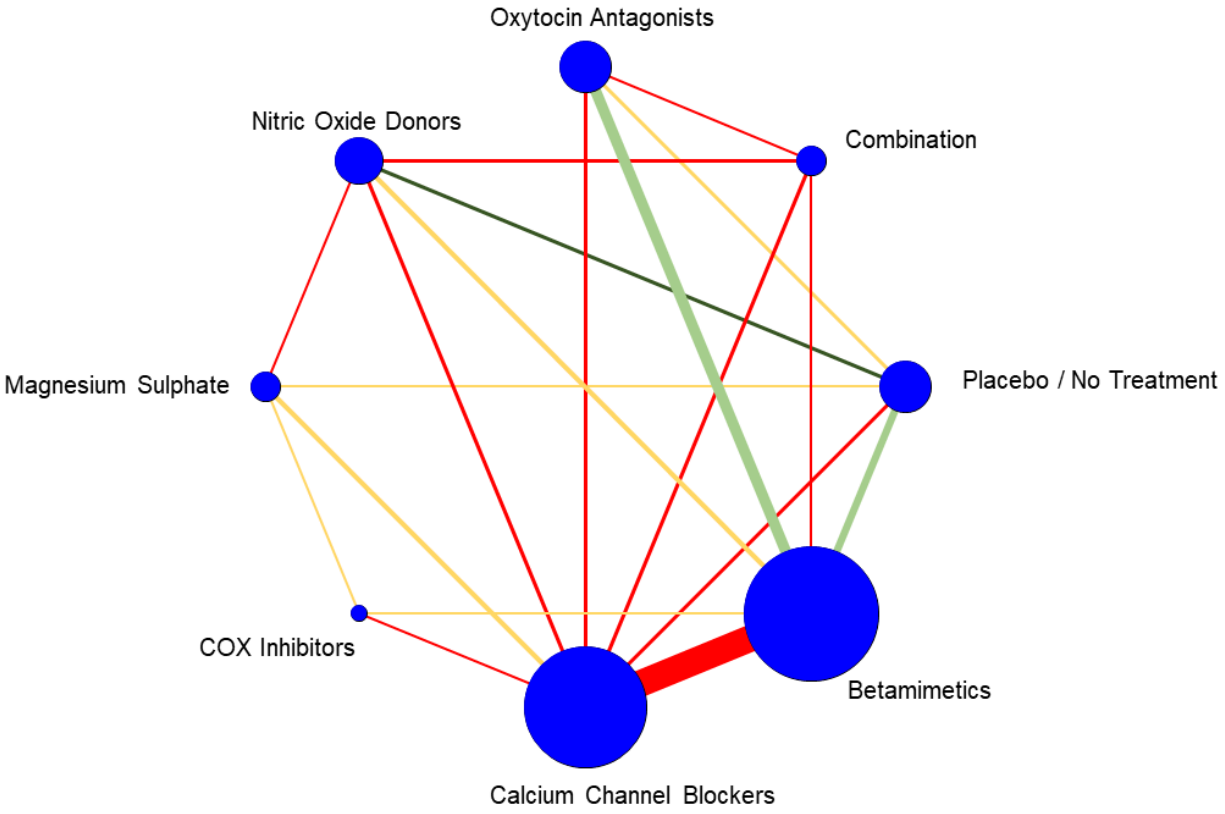
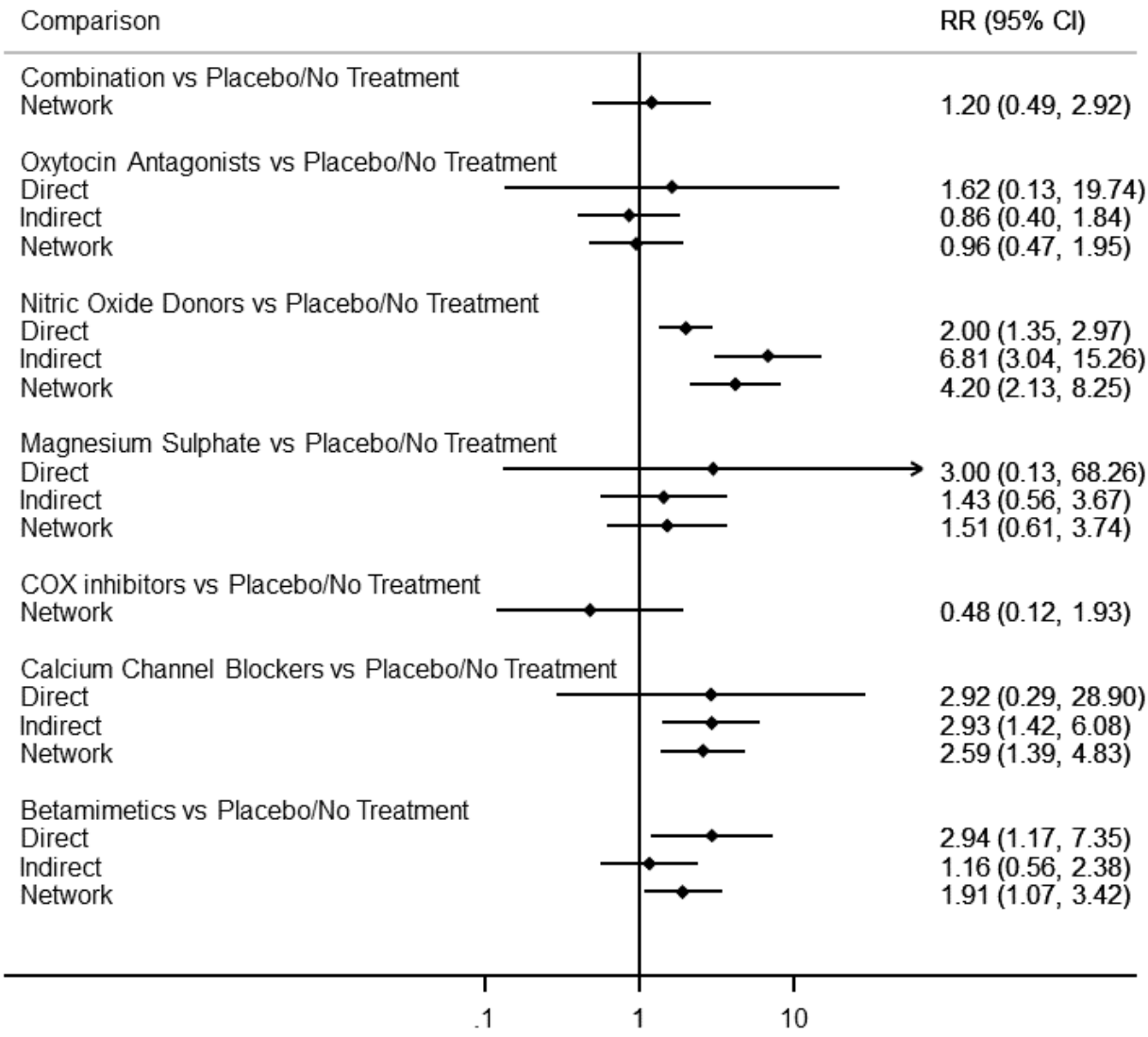


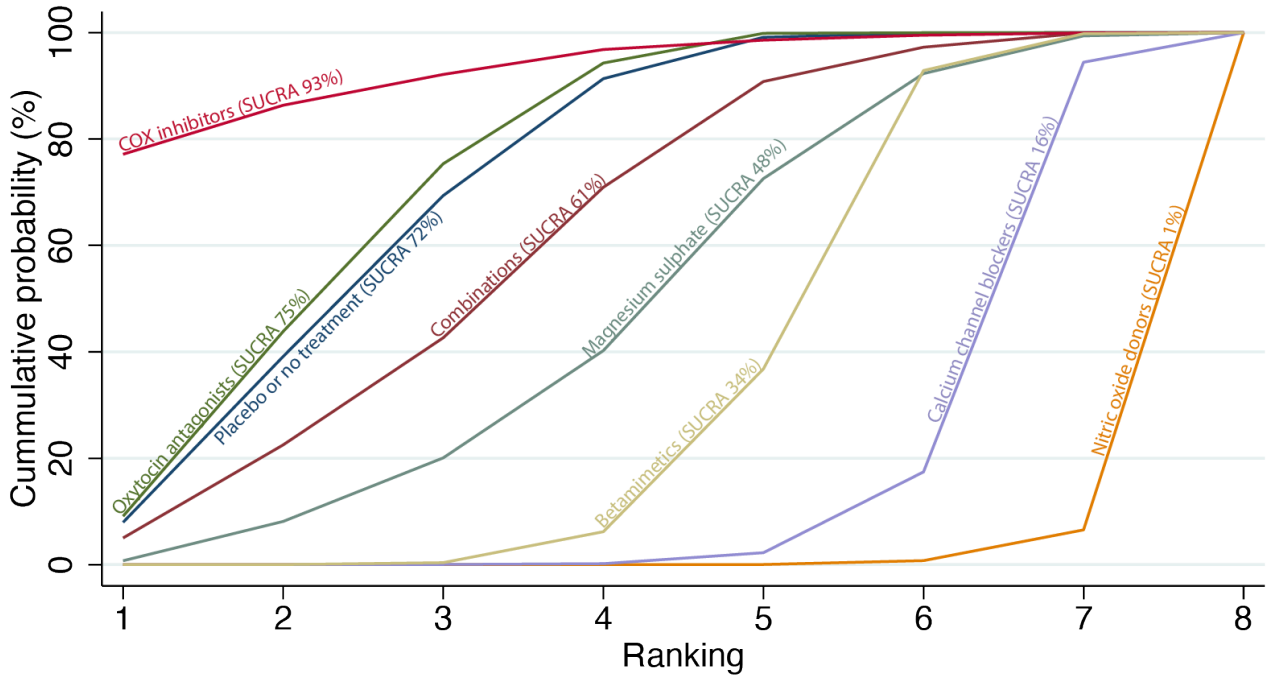
Figure 46. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for headache.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for headache are shown in Figure 47. The lowest ranked tocolytics for this outcome were the nitric oxide donors (SUCRA 1%), calcium channel blockers (SUCRA 16%), and betamimetics (SUCRA 34%).

Figure 47. Cumulative rankograms comparing each of the tocolytic drugs for headache. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



17. Nausea or vomiting

Network evidence

The network diagram for nausea or vomiting from tocolysis is presented in Figure 48. Relative effects from the network meta-analysis of 52 trials (6129 women) suggested that betamimetics probably (RR 1.91, 95% CI 1.25 to 2.91; moderate-certainty evidence) and COX inhibitors possibly (RR 2.54, 95% CI 1.18 to 5.48; low-certainty evidence) cause nausea or vomiting. Low certainty evidence suggests that calcium channel blockers (RR 0.67, 95% CI 0.39 to 1.15), oxytocin receptor antagonists (RR 0.96, 95% CI 0.56 to 1.64), and combinations of tocolytics (RR 1.33, 95% CI 0.69 to 2.54) are associated with a wide range of effects for this outcome compared with placebo or no treatment. The evidence for the magnesium sulphate, and nitric oxide donors, is of very low certainty, hence the effects remain uncertain (Figure 49; Appendix 3).

Figure 48. Network diagram for nausea or vomiting. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

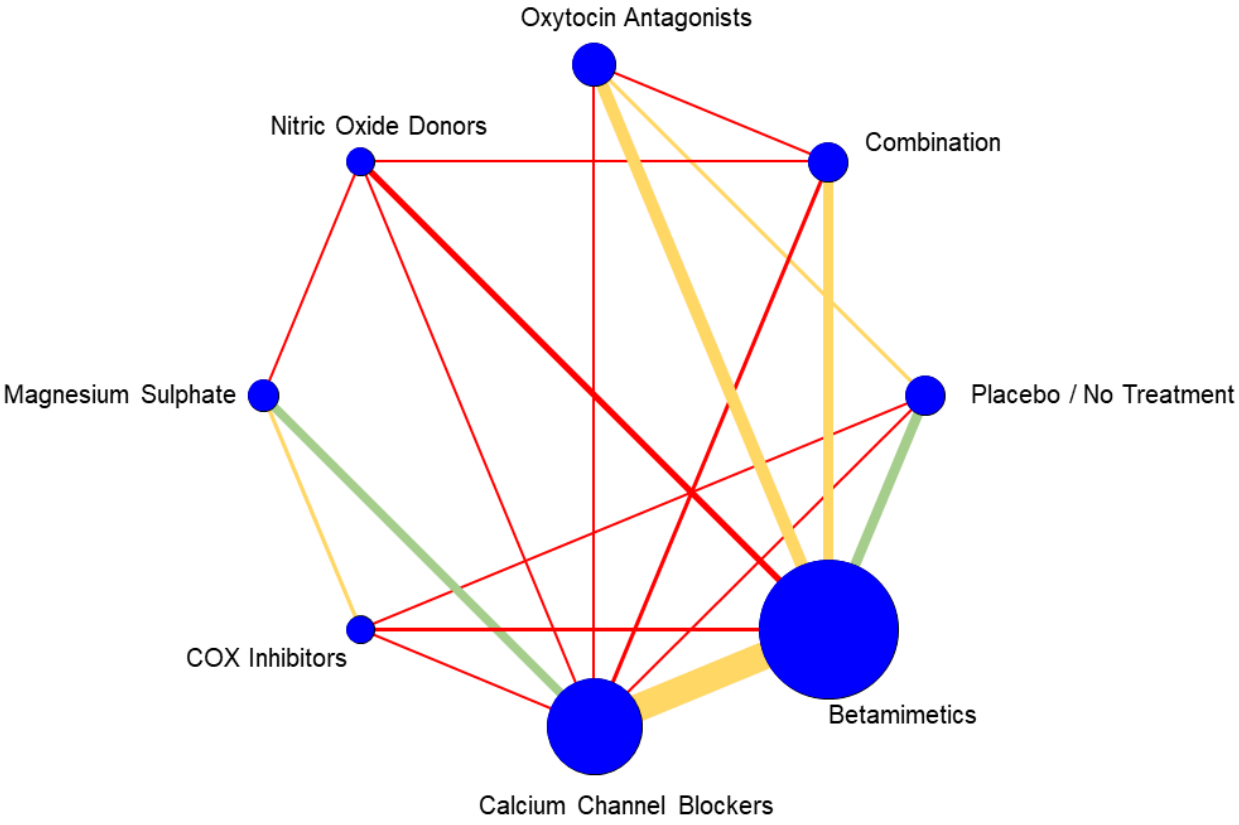
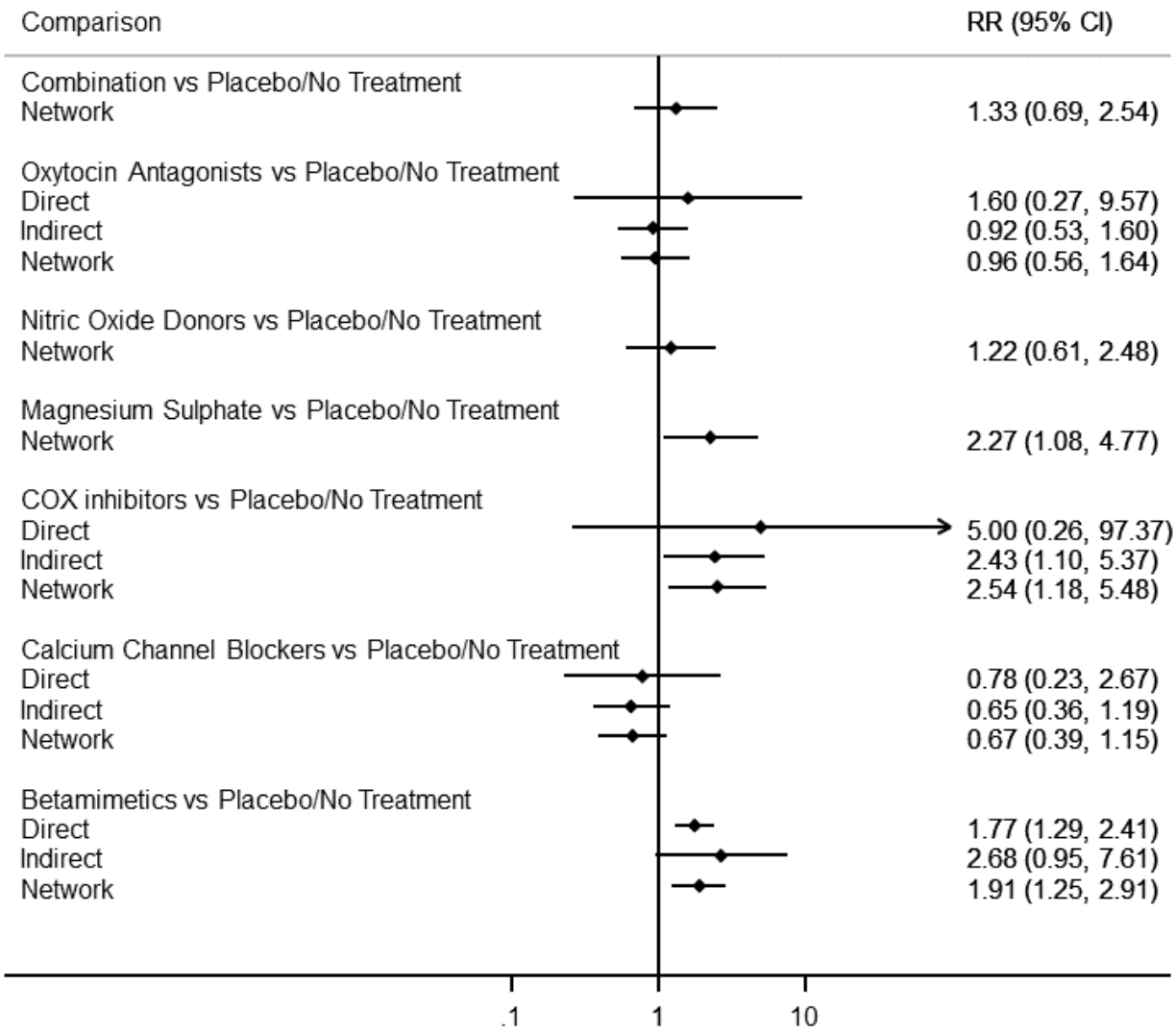


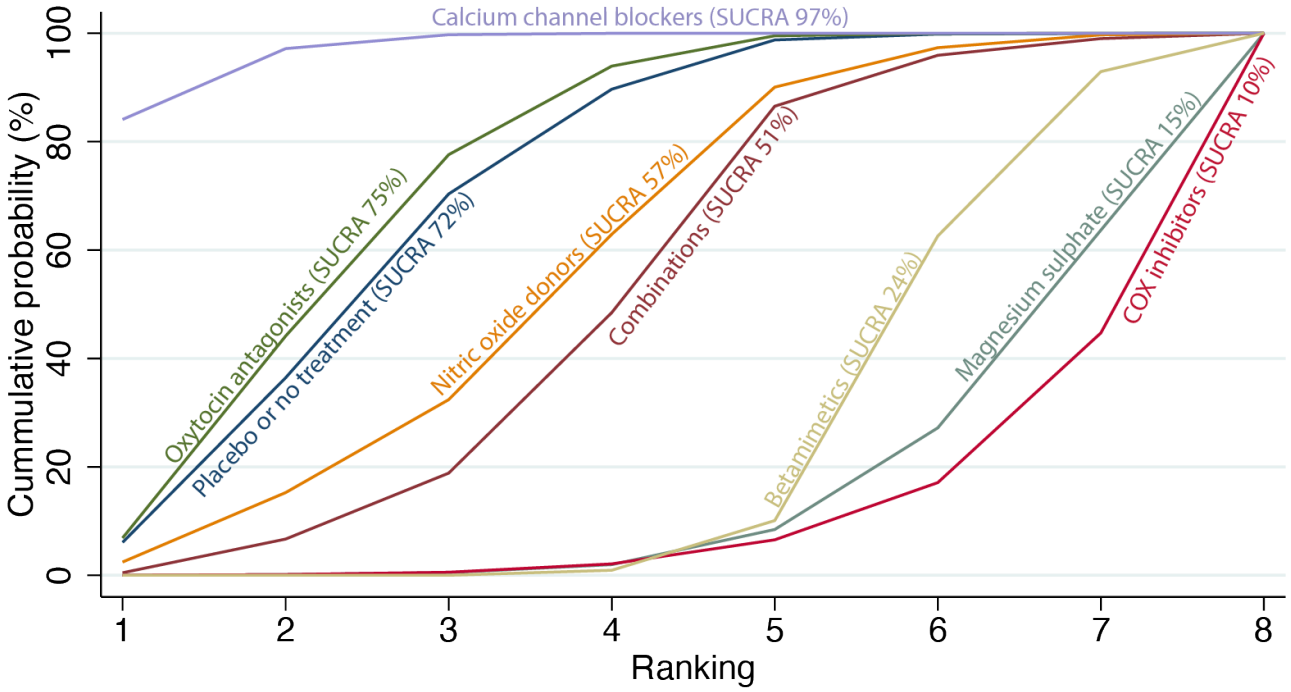
Figure 49. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for nausea or vomiting.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for nausea or vomiting are shown in Figure 50. The lowest ranked tocolytics for this outcome were the COX inhibitors (SUCRA 10%), magnesium sulphate (SUCRA 15%), and betamimetics (SUCRA 24%).

Figure 50. Cumulative rankograms comparing each of the tocolytic drugs for nausea or vomiting. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



18. Tachycardia

Network evidence

The network diagram for tachycardia from tocolysis is presented in Figure 51. Relative effects from the network meta-analysis of 41 trials (4939 women) suggested that betamimetics (RR 3.01, 95% CI 1.17 to 7.71; low-certainty evidence) possibly cause tachycardia. According to low-certainty evidence, oxytocin receptor antagonists (RR 0.23, 95% CI 0.08 to 0.67), and nitric oxide donors (RR 0.16, 95% CI 0.04 to 0.70) are associated with a lower risk of tachycardia compared with placebo or no treatment. COX inhibitors (RR 0.18, 95% CI 0.02 to 1.60) and combinations of tocolytics (RR 1.62, 95% CI 0.49 to 5.31) are associated with a wide range of effects for this outcome compared with placebo or no treatment. The evidence for calcium channel blockers, and magnesium sulphate is of very low certainty, hence the effects remain uncertain (Figure 52; Appendix 3).

Figure 51. Network diagram for tachycardia. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

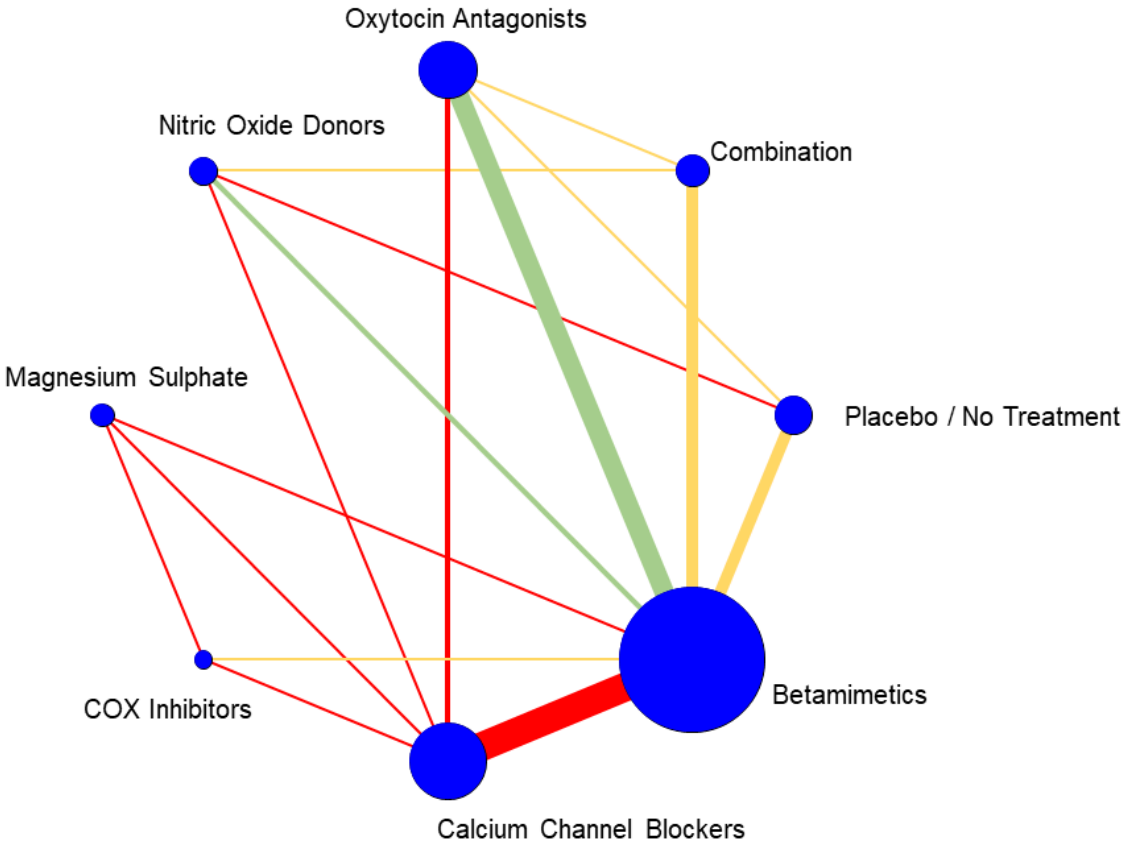
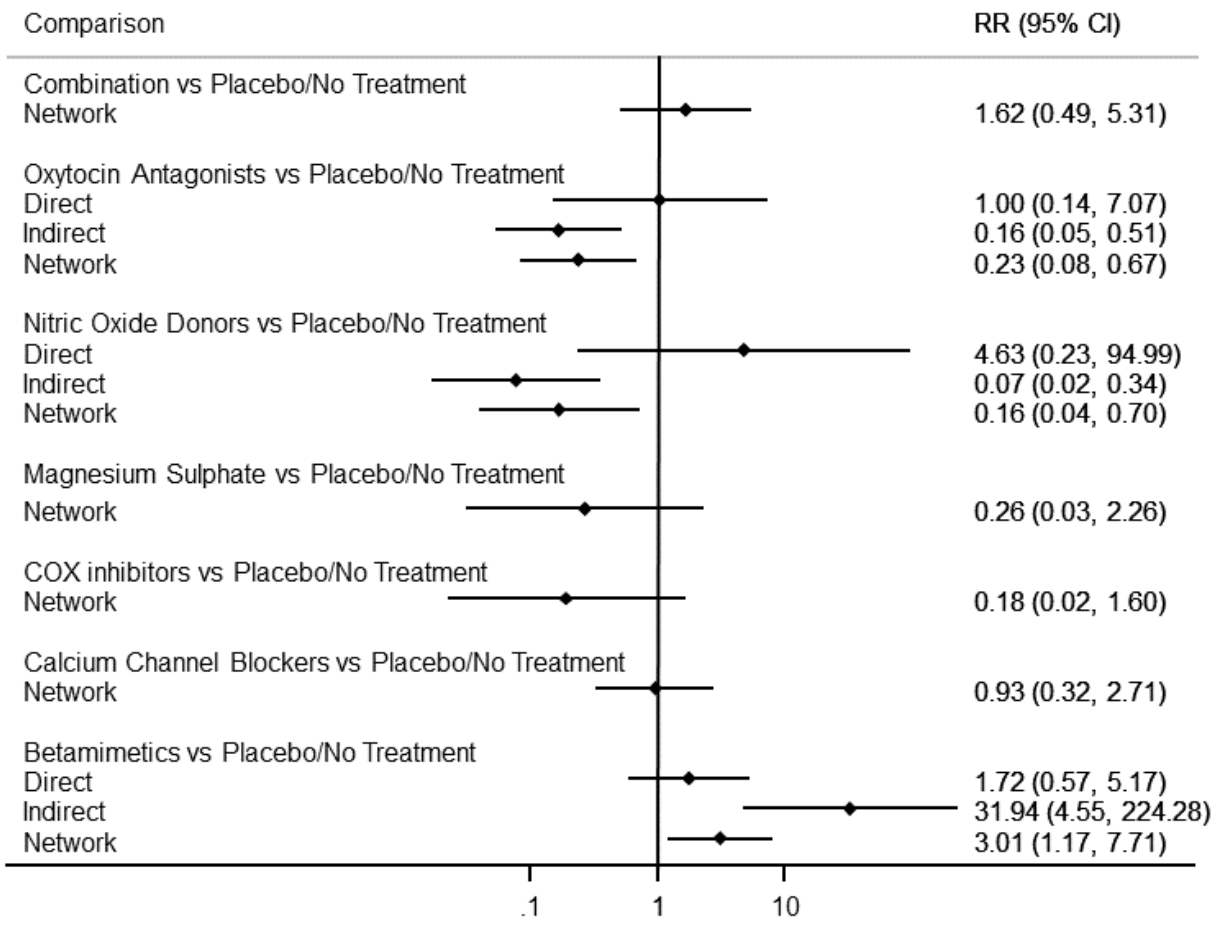


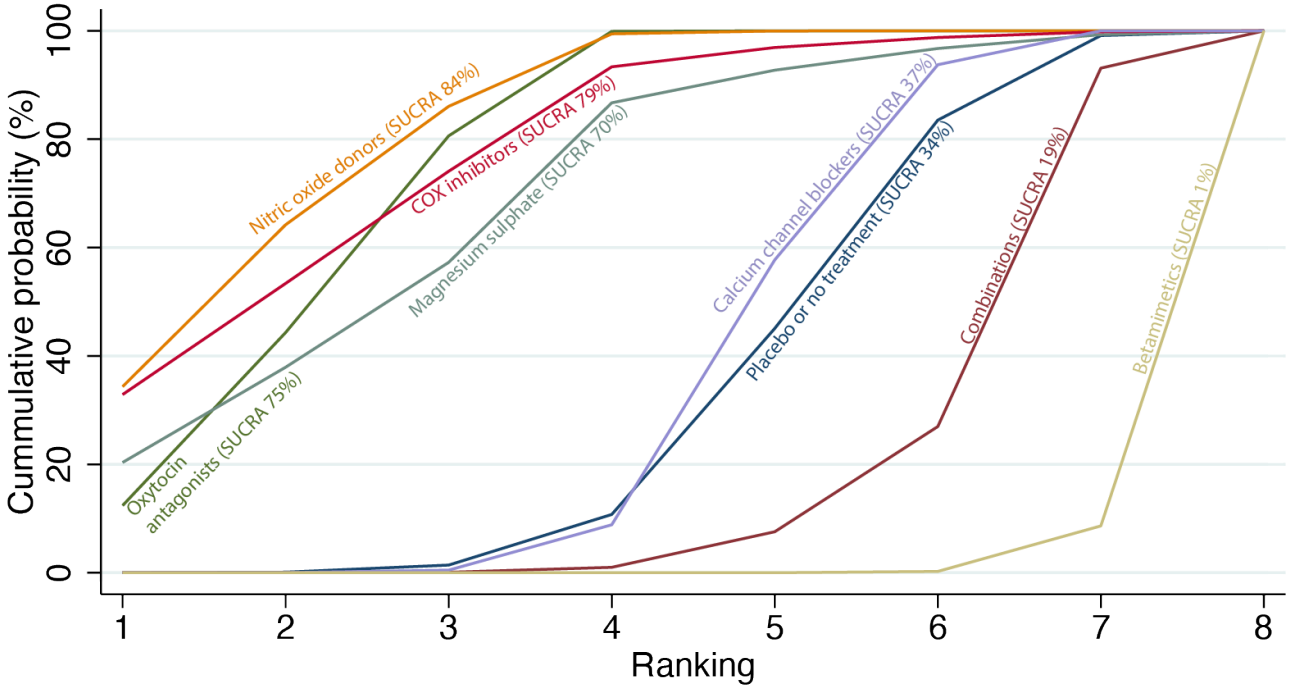
Figure 52. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for tachycardia.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for tachycardia are shown in Figure 53. The lowest ranked tocolytics for this outcome were betamimetics (SUCRA 1%), and combinations of tocolytics (SUCRA 19%). Highest ranked were the nitric oxide donors (SUCRA 84%), COX inhibitors (SUCRA 79%), and oxytocin receptor antagonists (SUCRA 75%).

Figure 53. Cumulative rankograms comparing each of the tocolytic drugs for tachycardia. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.

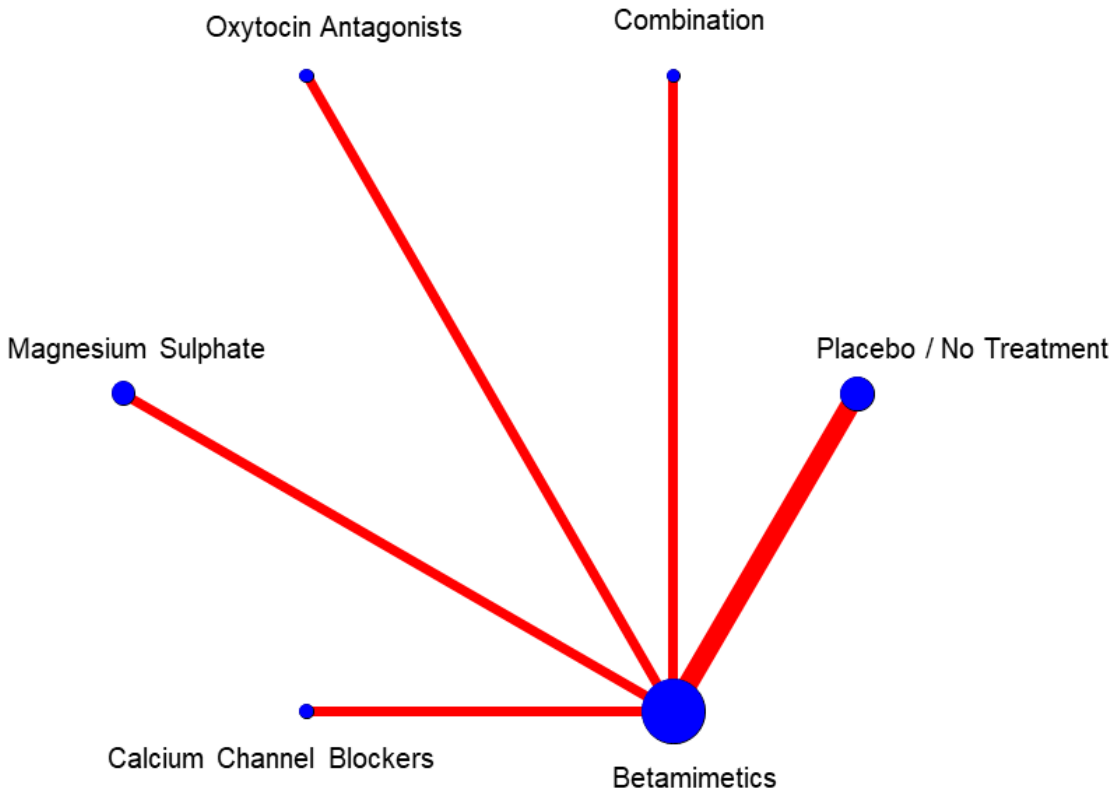


19. Maternal cardiac arrhythmias

Network evidence

The network diagram for maternal cardiac arrhythmias from tocolysis is presented in Figure 54. Due to insufficient trials reporting this outcome (10 trials, 1661 women), network meta-analysis was not possible, and so were unable to produce network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis (Data and analyses). Four trials compared betamimetics to placebo or no treatment resulting in very low-certainty evidence, so the effects for this comparison remain uncertain (Analysis 1.19; Appendix 3). There is no direct evidence comparing COX inhibitors, calcium channel blockers, magnesium sulphate, oxytocin receptor antagonists, nitric oxide donors, or combinations of tocolytics to placebo or no treatment (Appendix 3).

Figure 54. Network diagram for maternal cardiac arrhythmias. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.



20. Maternal hypotension

Network evidence

The network diagram for maternal hypotension from tocolysis is presented in Figure 55. Relative effects from low-certainty evidence from the network meta-analysis of 44 trials (4998 women) suggested that betamimetics (RR 2.51, 95% CI 0.58 to 10.89), oxytocin receptor antagonists (RR 0.95, 95% CI 0.18 to 5.06), and nitric oxide donors (RR 1.95, 95% CI 0.50 to 7.53) are associated with a wide range of effects for this outcome compared with placebo or no treatment. The evidence for COX inhibitors, calcium channel blockers, magnesium sulphate, and combinations of tocolytics is of very low certainty, hence the effects remain uncertain (Figure 56; Appendix 3).

Figure 55. Network diagram for hypotension. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

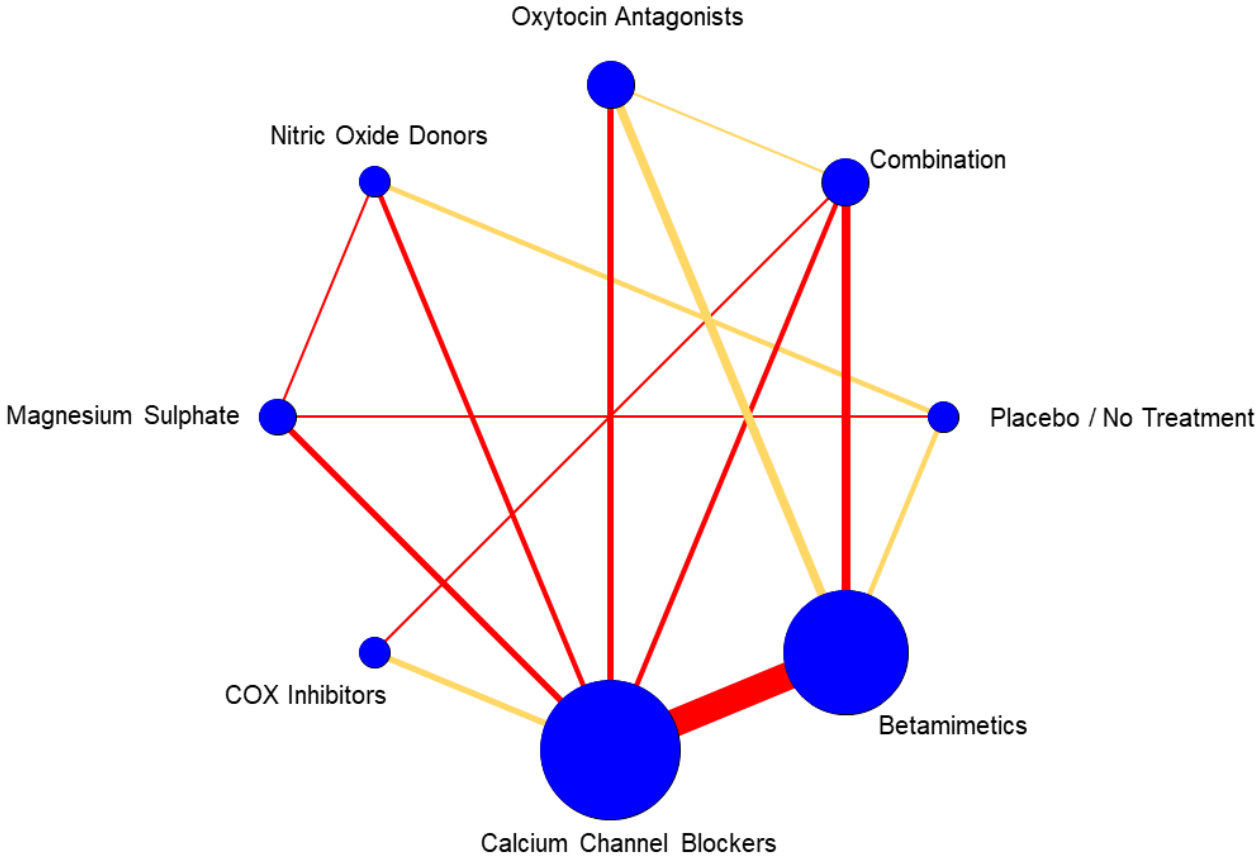
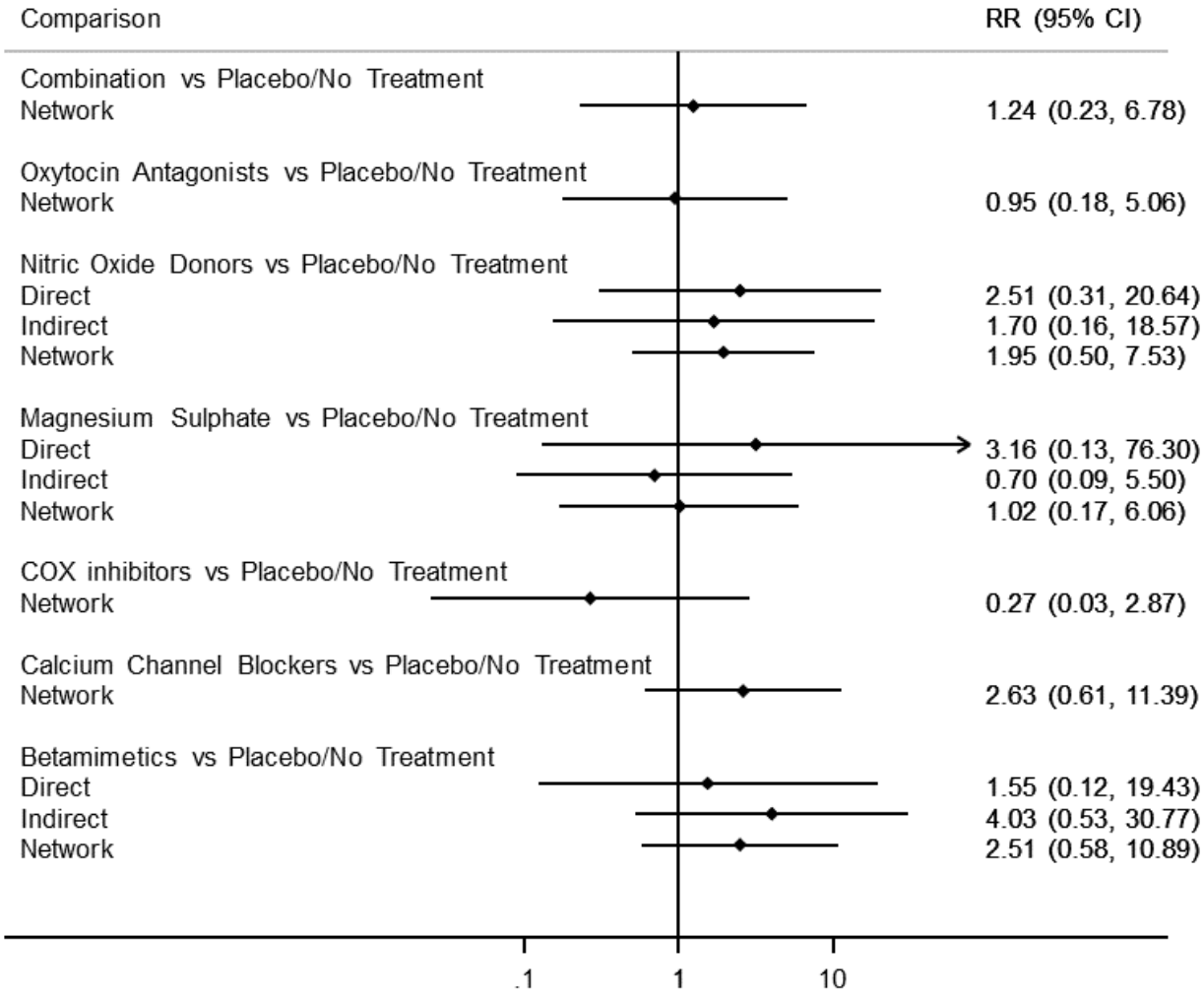


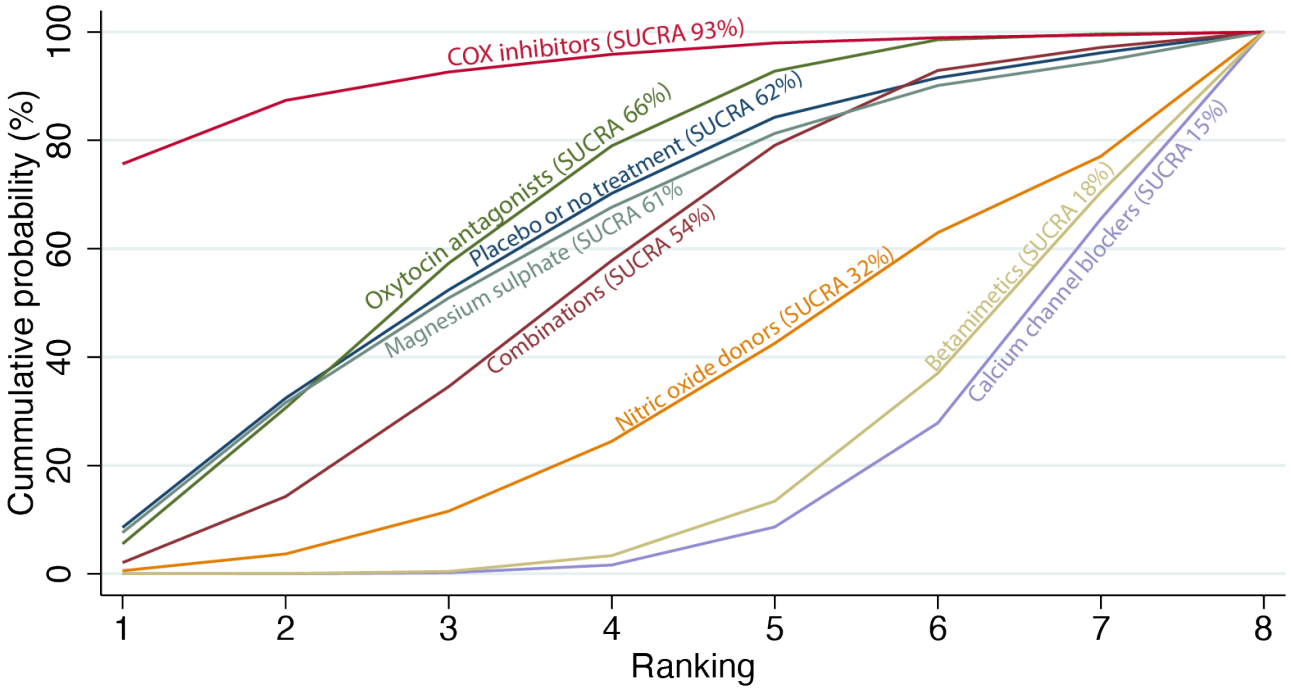
Figure 56. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for hypotension.



Tocolytic ranking

Cumulative probabilities for each tocolytic being at each possible rank for maternal hypotension are shown in Figure 57. The lowest ranked tocolytics for this outcome were calcium channel blockers (SUCRA 15%) and betamimetics (SUCRA 18%).

Figure 57. Cumulative rankograms comparing each of the tocolytic drugs for hypotension. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



21. Perinatal death

Network evidence

The network diagram for the outcome of perinatal death, including stillbirths and neonatal deaths before 28 days, is presented in Figure 58. Relative effects from the network meta-analysis of 79 trials (9547 babies) suggested that all tocolytics are associated with a wide range of effects for perinatal death when compared with placebo or no treatment as there were only few events (Figure 59; Appendix 3).

Figure 58. Network diagram for perinatal death. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

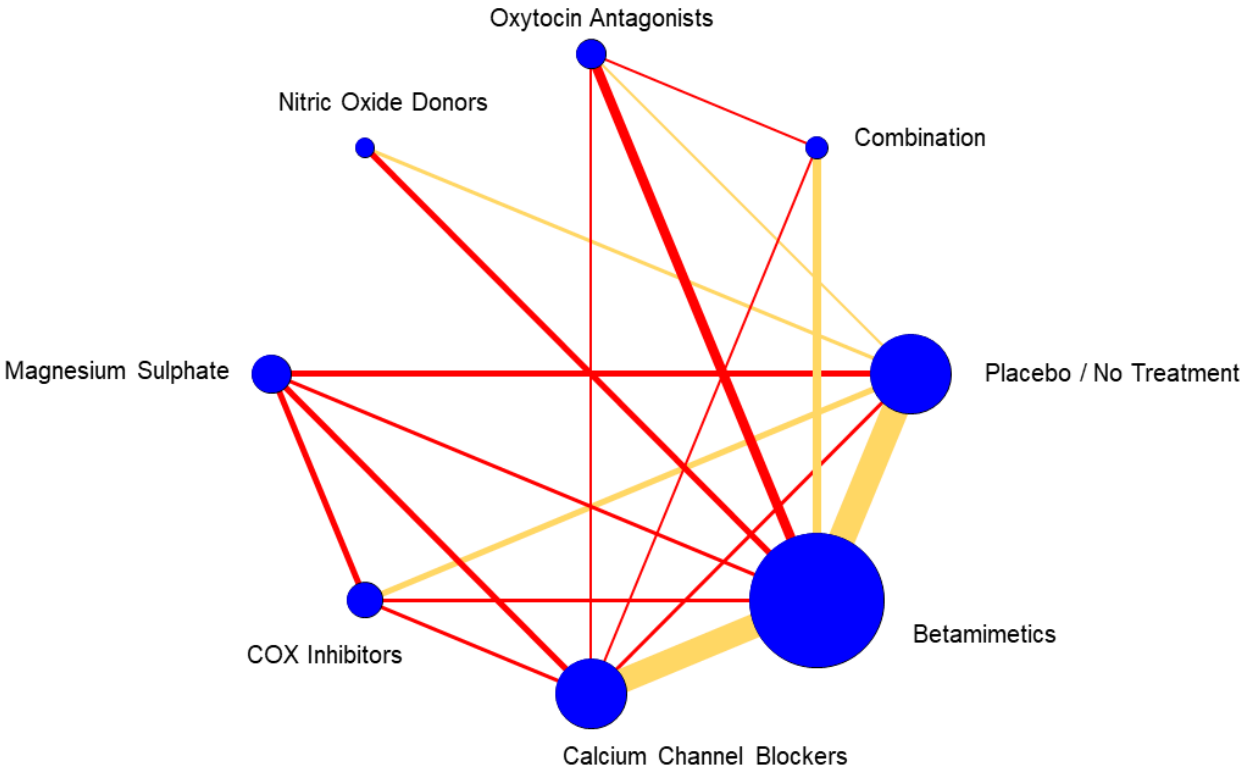
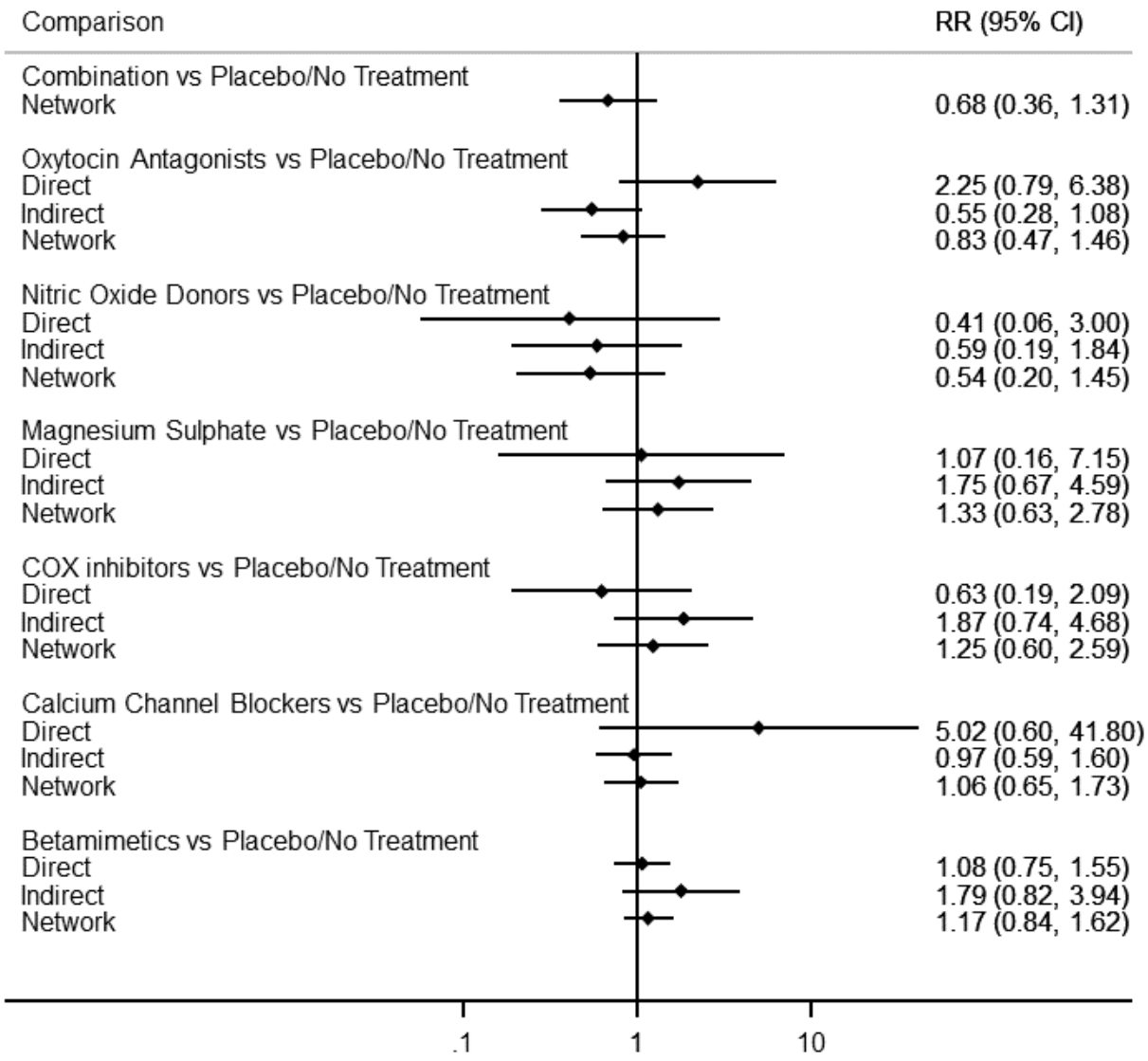


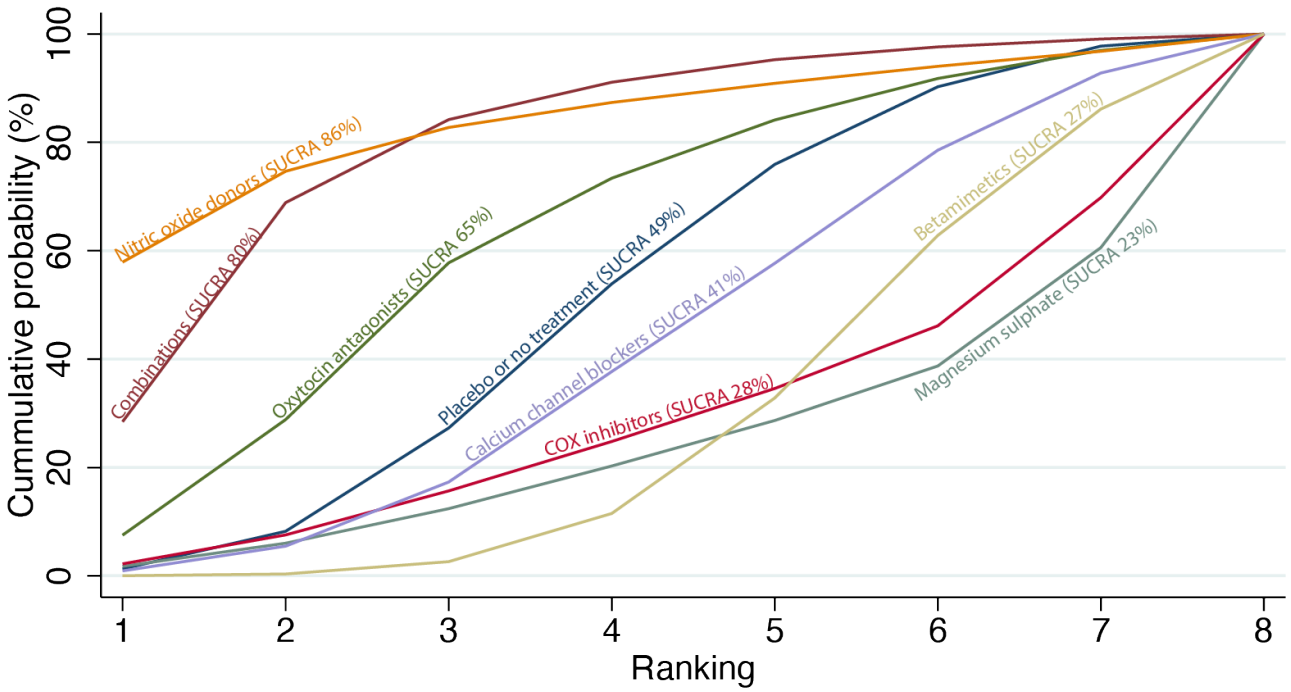
Figure 59. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for perinatal death.



Tocolytic ranking

The cumulative probabilities for each agent being at each possible rank for perinatal death are shown in Figure 60. The ranking for tocolytics was not clear for this outcome due to few events.

Figure 60. Cumulative rankograms comparing each of the tocolytic drugs for perinatal death. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



22. Stillbirth

Network evidence

The network diagram for the outcome of stillbirth, is presented in Figure 61. Relative effects from the network meta-analysis of 55 trials (6736 babies) suggested that all tocolytics are associated with a wide range of effects for stillbirth when compared with placebo or no treatment as there were few events (Figure 62; Appendix 3). There were no studies involving combinations of tocolytics.

Figure 61. Network diagram for stillbirth. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

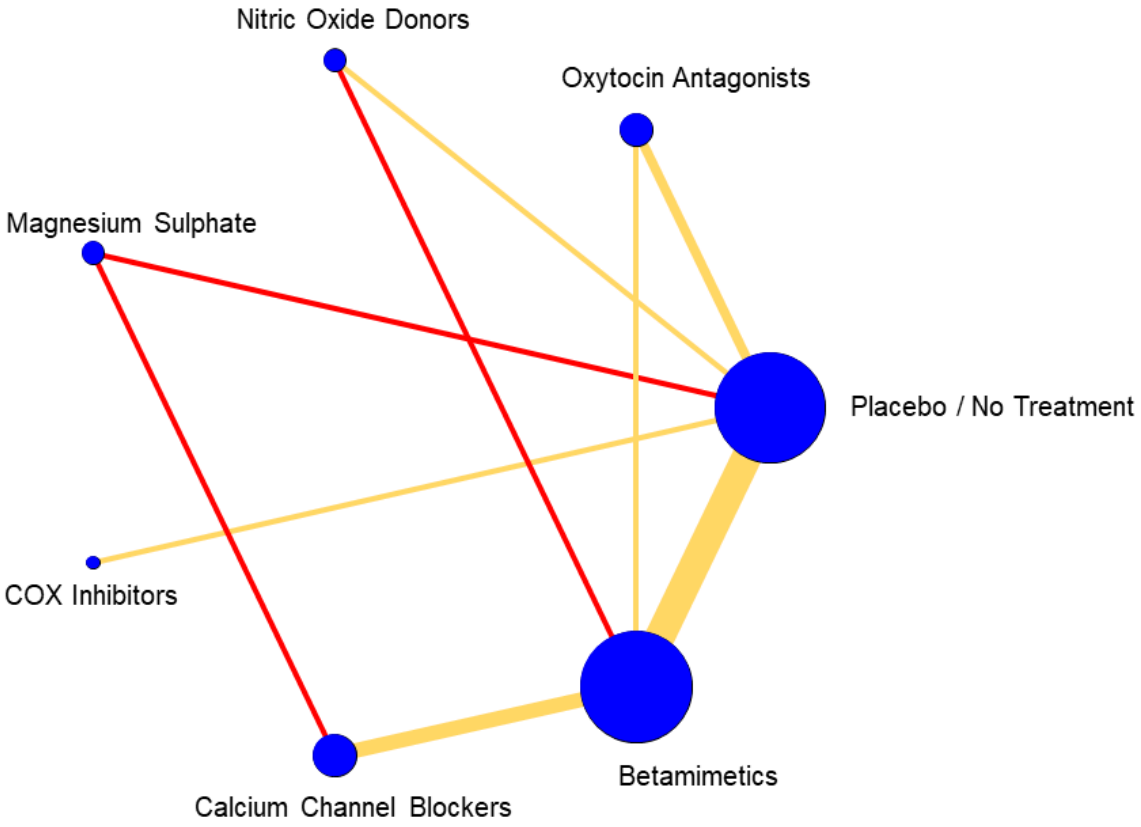
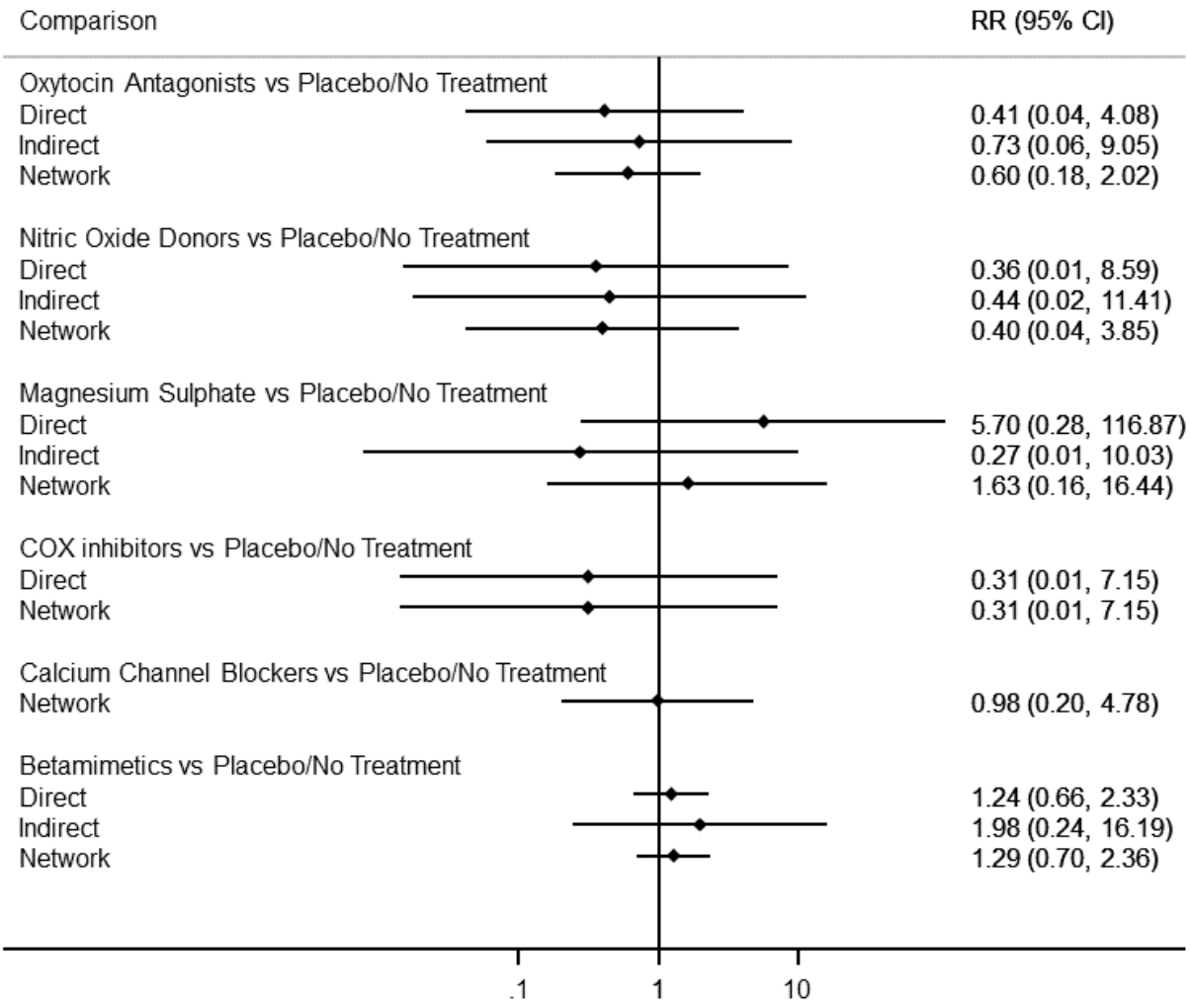


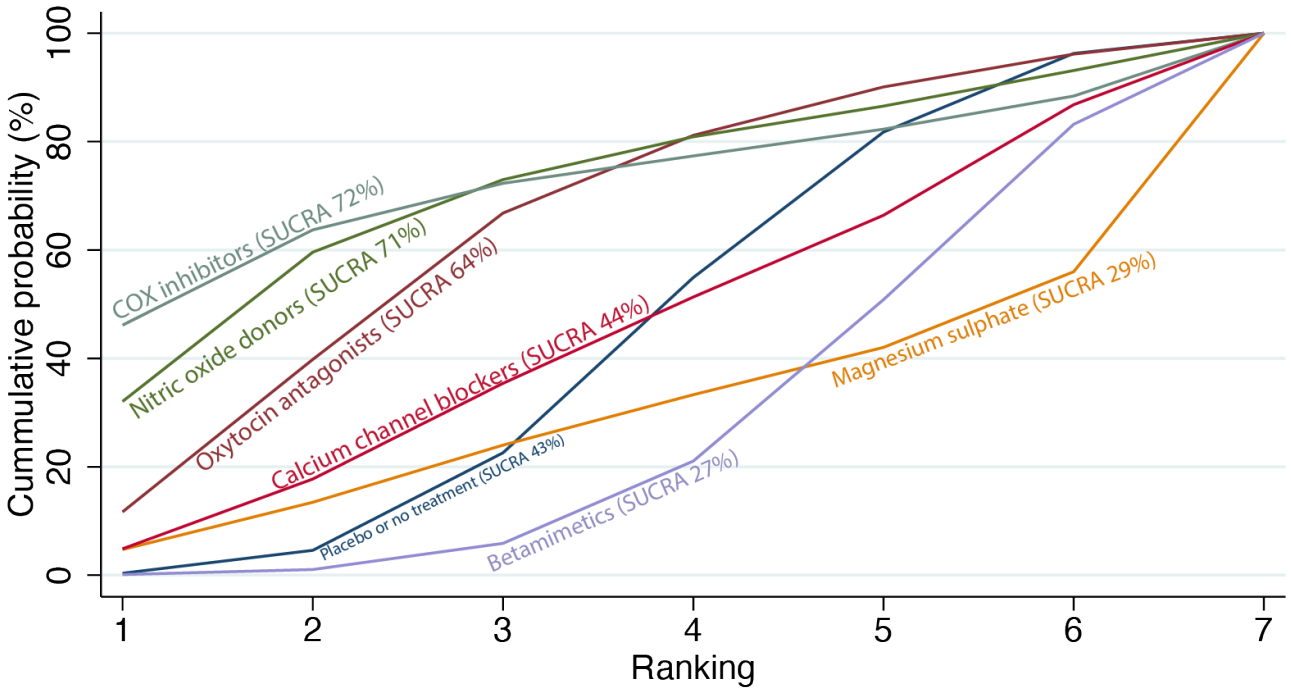
Figure 62. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for stillbirth.



Tocolytic ranking

The cumulative probabilities for each agent being at each possible rank for stillbirth are shown in Figure 63. The ranking for tocolytics was not clear for this outcome due to few events.

Figure 63. Cumulative rankograms comparing each of the tocolytic drugs for stillbirth. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.

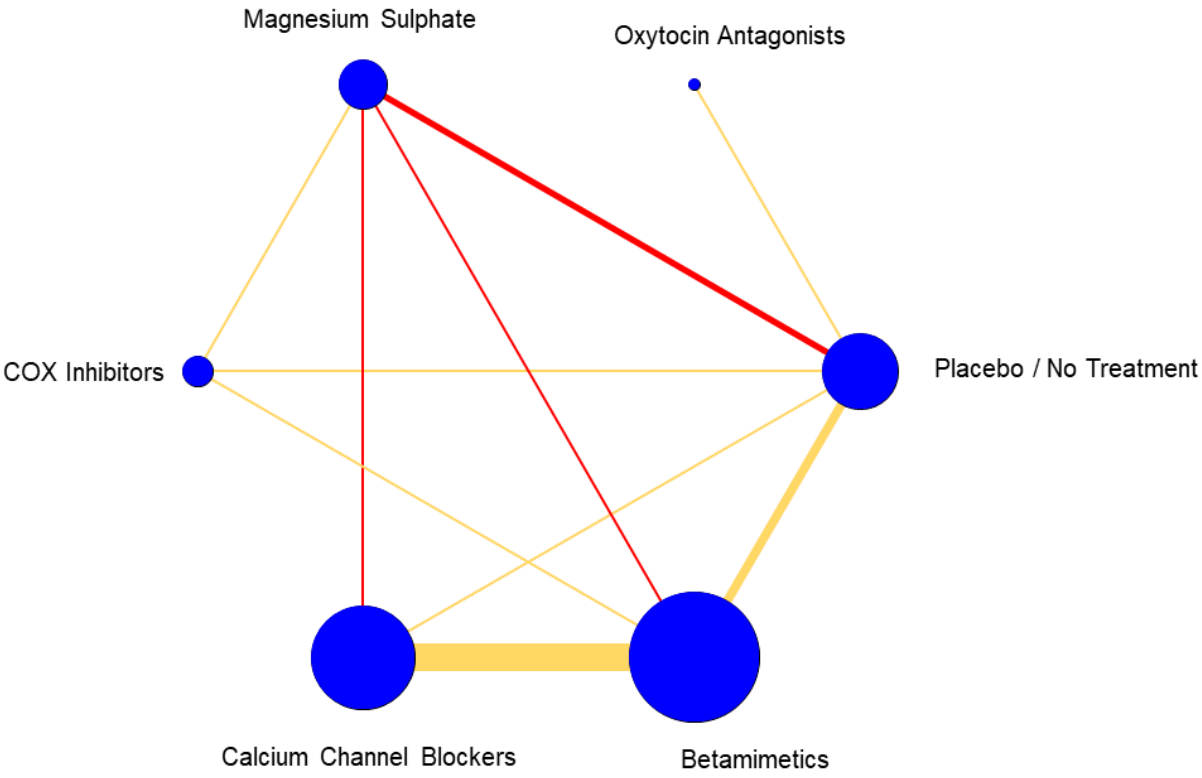


23. Neonatal death before 7 days

Network evidence

The network diagram for neonatal death before 7 days is presented in Figure 64. Due to the small number of events in the trials reporting this outcome (40 trials, 4501 babies), network meta-analysis was not possible, and so we were unable to produce network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis (Data and analyses). Direct evidence between betamimetics (Analysis 1.23), COX inhibitors (Analysis 2.23), calcium channel blockers (,Analysis 3.23) magnesium sulphate (Analysis 4.23), and oxytocin receptor antagonists (Analysis 5.23) versus placebo or no treatment is available, resulting in a wide range of effects (Appendix 3). There is no direct evidence comparing nitric oxide donors, and combinations of tocolytics to placebo or no treatment (Appendix 3).

Figure 64. Network diagram for neonatal death before 7 days. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.



24. Neurodevelopmental morbidity

Network evidence

The network diagram for neurodevelopmental morbidity is presented in Figure 65. Relative effects from low-certainty evidence from the network meta-analysis of 41 trials (6378 babies) suggested that calcium channel blockers (RR 0.51, 95% CI 0.30 to 0.85; low-certainty evidence) possibly reduce the risk of neurodevelopmental morbidity. Betamimetics (RR 0.86, 95% CI 0.59 to 1.25; low-certainty evidence), oxytocin receptor antagonists (RR 0.74, 95% CI 0.47 to 1.16; moderate-certainty evidence), and nitric oxide donors (RR 0.39, 95% CI 0.12 to 1.32; low-certainty evidence) are associated with a wide range of effects for this outcome compared with placebo or no treatment. The evidence for COX inhibitors, magnesium sulphate, and combinations of tocolytics is of very low certainty, hence the effects remain uncertain (Figure 66; Appendix 3).

Figure 65. Network diagram for neurodevelopmental morbidity. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

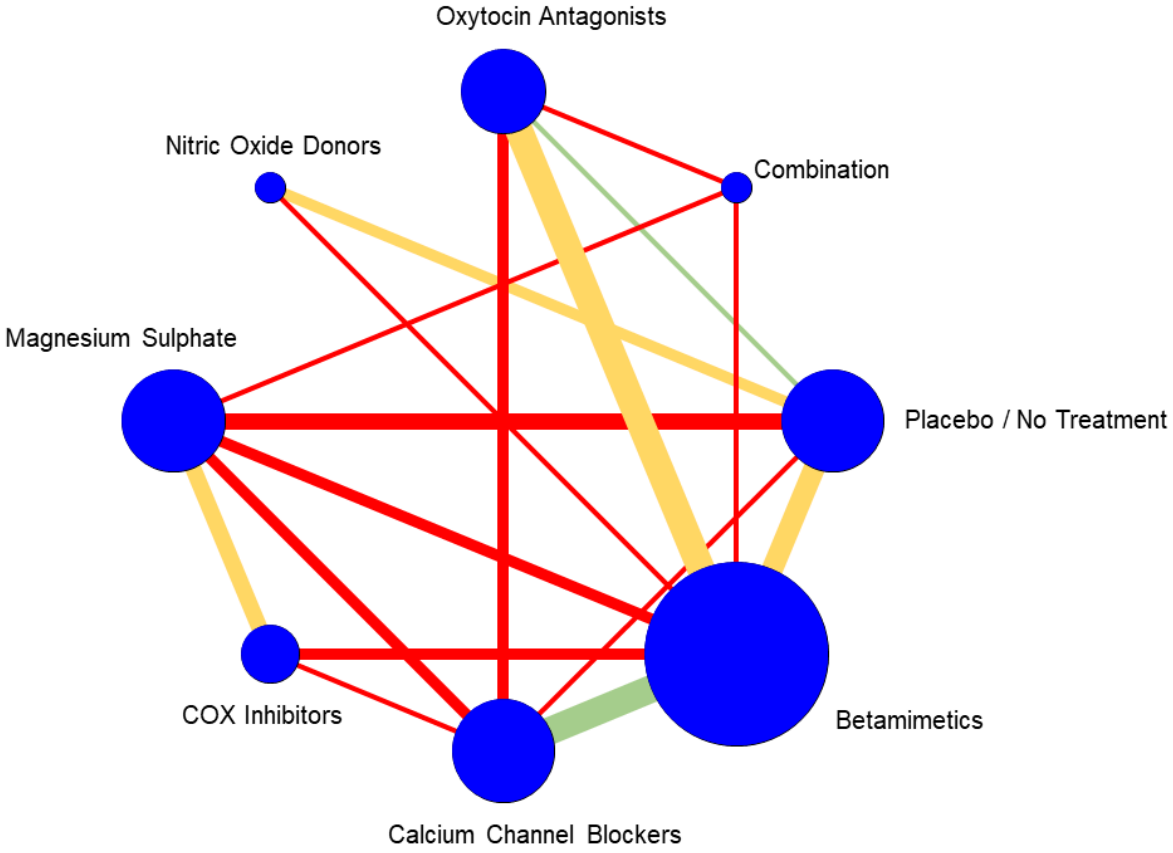
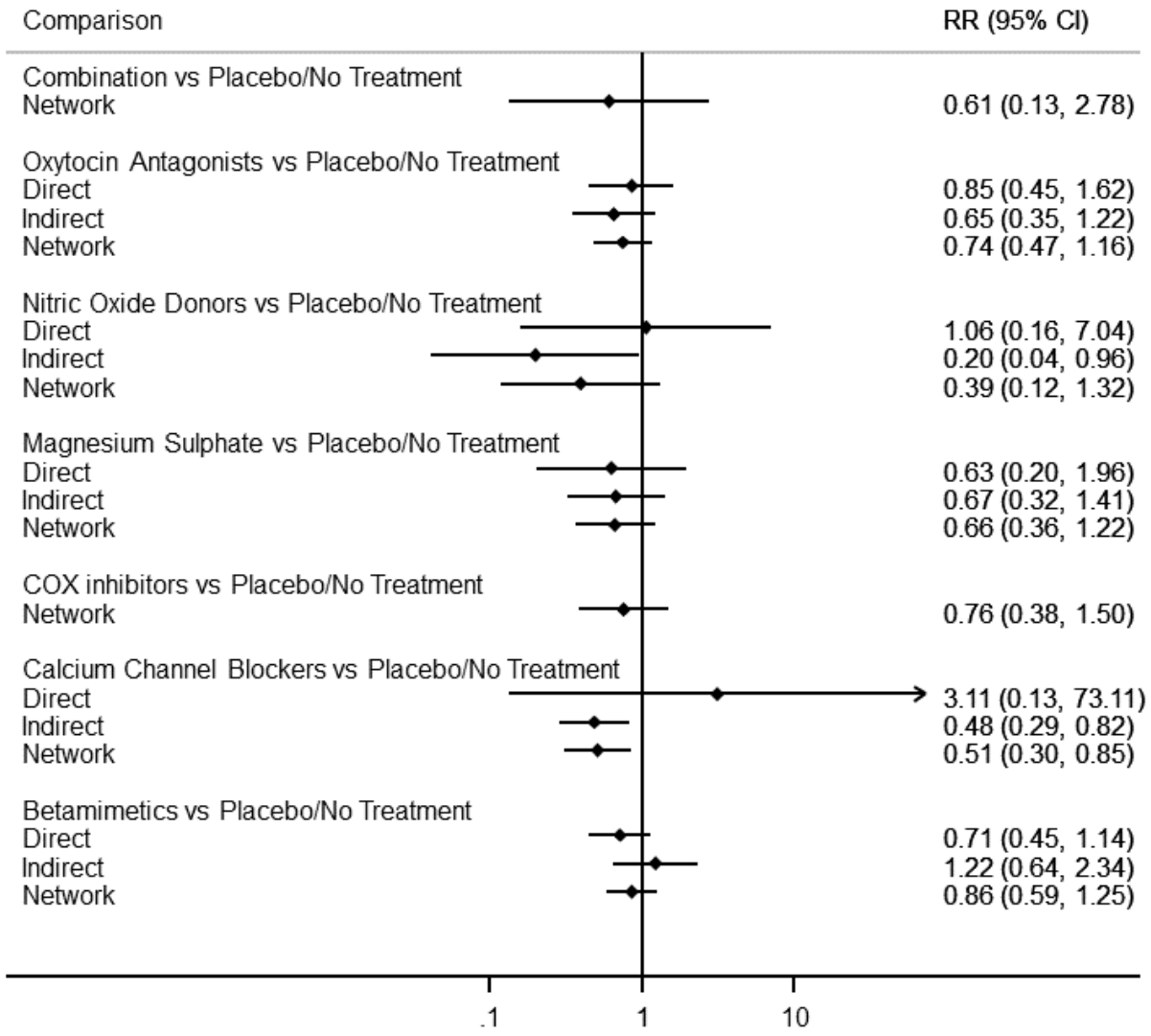


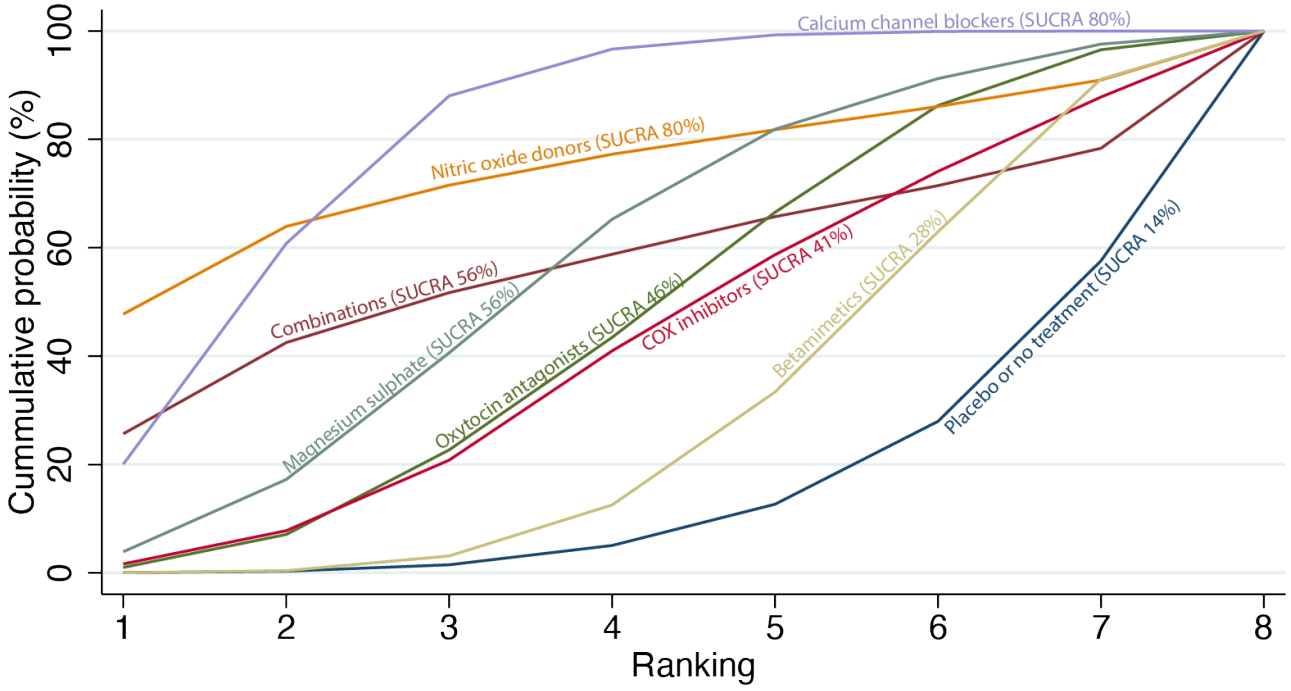
Figure 66. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for neurodevelopmental morbidity.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for neurodevelopmental morbidity are shown in Figure 67. The highest ranked tocolytics for this outcome were the calcium channel blockers (SUCRA 80%), and nitric oxide donors (SUCRA 80%), meanwhile placebo or no treatment was ranked the lowest (SUCRA 14%).

Figure 67. Cumulative rankograms comparing each of the tocolytic drugs for neurodevelopmental morbidity. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



25. Gastrointestinal morbidity

Network evidence

The network diagram for gastrointestinal morbidity is presented in Figure 68. Relative effects from low certainty evidence from the network meta-analysis of 32 trials (4549 babies) suggested that COX inhibitors (RR 1.12, 95% CI 0.47 to 2.64), oxytocin receptor antagonists (RR 0.38, 95% CI 0.12 to 1.22), and nitric oxide donors (RR 0.88, 95% CI 0.29 to 2.71) are associated with a wide range of effects for this outcome compared with placebo or no treatment. The evidence for betamimetics, calcium channel blockers, magnesium sulphate, and combinations of tocolytics is of very low certainty, hence the effects remain uncertain (Figure 69; Appendix 3).

Figure 68. Network diagram for gastrointestinal morbidity. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

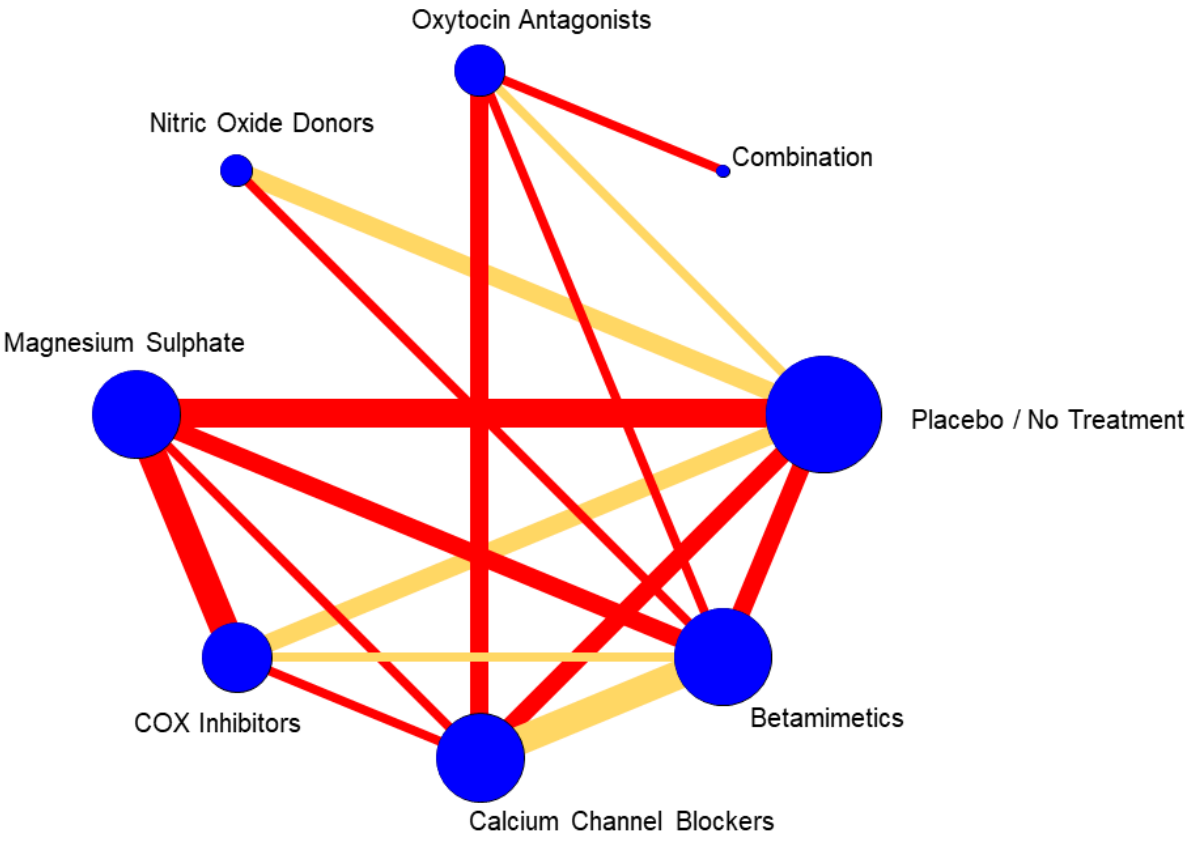
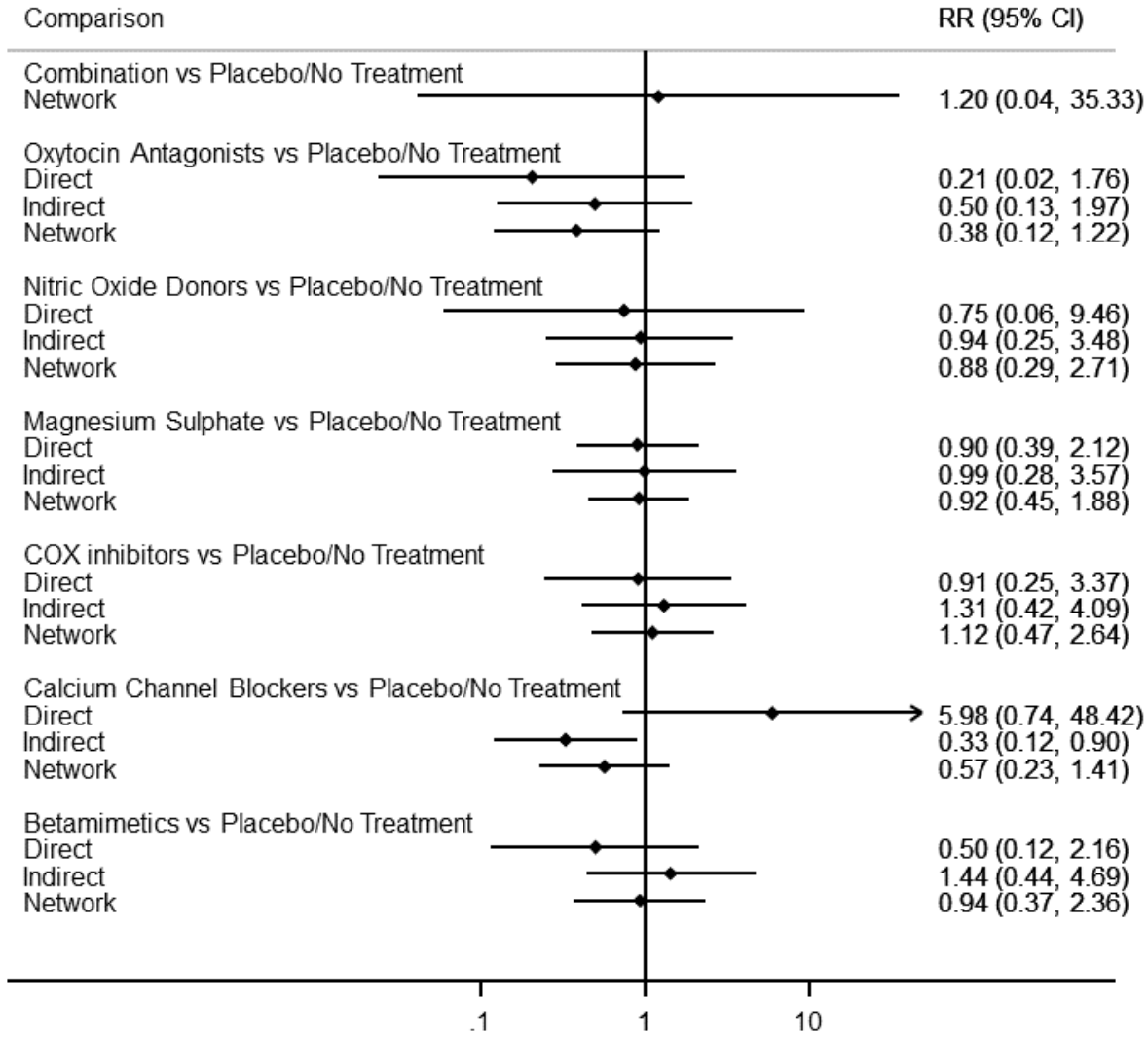


Figure 69. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for gastrointestinal morbidity.

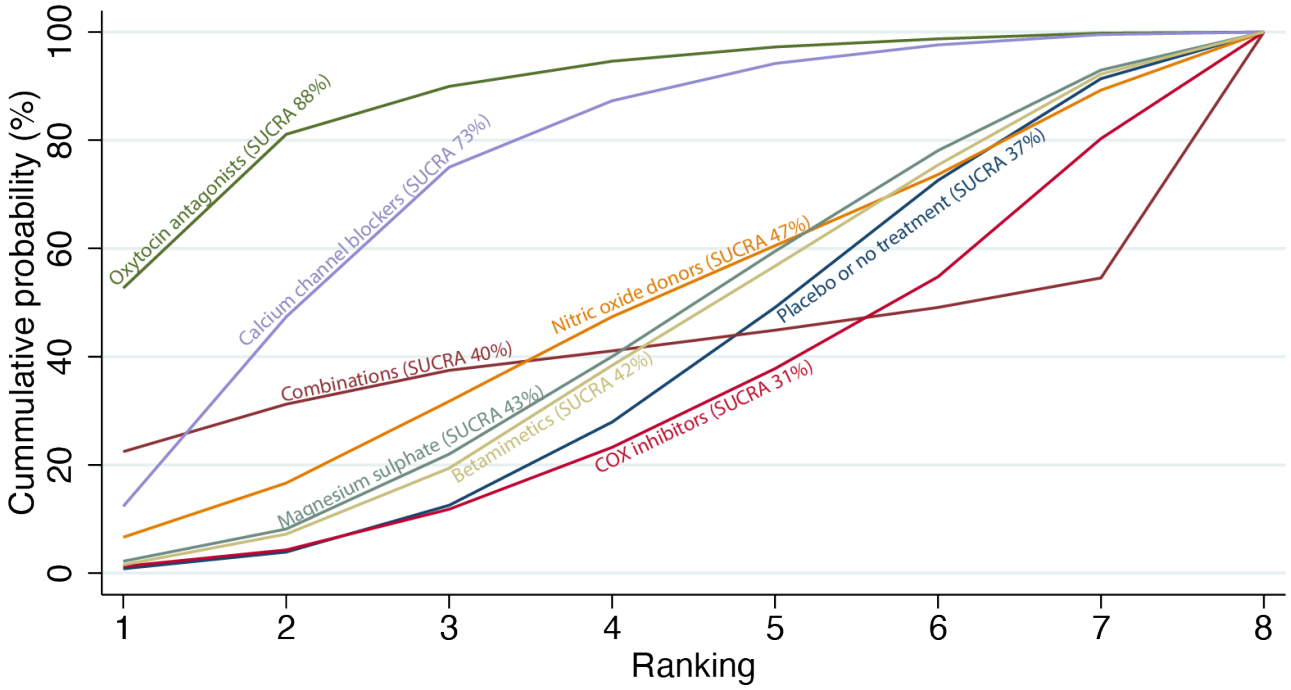


Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for gastrointestinal morbidity are shown in Figure 70.

The highest ranked tocolytics for this outcome were the oxytocin receptor antagonists (SUCRA 88%), and the calcium channel blockers (SUCRA 73%). COX inhibitors (SUCRA 31%), and placebo or no treatment (SUCRA 37%) were ranked the lowest.

Figure 70. Cumulative rankograms comparing each of the tocolytic drugs for gastrointestinal morbidity. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



26. Respiratory morbidity

Network evidence

The network diagram for respiratory morbidity is presented in Figure 71. Relative effects of from the network meta-analysis of 60 trials (8091 babies) suggested that calcium channel blockers (RR 0.68, 95% CI 0.53 to 0.88; low-certainty evidence) possibly reduce the risk of respiratory morbidity, meanwhile betamimetics (RR 0.95, 95% CI 0.81 to 1.13; moderate-certainty evidence) probably make little to no difference. COX inhibitors (RR 0.94, 95% CI 0.70 to 1.28; low-certainty evidence), magnesium sulphate (RR 0.94, 95% CI 0.72 to 1.23; low-certainty evidence), and oxytocin receptor antagonists (RR 1.07, 95% CI 0.86 to 1.33; moderate-certainty evidence) are associated with a wide range of effects for this outcome compared with placebo or no treatment. The evidence for nitric oxide donors and combinations of tocolytics is of very low certainty, hence the effects remain uncertain (Figure 72; Appendix 3).

Figure 71. Network diagram for respiratory morbidity. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

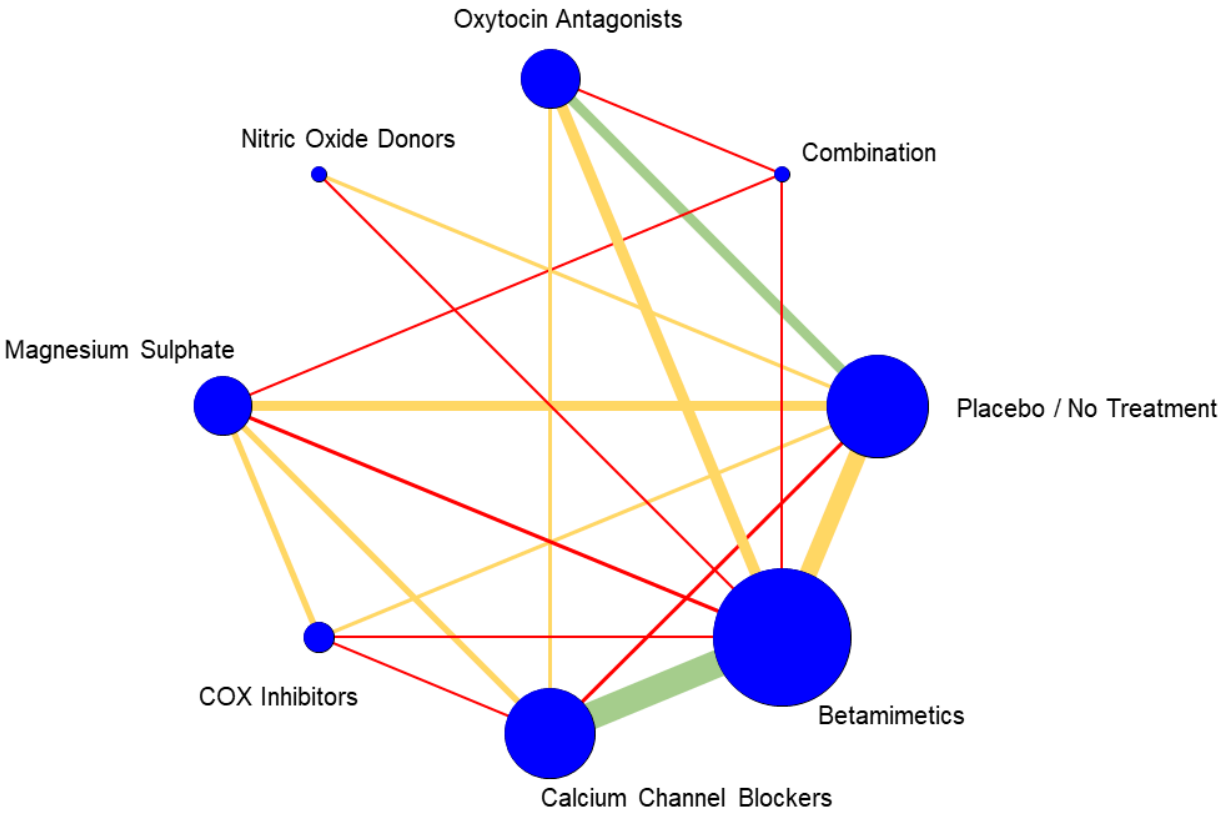
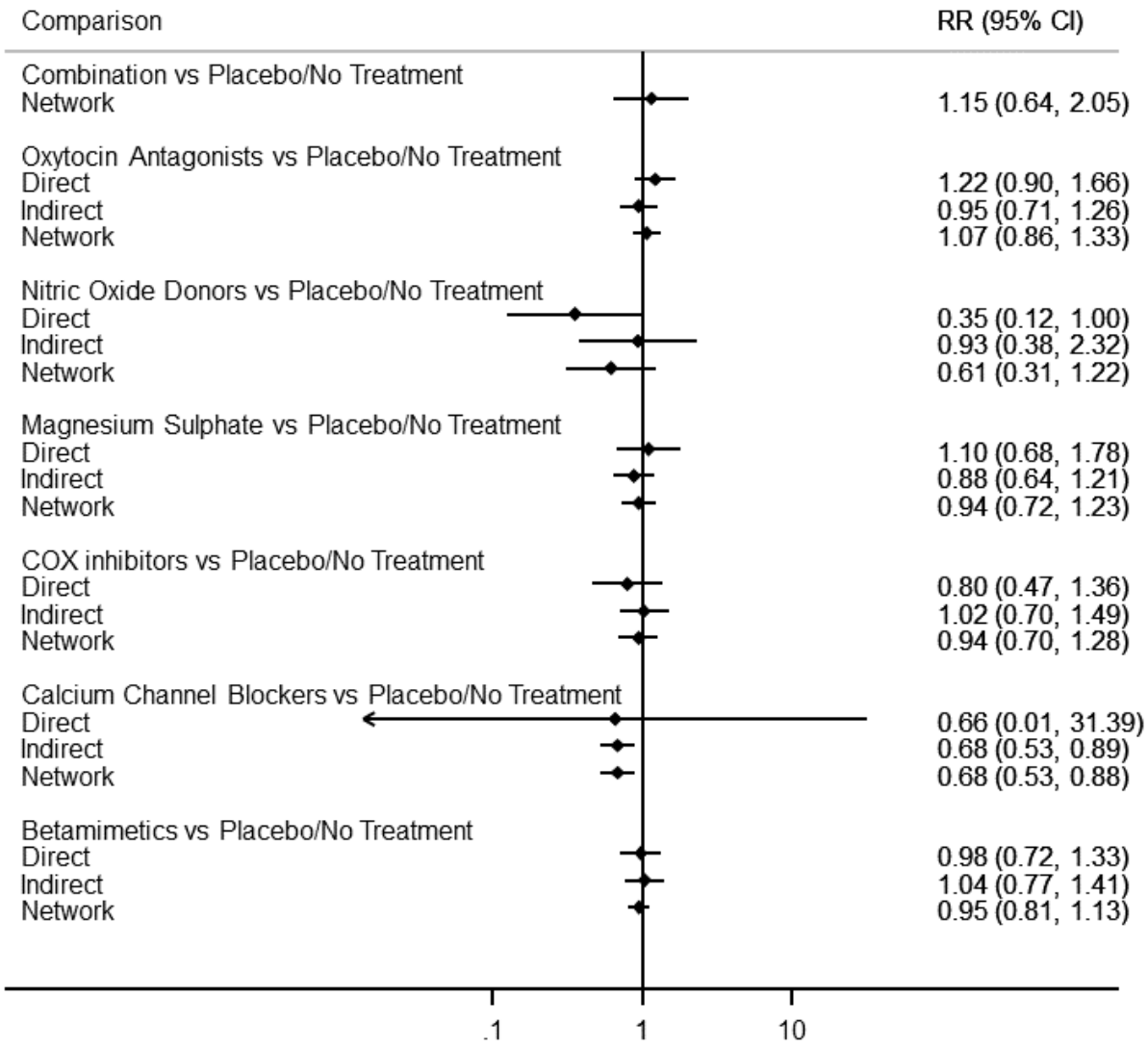


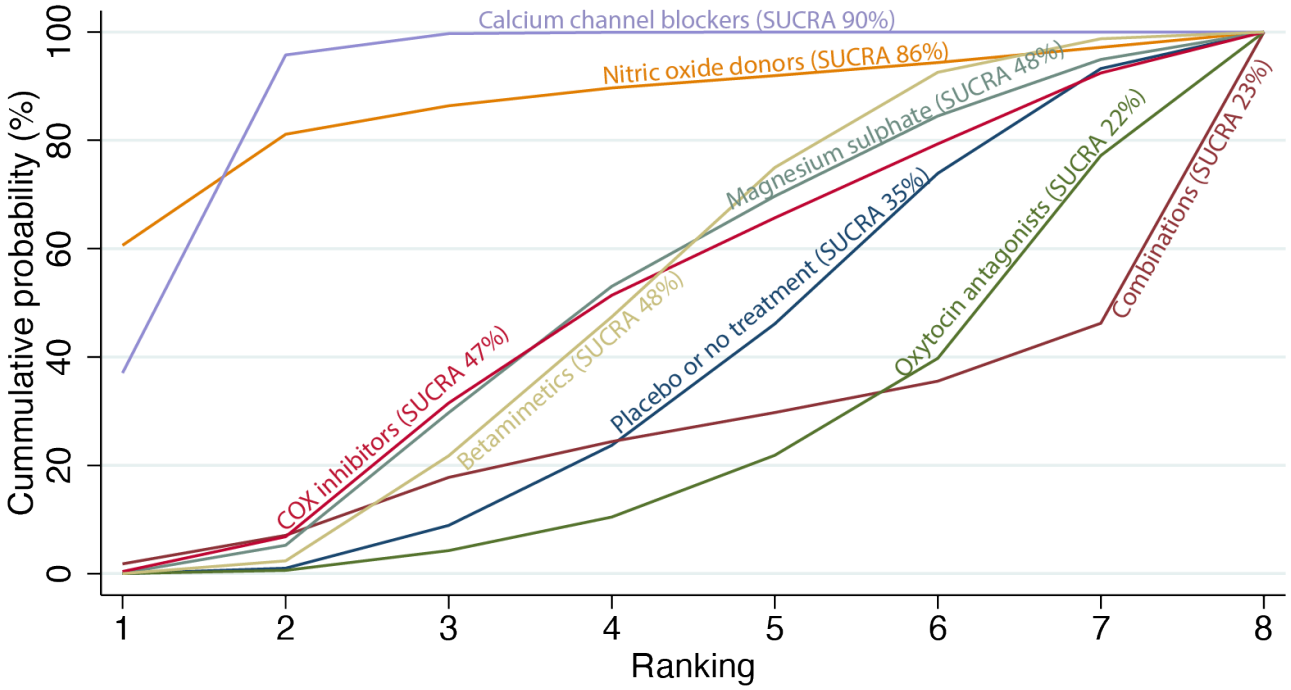
Figure 72. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for respiratory morbidity.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for respiratory morbidity are shown in Figure 73. The highest ranked tocolytics for this outcome were the calcium channel blockers (SUCRA 90%) and nitric oxide donors (SUCRA 86%). Oxytocin receptor antagonists (SUCRA 22%) and combinations of tocolytics (SUCRA 23%) were ranked the lowest.

Figure 73. Cumulative rankograms comparing each of the tocolytic drugs for respiratory morbidity. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



27. Mean birthweight

Network evidence

The network diagram for birthweight as a continuous outcome in grams is presented in Figure 74. Network meta-analysis of 77 trials (8258 babies) suggested that nitric oxide donors (MD 425.53 grams more, 95% CI 224.32 more to 626.74 more; low-certainty evidence) possibly result in neonates with a higher birthweight (Figure 75; Appendix 3). Moderate-certainty evidence suggests that there is probably little or no difference between betamimetics (MD 5.52 grams fewer, 95% CI 85.23 fewer to 74.18 more), calcium channel blockers (MD 84.08 grams more, 95% CI 3.22 fewer to 171.38 more), oxytocin receptor antagonists (MD 0.21 grams more, 95% CI 97.80 fewer to 98.22 more), and possibly with magnesium sulphate (MD 21.07 grams more, 95% CI 78.12 fewer to 120.27 more) compared with placebo or no treatment (Figure 75; Appendix 3). The effects for COX inhibitors and combinations of tocolytics were unclear because the certainty of the evidence was very low (Appendix 3).

Figure 74. Network diagram for mean birthweight. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

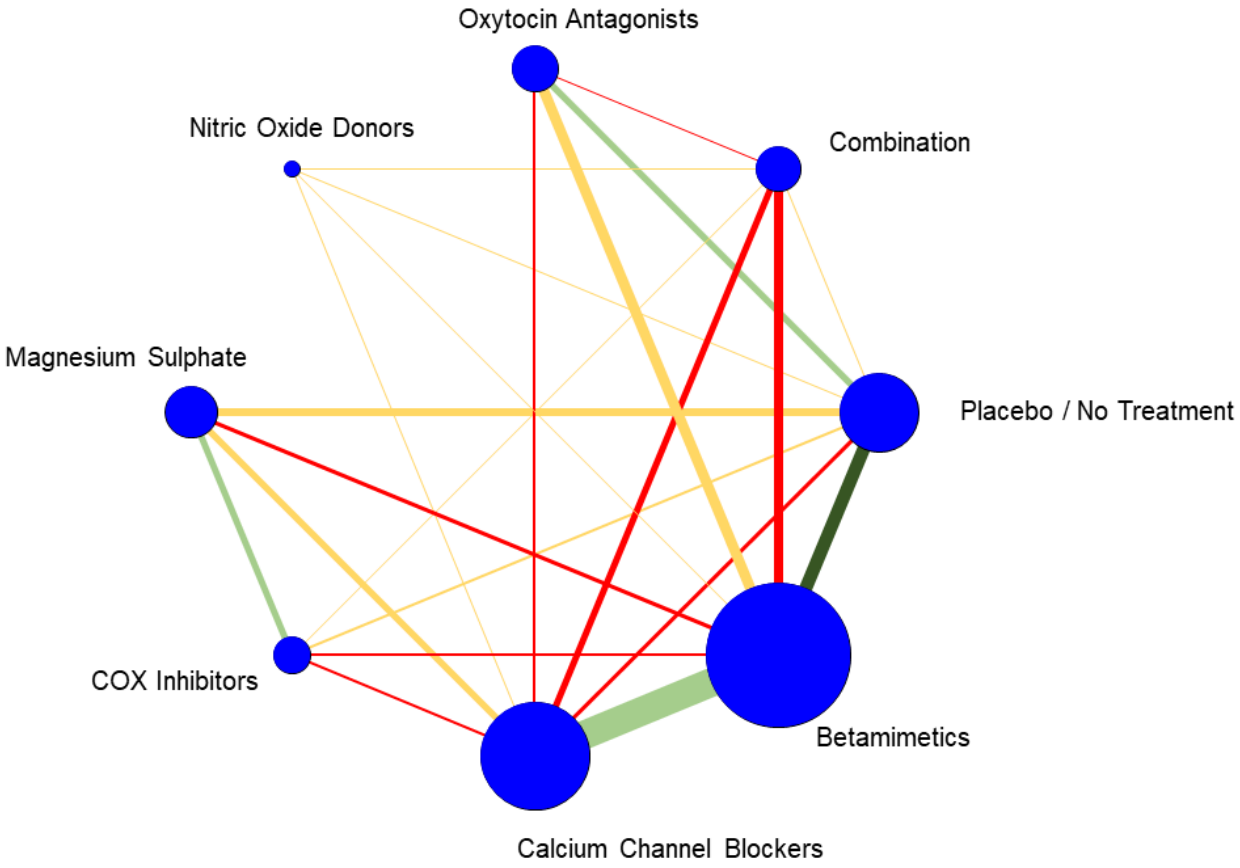
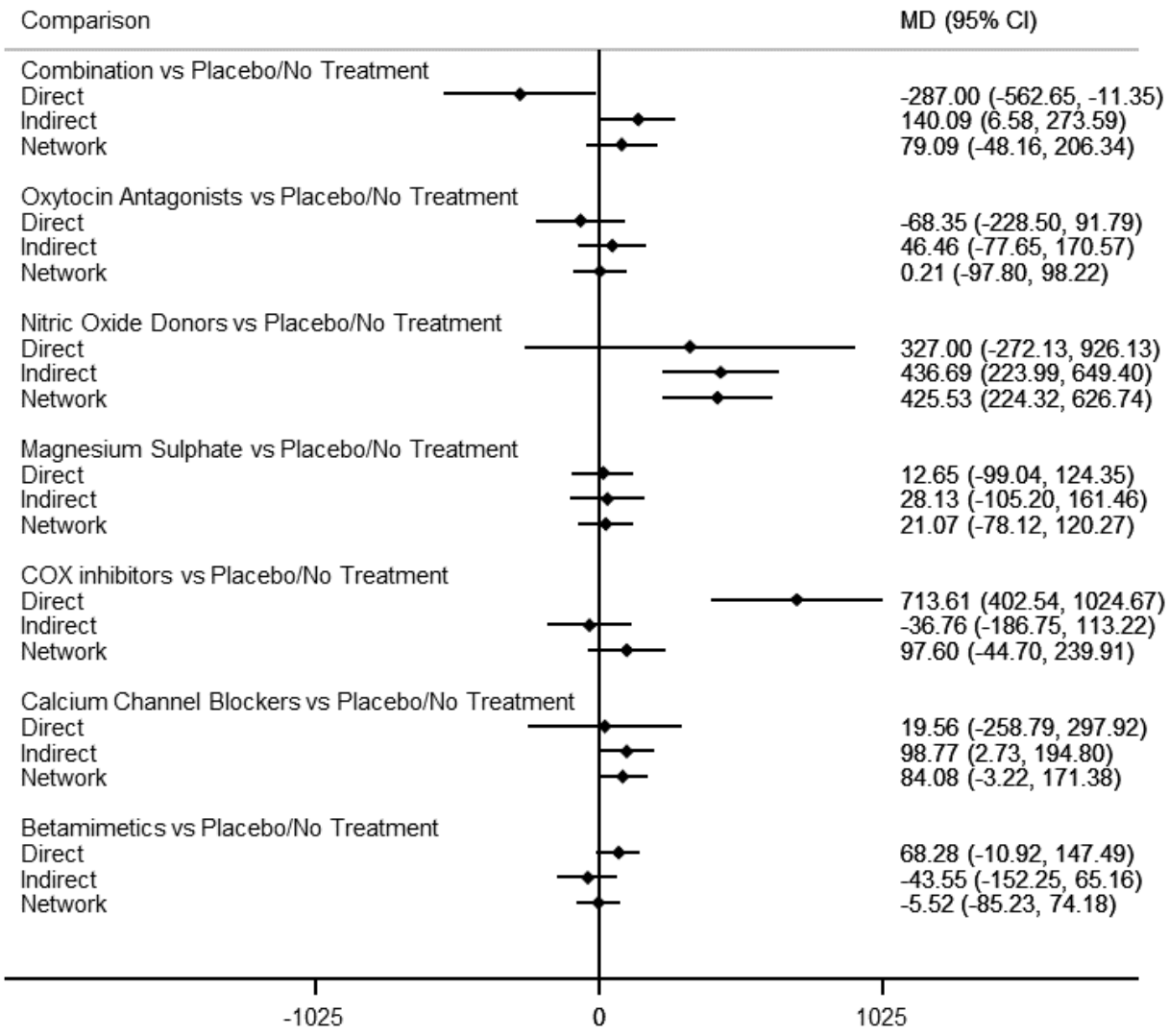


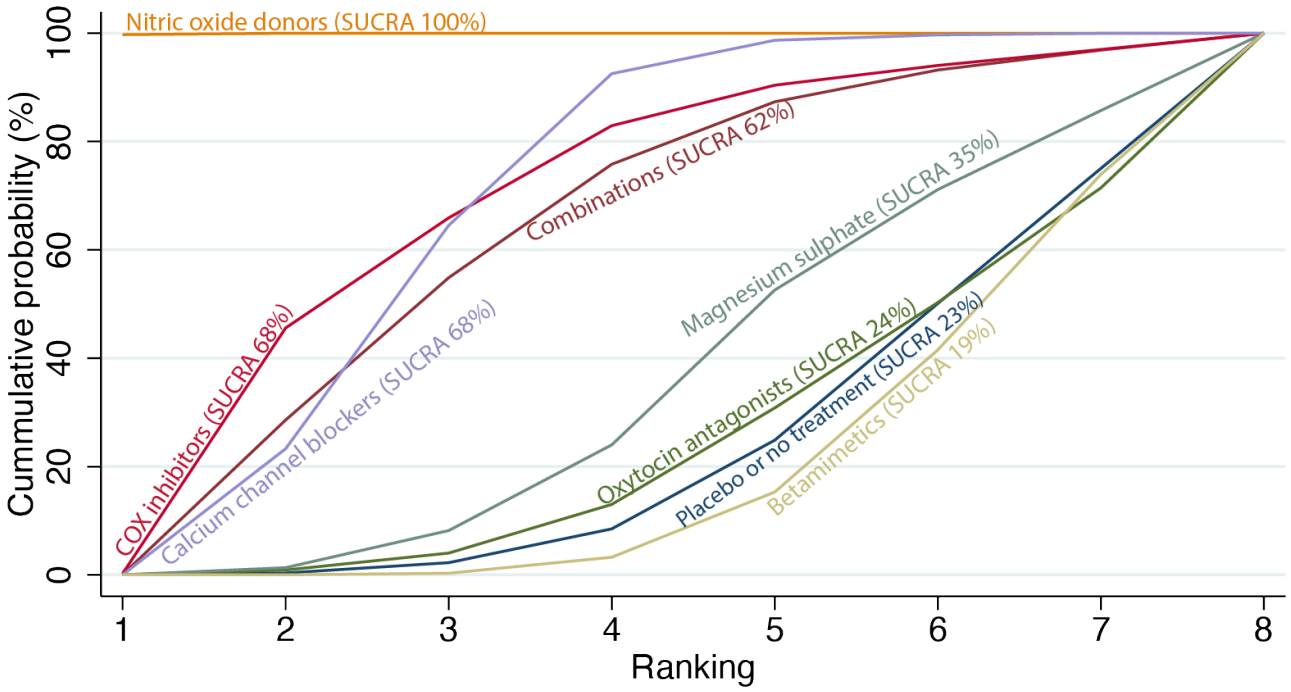
Figure 75. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for mean birthweight.



Tocolytic ranking

Figure 76 shows the cumulative probabilities for each agent being at each possible rank for birthweight as a continuous outcome. The highest ranked tocolytics were the nitric oxide donors (SUCRA 100%) and lowest ranked were betamimetics (SUCRA 19%) and placebo or no treatment (SUCRA 23%).

Figure 76. Cumulative rankograms comparing each of the tocolytic drugs for mean birthweight. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



28. Birthweight less than 2000 g

Network evidence

The network diagram for neonate birthweight less than 2000 g is presented in Figure 77. Relative effects from the network meta-analysis of seven trials (522 babies) suggested that calcium channel blockers (RR 0.49, 95% CI 0.28 to 0.87; low-certainty evidence) possibly reduce the risk of a neonate being born with a birthweight less than 2000 g, meanwhile other tocolytics are associated with a wide range of effects for this outcome when compared with placebo or no treatment as there were insufficient studies (Figure 78; Appendix 3). There is no direct, indirect or network evidence comparing oxytocin receptor antagonists, and nitric oxide donors with placebo or no treatment (Appendix 3).

Figure 77. Network diagram for birthweight of less than 2000 g. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

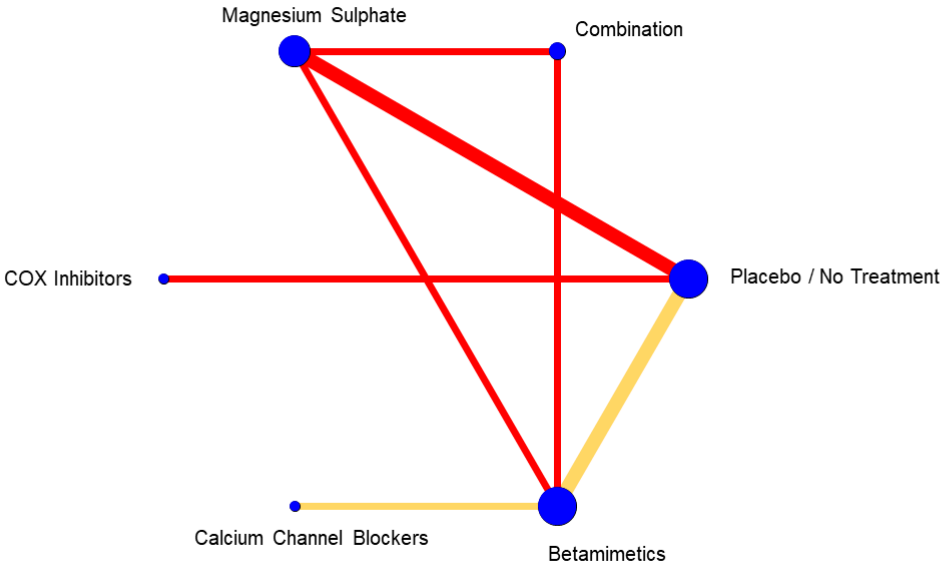
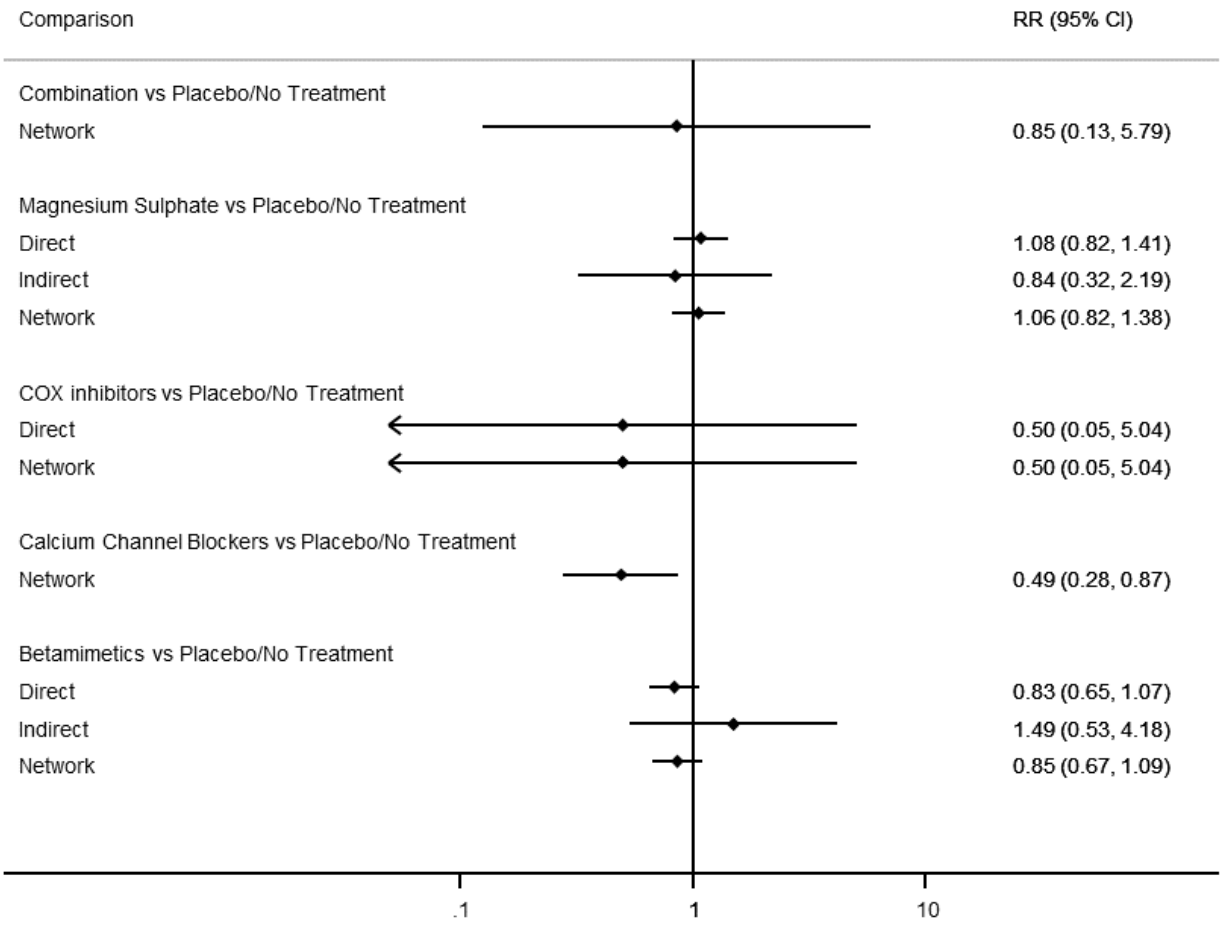


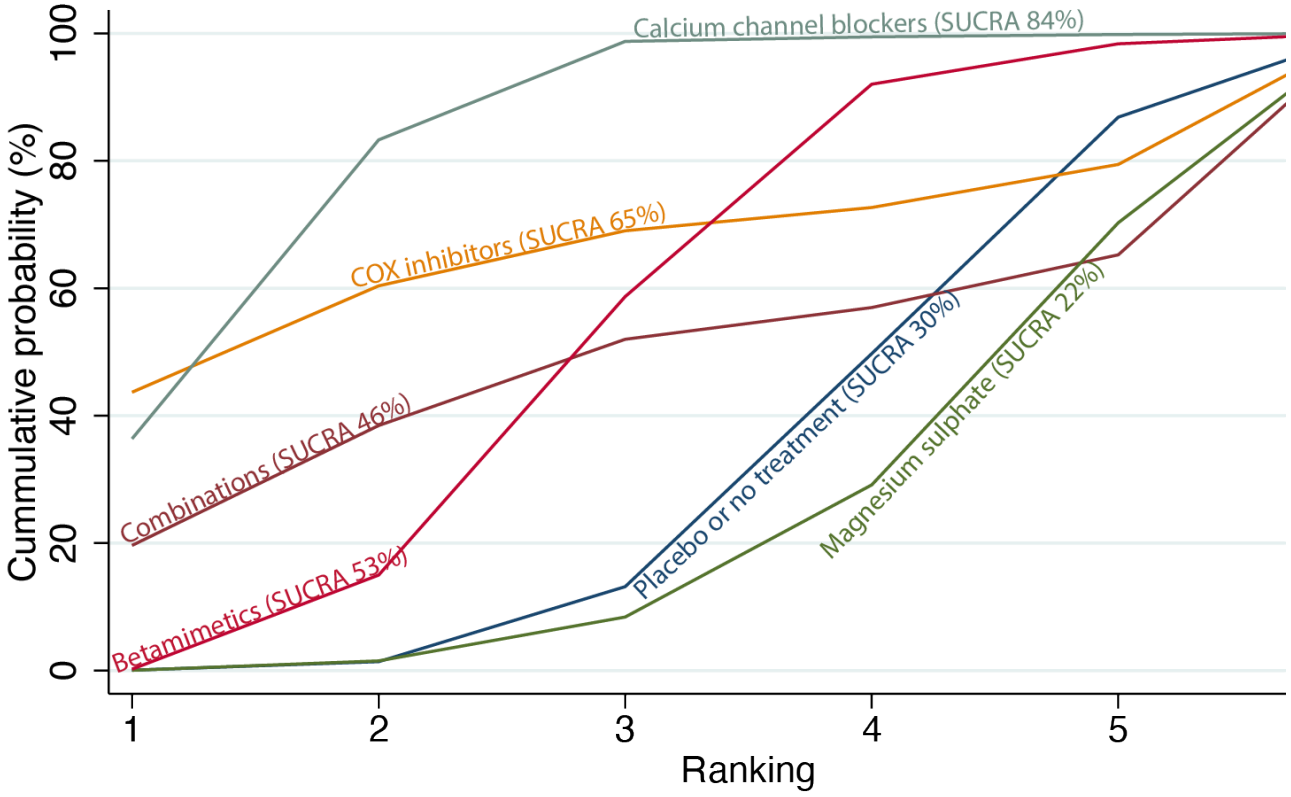
Figure 78. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for birthweight of less than 2000 g.



Tocolytic ranking

The cumulative probabilities for each agent being at each possible rank for birthweight less than 2000 g are shown in Figure 79. The ranking for tocolytics was not clear for this outcome due to few studies.

Figure 79. Cumulative rankograms comparing each of the tocolytic drugs for birthweight of less than 2000 g. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



29. Birthweight less than 2500 g

Network evidence

The network diagram for neonate birthweight less than 2500 g is presented in Figure 80. Relative effects from the network meta-analysis of 27 trials (3592 babies) suggested that betamimetics (RR 0.92, 95% CI 0.85 to 1.00; moderate-certainty evidence), and calcium channel blockers (RR 0.80, 95% CI 0.69 to 0.93; moderate-certainty evidence) probably result in fewer neonates born with a birthweight less than 2500 g. Low-certainty evidence suggests that COX inhibitors (RR 0.21, 95% CI 0.07 to 0.62), nitric oxide donors (RR 0.40, 95% CI 0.24 to 0.69), and combinations of tocolytics (RR 0.74, 95% CI 0.59 to 0.93) also possibly result in fewer neonates born with a birthweight less than 2500 g. Magnesium sulphate (RR 0.94, 95% CI 0.84 to 1.06), and oxytocin receptor antagonists (RR 0.94, 95% CI 0.79 to 1.12) possibly make little or no difference to this outcome (Figure 81; Appendix 3).

Figure 80. Network diagram for birthweight of less than 2500 g. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

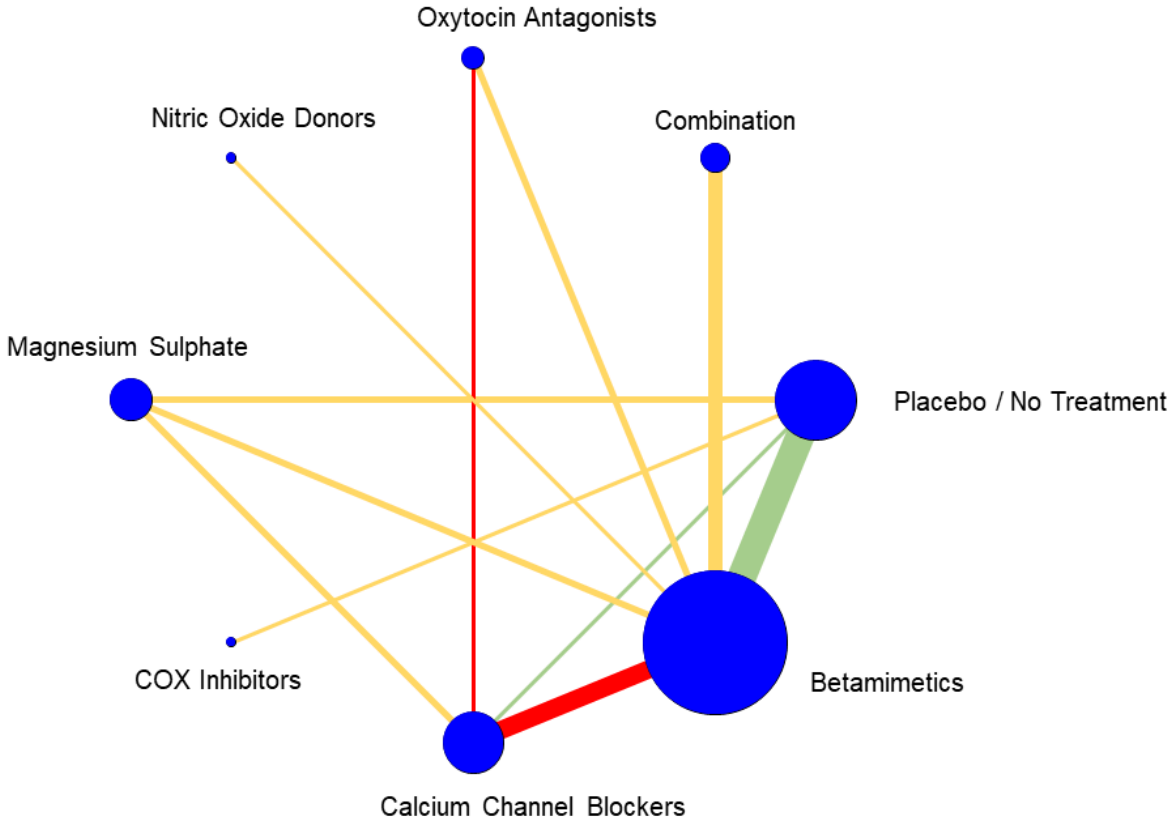
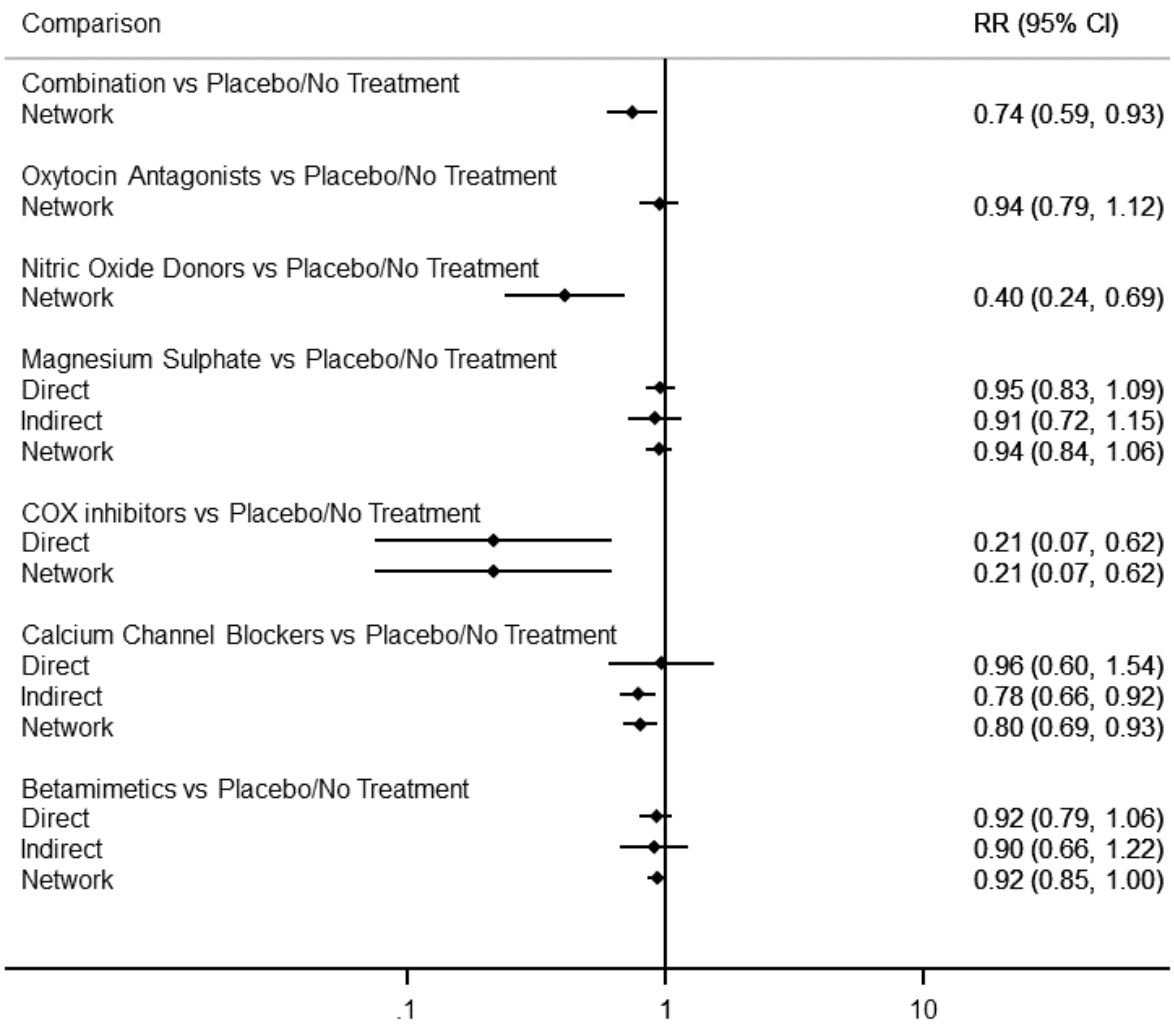


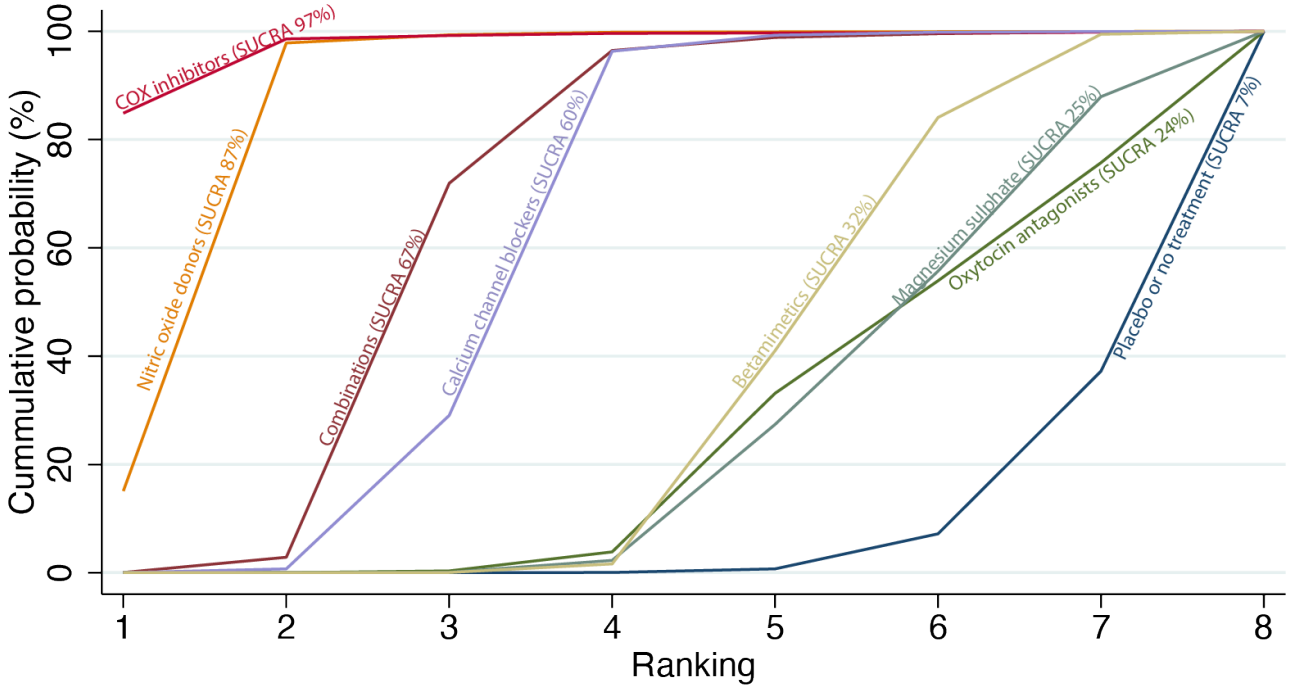
Figure 81. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for birthweight of less than 2500 g.



Tocolytic ranking

The cumulative probabilities for each agent being at each possible rank for birthweight less than 2500 g are shown in Figure 82. The highest ranked tocolytics were the COX inhibitors (SUCRA 97%), and nitric oxide donors (SUCRA 87%) and lowest ranked was placebo or no treatment (SUCRA 7%).

Figure 82. Cumulative rankograms comparing each of the tocolytic drugs for birthweight of less than 2500 g. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



30. Gestational age at birth

Network evidence

The network diagram for gestational age at birth as a continuous outcome in weeks is presented in Figure 83. Network meta-analysis of 66 trials (7451 women) suggested that nitric oxide donors (MD 1.35 weeks more, 95% CI 0.37 more to 2.32 more; low-certainty evidence) possibly result in neonates with a more advanced gestational age at birth (Figure 84; Appendix 3). Moderate-certainty evidence suggests that there is probably little or no difference between betamimetics (MD 0.23 weeks fewer (95% CI 0.70 fewer to 0.23 more), calcium channel blockers (MD 0.24 weeks more, 95% CI 0.25 fewer to 0.73 more) than placebo or no treatment (Figure 84; Appendix 3). Similarly, oxytocin receptor antagonists possibly make little to no difference (MD 0.08 weeks fewer, 95% CI 0.70 fewer to 0.55 more) to this outcome. The effects for COX inhibitors, magnesium sulphate, and combinations of tocolytics were unclear because the certainty of the evidence was very low (Appendix 3).

Figure 83. Network diagram for gestational age at birth. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

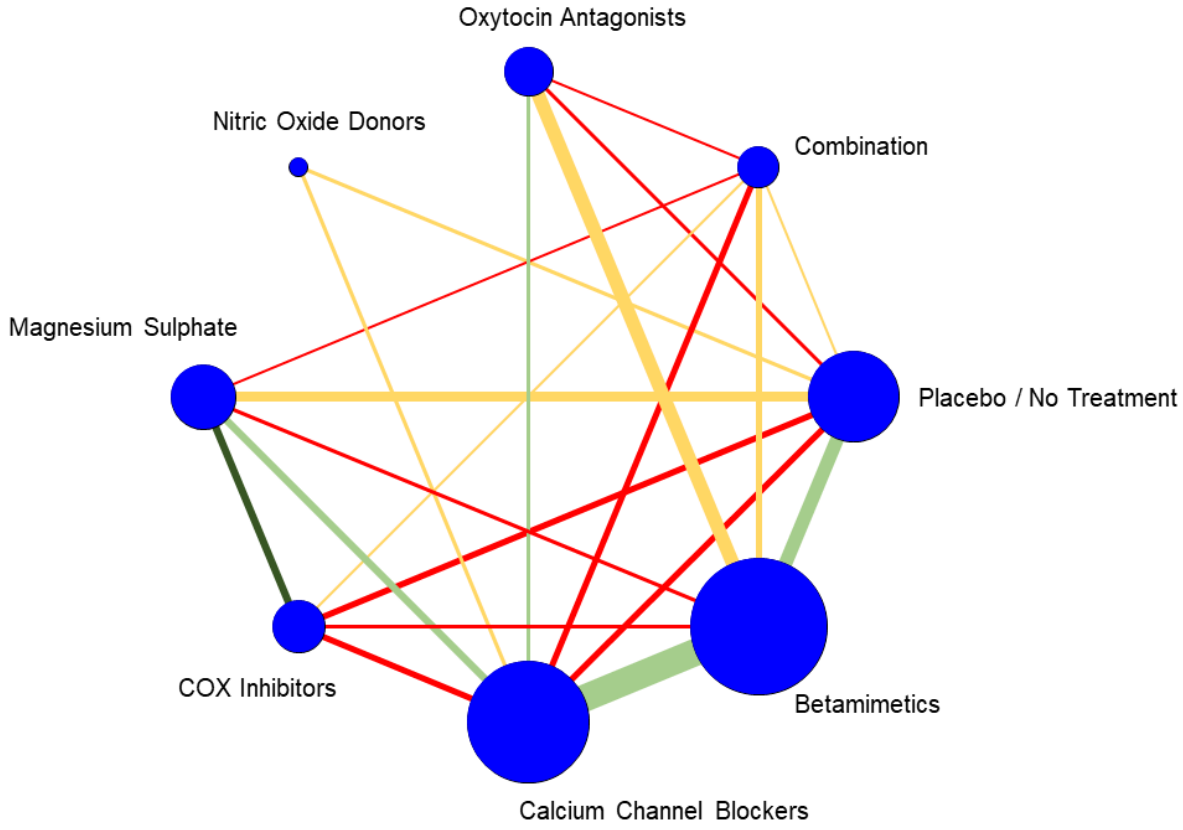
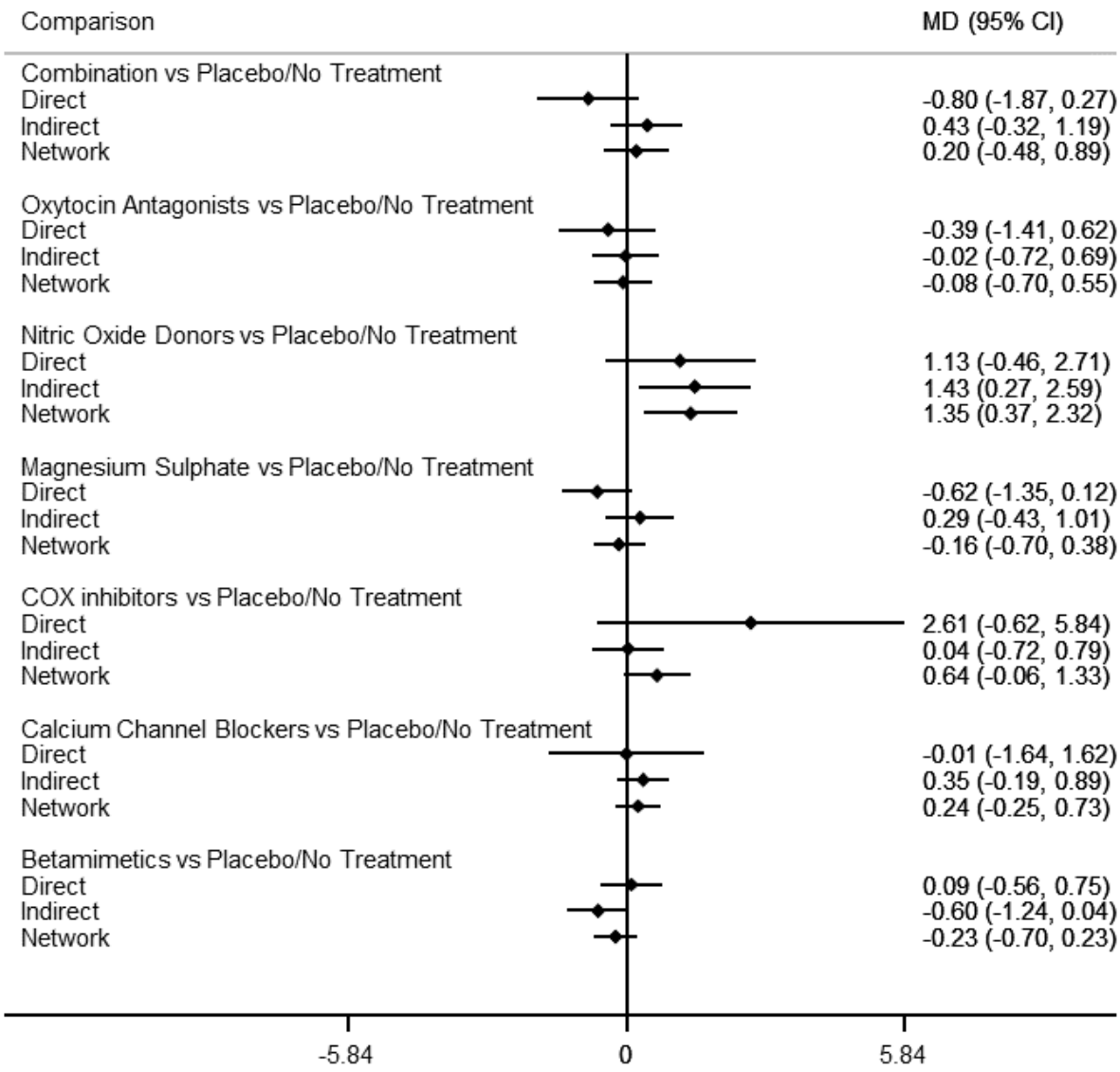


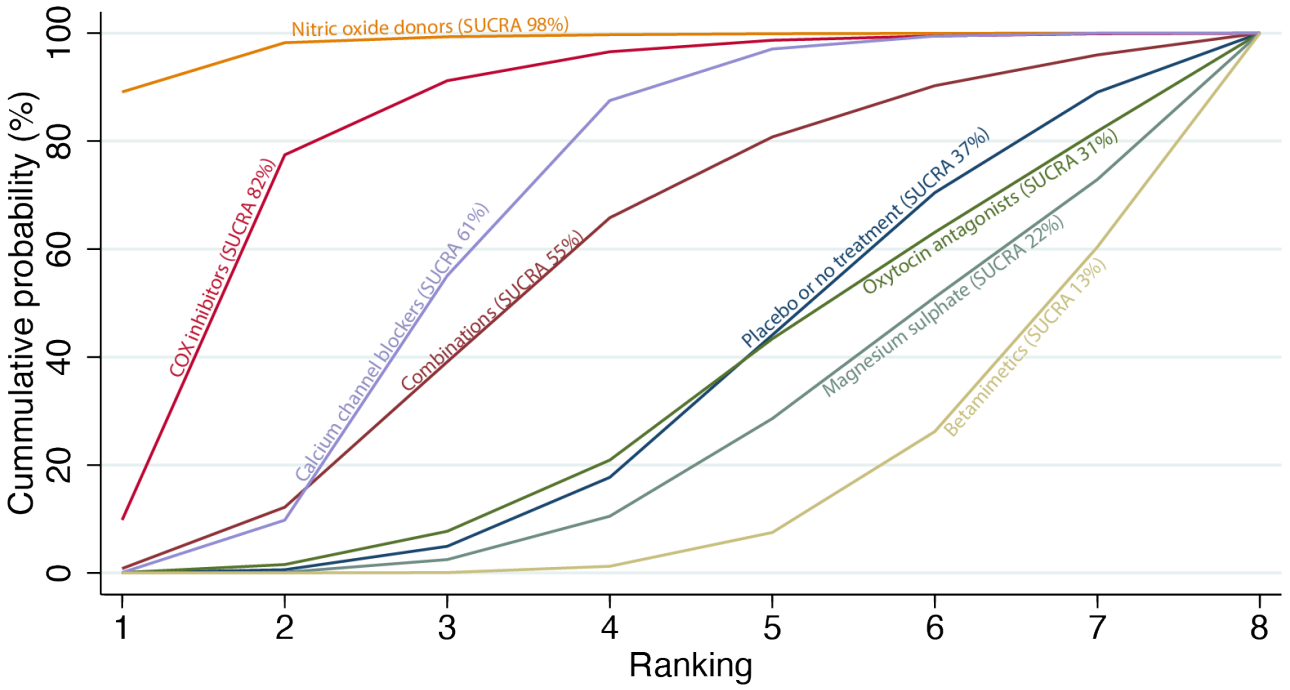
Figure 84. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for gestational age at birth.



Tocolytic ranking

Figure 85 shows the cumulative probabilities for each agent being at each possible rank for gestational age at birth as a continuous outcome. The highest ranked tocolytics were the nitric oxide donors (SUCRA 98%) and COX inhibitors (SUCRA 82%) and lowest ranked were the betamimetics (SUCRA 13%).

Figure 85. Cumulative rankograms comparing each of the tocolytic drugs for gestational age at birth. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



31. Neonatal infection

Network evidence

The network diagram for neonatal infection is presented in Figure 86. Relative effects from the network meta-analysis of 33 trials (5070 babies) suggested that tocolytics are associated with a wide range of effects for neonatal infection when compared with placebo or no treatment (Figure 87; Appendix 3). There were no studies involving nitric oxide donors and the effects for combinations of tocolytics were unclear because the certainty of the evidence was very low (Appendix 3)

Figure 86. Network diagram for neonatal infection. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

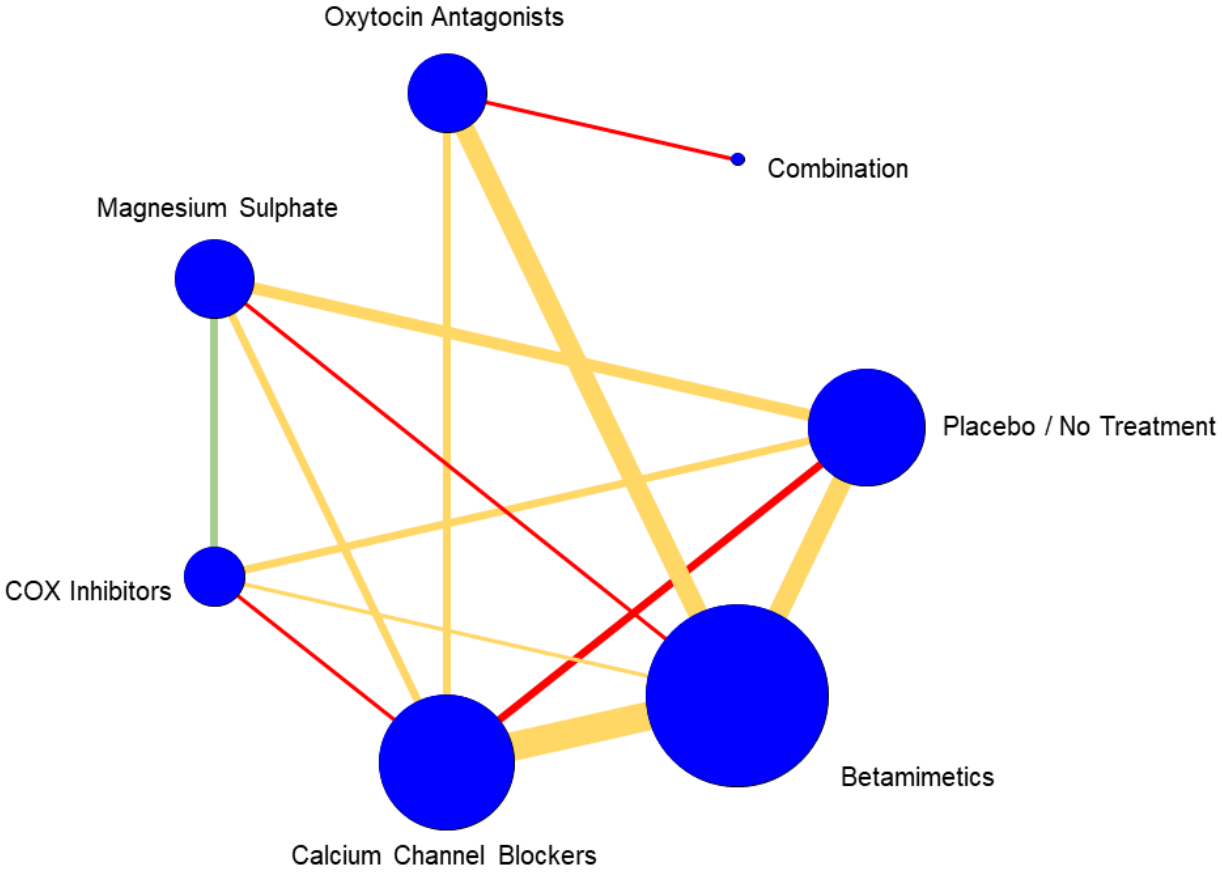
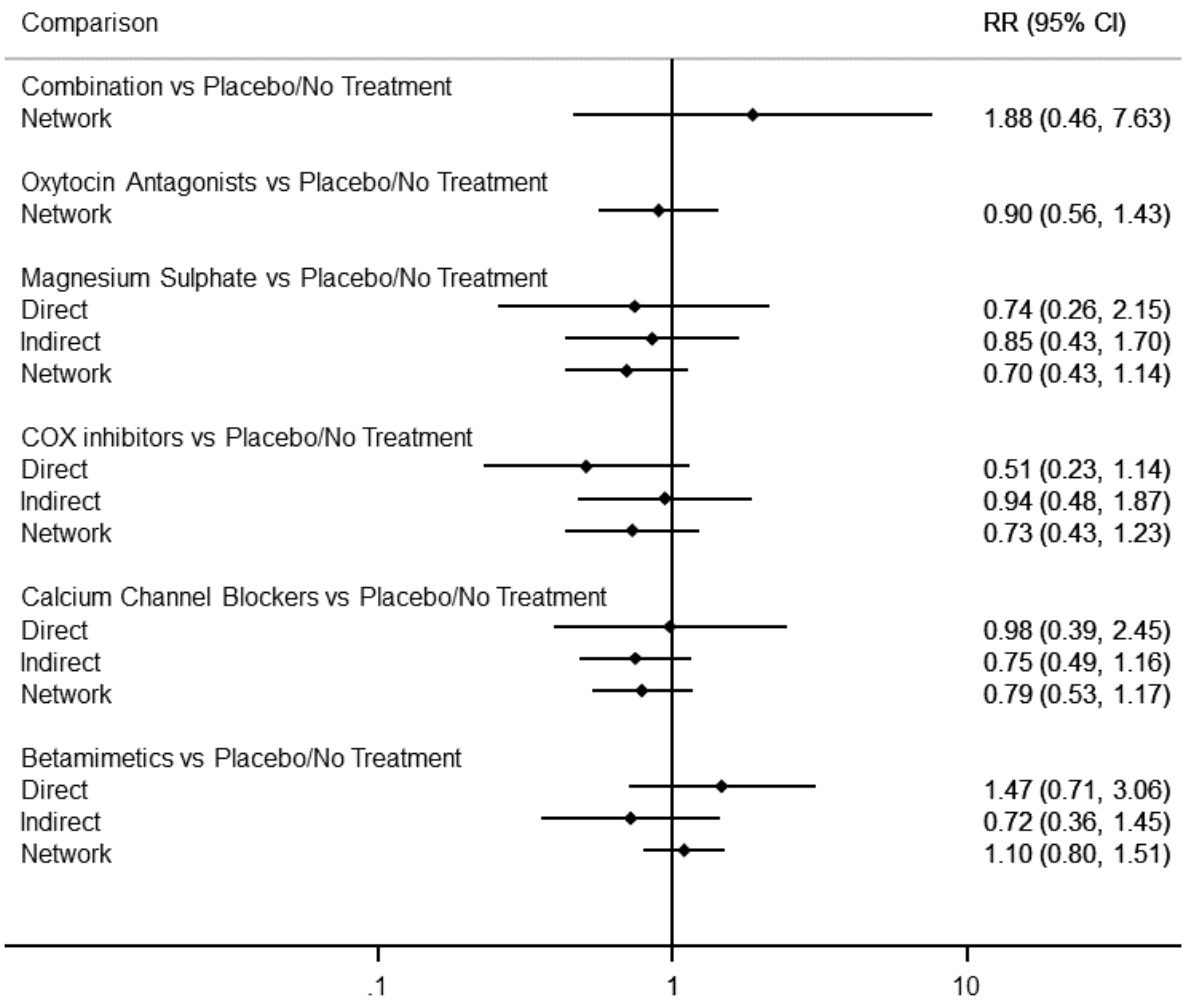


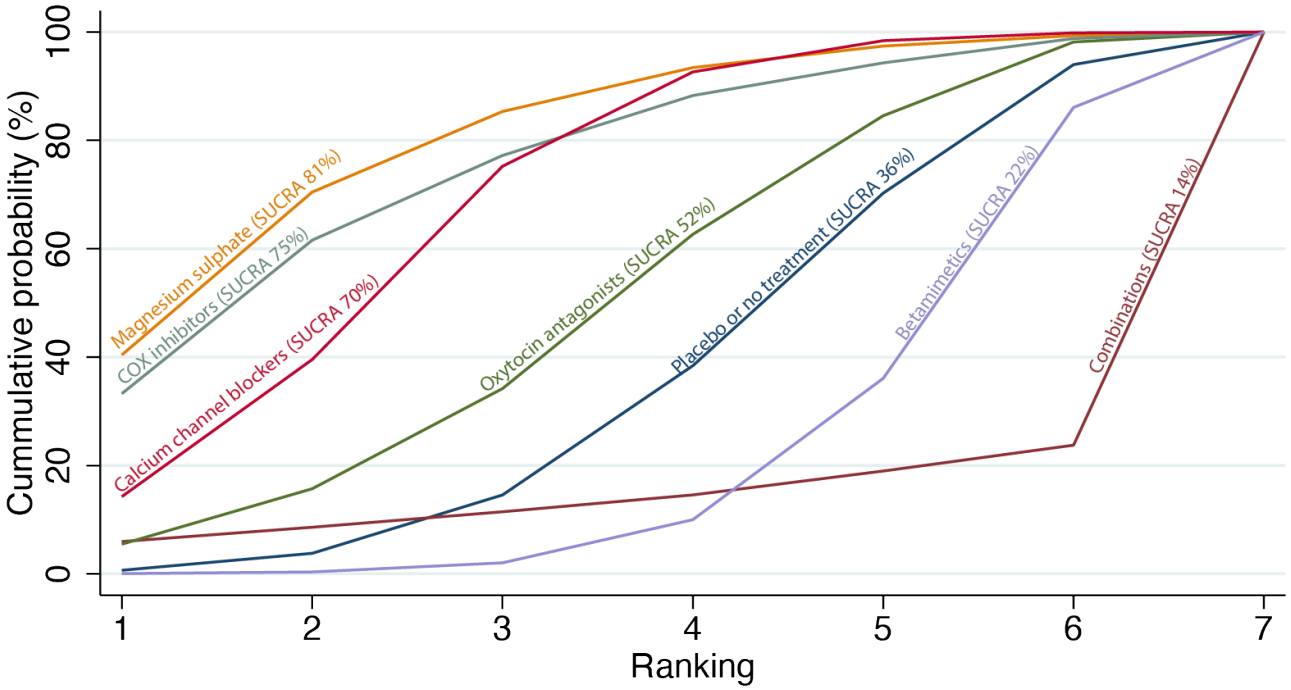
Figure 87. Forest plot with relative risk ratios and 95% confidence intervals from pairwise, indirect and network (combining direct and indirect) analyses for neonatal infection.



Tocolytic ranking

The cumulative probabilities for each tocolytic being at each possible rank for neonatal infection are shown in Figure 88. The highest ranked tocolytics were the magnesium sulphate (SUCRA 81%) and COX inhibitors (SUCRA 75%) and lowest ranked were the combinations of tocolytics (SUCRA 14%).

Figure 88. Cumulative rankograms comparing each of the tocolytic drugs for neonatal infection. Ranking indicates the cumulative probability of being the best agent, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SURface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available agents.



The certainty of the evidence (grading of the results) considers the heterogeneity and inconsistency for all outcomes mentioned above, and all of the tocolytic comparisons stated in the results.

Subgroup analyses

Subgroup analyses did not reveal any substantial differences in the effects of different tocolytics by the duration of tocolysis (suppression alone versus suppression plus long-term maintenance). We carried out a post hoc subgroup analysis according to the use of rescue tocolysis and the effects were consistent in both subgroups. Rescue tocolysis was defined as instances where the first tocolytic failed to delay preterm labour and another tocolytic had to be used. In addition, we planned a subgroup analysis according to the gestational age at trial entry, whether amniotic membranes were ruptured or not and whether the trial included singleton or multiple pregnancies, but sufficient studies were not available for these subgroup analyses.

Sensitivity analysis

We carried out prespecified sensitivity analyses by restricting our analyses to studies with no co-interventions such as progesterone, to studies at low risk of bias and studies that were placebo-controlled. We also performed sensitivity analyses according to the choice of relative effect measure (risk ratio versus odds ratio), the statistical model (fixed-effect versus random-effects model), and by removing studies conducted before 1990. The sensitivity analyses show that the overall results are not affected by the above mentioned criteria or decisions.

DISCUSSION

Summary of main results

The network meta-analysis involved six tocolytic drug classes, combinations of tocolytic drugs, and placebo or no tocolytic treatment. Most trials included women in threatened preterm birth, with a singleton pregnancy between 24 and 34 weeks. Overall, the evidence presented varied widely in quality, and our confidence in the effect estimates ranged from very low to high.

Primary outcomes

Delay in birth

Relative effects from the network meta-analysis suggested that all the classes of tocolytics that we assessed are probably effective in delaying preterm birth when compared with placebo or no treatment. Specifically, betamimetics are possibly effective in delaying preterm birth by 48 hours, and 7 days. COX inhibitors are possibly effective in delaying preterm birth by 48 hours. Calcium channel blockers are possibly effective in delaying preterm birth by 48 hours, probably effective in delaying preterm birth by 7 days, and result in a significant pregnancy prolongation. Magnesium sulphate is probably effective in delaying preterm birth by 48 hours. Oxytocin receptor antagonists are effective in delaying preterm birth by 7 days, and probably by 48 hours, and also possibly result in a mean pregnancy prolongation of 10 days. Nitric oxide donors are probably effective in delaying preterm birth by 48 hours, and 7 days. Combinations of tocolytics - largely based on the combination of betamimetics with magnesium sulphate - are probably effective in delaying preterm birth by 48 hours, and 7 days.

The highest ranked tocolytics for delaying preterm birth by 48 hours, 7 days, and delay in birth as a continuous outcome are the nitric oxide donors, calcium channel blockers, oxytocin receptor antagonists and combinations of tocolytics.

Cessation of treatment due to adverse effects

Relative effects from the network meta-analysis suggested that betamimetics, calcium channel blockers, magnesium sulphate and combinations of tocolytics are probably more likely to result in cessation of treatment due to adverse effects.

Neonatal death, serious adverse effects and maternal infection

For the remaining pre-specified primary outcomes including neonatal death at 28 days, serious adverse effects and maternal infection, tocolytics are associated with a wide range of treatment effects compared with placebo or no treatment for so their effects remain uncertain.

Secondary outcomes

Neonatal morbidity, gestational age and birthweight

For the secondary outcomes, calcium channel blockers possibly reduce the risk of neurodevelopmental morbidity, and the risk of respiratory morbidity, and result in fewer neonates born with a birthweight less than 2000 g. Nitric oxide donors possibly result in neonates with a higher birthweight, fewer neonates born with a birthweight less than 2500 g, and a more advanced gestational age at birth. Combinations of tocolytics possibly result in fewer neonates born with a birthweight less than 2500 g.

Maternal adverse effects

In terms of adverse effects, betamimetics probably cause dyspnoea, palpitations, nausea or vomiting, and possibly headache, and tachycardia compared with placebo or no treatment. COX inhibitors possibly cause nausea or vomiting. Calcium channel blockers possibly cause headache. Nitric oxide donors probably cause headache.

Subgroup analyses

Subgroup analyses did not reveal any substantial differences in the effects of different tocolytics by the duration of tocolysis (acute suppression alone versus acute suppression plus long-term maintenance). We carried out a post hoc subgroup analysis according to the use of rescue tocolysis and the effects were consistent in both subgroups. There are insufficient data to perform subgroup analyses by: gestational age at trial entry (fewer than 32/40 completed weeks versus 32/40 completed weeks or more); status of amniotic membranes (women with ruptured membranes versus women with intact membranes); and number of fetuses (singleton versus multiple pregnancy).

Overall completeness and applicability of evidence

This network meta-analysis provides the relative effectiveness of all tocolytics in a coherent and methodologically robust way across important clinical outcomes by combining both direct and indirect evidence, thus increasing the statistical power and confidence in the results. We found that most of the included trials reported several of the primary outcomes and most of the secondary outcomes. This increased the power across most of our analyses and contributed to the consistency in the ranking across most outcomes.

We were thorough in our evaluation of the important potential treatment effect modifiers (gestational age, amniotic membranes, multiple pregnancy, and duration of tocolysis). We did not encounter important differences in the distribution of the effect modifiers between the different comparisons. The results of the network meta-analyses were mostly consistent and where there was significant inconsistency this was likely due to unstable estimates from a low number of events.

Women recruited to the included studies were predominantly between 24 to 34 weeks of gestation, in hospital settings and with singleton pregnancies. Our findings may not be readily generalisable to other gestations or multiple pregnancies. Trials often varied in the regimen used for the tocolytics with several studies using a short course of tocolysis for up to 48 hours while others continued use of tocolysis for longer; in some trials up to the time of birth. The observed effects for the tocolytics were consistent in both subgroups.

Quality of the evidence

We acknowledge that there is no single established approach for assessing the certainty of the effect estimates generated by the network meta-analysis. We applied the rigorous method for appraising quality of network evidence as proposed by the GRADE Working group. Overall, the evidence presented varied widely in quality, and our confidence in the effect estimates ranged from very low to high certainty. When we compared placebo or no treatment with all tocolytic drugs and combinations of tocolytics, most individual outcomes included a range in quality of evidence, and this was equally true for our most important outcomes. Our reasons for downgrading the evidence also varied across comparisons and outcomes.

Potential biases in the review process

The evidence for this review is derived from trials identified from a detailed, systematic search process without language restriction. This search was conducted in consultation with Cochrane Pregnancy and Childbirth's Information Specialist. It is possible (but unlikely) that additional trials have been published but not identified. It is also possible that there are other trials, additional to those of which we are aware, that have been conducted but are not yet published. Should any such trials be identified, we will include them in updates of this review. We performed a systematic search but we cannot be sure we identified all relevant trials. We prepublished and followed our protocol (New Reference). At least two review authors (AW, EM, AM, EL, AP, VAH, IG) independently assessed all studies, extracted data and graded evidence. At least two review authors (AW, VAH, IG) appraised studies published during and after 2010 for trustworthiness in accordance with set criteria (Appendix 2).

Before we could carry out the GRADE assessment of the network meta-analysis evidence, we had to determine the methodology for this process because there is no well-established approach or accompanying tools such as software. At least two review authors (AW, AP, VAH) undertook all GRADE assessments, in consultation with IG where additional decision making was required.

The earliest included trial was conducted in 1966 (Adam 1966), and in the decades since, clinical care for newborns has dramatically improved. These temporal changes could have contributed to heterogeneity and increased the uncertainty of findings. However, we carried out a sensitivity analysis by removing trials published before 1990 and this did not vary the ranking of the tocolytics substantially. As administration of corticosteroids for fetal lung maturation, and magnesium sulphate for neuroprotection have become increasingly available this could perhaps have also led to apparent changes in neonatal outcomes.

A source of heterogeneity and inconsistency was the use of rescue tocolysis where the first tocolytic failed to delay preterm labour. This varied substantially with some studies routinely administering a second-line tocolytic, while others did not describe or use any rescue tocolysis if the first tocolytic was judged as failed. We did carry out a post-hoc subgroup analysis to examine subgroup effects of the rescue tocolysis and the effects were consistent in both subgroups.

The trials included in the review recruited women with varied clinical characteristics, and it is important to consider this when interpreting results. The inclusion criteria were not always reported in detail and, when they were, these varied across trials. Lastly, not all trials reported data on adverse effects, hence these analyses were often underpowered.

Data from 17 ongoing studies may inform future updates of this review.

Agreements and disagreements with other studies or reviews

Our results agree with existing Cochrane Reviews (Crowther 2014; Duckitt 2014; Flenady 2014a; Flenady 2014b; Neilson 2014; Reinebrant 2015), that focus on the comparison of a tocolytic drug versus another (direct comparisons). However, this network meta-analysis has several more studies than included in the previous reviews because of its nature of comparing all available tocolytic drugs in one single analysis and because it is the most up-to-date, including recently published trials. Hence, some estimates differ slightly, as expected.

A similar network meta-analysis on this topic has previously been conducted (Haas 2012), which concluded that COX inhibitors and calcium channel blockers had the highest probability to delay preterm birth by 48 hours. This review was conducted almost a decade ago with fewer trials included, which resulted in lower power and may account for the different conclusions reached. We have also applied the trustworthiness tool from Cochrane, which may have resulted in some trials with implausible results (e.g. massive risk reduction for main outcomes with small sample size) to be eliminated from the review.

AUTHORS' CONCLUSIONS

Implications for practice

This review shows that all tocolytic classes that we assessed are effective in delaying preterm birth when compared with placebo or no treatment based mostly on moderate- and low-certainty evidence. Evidence suggests that tocolytics are associated with adverse effects. Betamimetics or combinations of tocolytics involving betamimetics often result in cessation of treatment because of adverse effects.

In deciding which tocolytic option to use, healthcare providers should carefully consider the clinical rationale and circumstances for the individual pregnancy surrounding the need for prolonging the time of birth (for instance antenatal use of corticosteroids or magnesium sulphate for fetal lung maturation or neuroprotection). From a safety standpoint, clinicians should assess the current clinical condition of potentially eligible women against the adverse effects of a particular tocolytic to avoid exacerbating underlying health problems.

Policy makers could consider the various options when considering implementation strategies, and building or supporting health service delivery.

Before making decisions, policymakers would need to balance the desirable and undesirable effects of the range of effective tocolytics presented with their available resources and other contextual issues. An economic assessment would need to assess the consequences of tocolytics, with consideration of differences between their effects (benefits and harms), supply costs, and other resource requirements (staffing and training, equipment and infrastructure, staff time, supplies, supervision, and monitoring). Other important considerations for decision-making include the potential impact of introducing or scaling up tocolytic drugs on health equity, acceptability to key stakeholders and feasibility of using these drugs in routine clinical practice.

Implications for research

Most of the evidence presented in this review are of moderate or low certainty. Further high-quality large trials are required to improve the certainty of the evidence. A majority of the trials had fewer than 100 participants which meant that neonatal and safety outcomes had very few events and analyses were often underpowered.

Trials evaluating magnesium sulphate only for neuroprotection were excluded. For trials evaluated a tocolytic and participants received magnesium sulphate for perinatal optimisation this was noted as a co-intervention. It is appreciated that perinatal optimisation now includes magnesium sulphate and the tocolytic benefit of this practice should be appreciated.

Future trials should examine the effectiveness of the tocolytics separate for the subgroups of women according to their gestational age, intact from ruptured membranes and singleton from multiple pregnancies.

Reporting of future trials need to include the critical and important outcomes set by WHO (WHO 2015) for interventions to improve preterm birth outcomes, as this would strengthen future evidence synthesis.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adam 1966

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	48 women were randomised from 1 centre in Australia in 1965 (further dates NR) Population: women with threatened preterm birth < 37 weeks' gestation with intact membranes Definition of threatened preterm birth: NR Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding) and cervical dilation > 4 cm, confirmed ruptured membranes
Interventions	Isoxuprine 80 mg administered by IM injection in the first 24 h followed by 40-60 mg administered orally daily vs placebo

Adam 1966 *(Continued)*

Outcomes	Neonatal death before 28 d, perinatal death, stillbirth, neonatal death before 7 d
Notes	Mead Johnson Pty Ltd supplied the medications. No other COI reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 women were excluded from the analyses due to loss to follow-up (< 10%). Numbers were similar across both arms. All other women included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics NR. No other obvious bias

Ally 1992

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	107 women were randomised from centres in France (number NR) between April 1988 and March 1990 Population: women with threatened preterm birth between 22+0 and 35+0 weeks with intact membranes Definition of threatened preterm birth: not defined Exclusion criteria: comprised contraindications to tocolysis (suspected intrauterine infection), rupture of membranes, nephropathy
Interventions	Magnesium gluconate 200 mg/kg body weight followed by ritodrine 100 mg administered IV vs ritodrine 100 mg IV
Outcomes	Pregnancy prolongation, cessation of treatment due to AEs, GA at birth, nausea or vomiting, maternal hypotension, mean birthweight, tachycardia
Notes	No COI

Ally 1992 *(Continued)*

Funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number list
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 women excluded from the study (< 10%) (groups not stated) for medical reasons
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar, no other bias reported

Al Omari 2013

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	100 women were randomised from 2 centres in the United Arab Emirates between April 2007 and September 2010 Population: women with threatened preterm birth between 24+0 to 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 30 min with cervical dilation up to 3 cm and effacement of ≥ 50% Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection), indications for imminent birth, ruptured membranes, multiple pregnancy, prior tocolytic use, maternal medical conditions (diabetes other than diet-controlled, hypertension or other chronic conditions), a fetus showing signs of non-reassuring well-being
Interventions	Atosiban 6.7 mg administered by IV bolus, followed by 18 mg/h for 3 h followed by 6 mg/h for 48 h vs nifedipine 10 mg orally every 15 min until contractions stopped with a maximum dose of 40 mg in the 1st h followed by maintenance dose of 10 mg every 6 h for 48 h alongside of atosiban 6.7 mg administered by IV bolus, followed by 18 mg/h for 3 h followed by 6 mg/h for 48 h
Outcomes	Delay by 48 h, delay by 7 d, perinatal death, GA at birth, nausea or vomiting, pulmonary oedema, arrhythmias, SAEs, tachycardia, hypotension, headache, mean birthweight, neonatal death before 28 d,

Al Omari 2013 *(Continued)*

	gastrointestinal morbidity, neurodevelopmental morbidity, neonatal infection, pregnancy prolongation, cessation of treatment due to AEs
Notes	Rescue tocolysis was given with salbutamol if the study drug failed due to labour progress or intolerable AEs. No women received rescue tocolysis as labour progressed too quickly for those who required it. No COI Funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers
Allocation concealment (selection bias)	Unclear risk	Folded slips
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	8 women were excluded from the analysis, a per-protocol analysis was conducted, women who did not receive the intervention were excluded from analysis plus 2 women were lost to follow-up (total: 3 in atosiban arm and 5 in combination arm), totaling 10% in 1 arm
Selective reporting (reporting bias)	Unclear risk	The outcomes reported match the study protocol that was registered retrospectively NCT01429545
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Al Qattan 2000

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	60 women were randomised from 1 centre in Kuwait. Population: women with threatened preterm birth between 24+0 and 34+0 weeks' gestation with a singleton pregnancy Definition of threatened preterm birth: at least 2 regular uterine contractions in 10 min with cervical dilation or effacement Exclusion criteria: contraindications for tocolysis (severe vaginal bleeding or suspected intrauterine infection), maternal medical disease, severe pre-eclampsia or eclampsia, premature rupture of mem-

Al Qattan 2000 *(Continued)*

	branes, polyhydramnios, cervical dilation > 4 cm, a fetus showing signs of non-reassuring well-being, malformations or demise, breech presentation
Interventions	Nifedipine 30 mg administered orally followed by 20 mg in 2 h if uterine contractions persisted, followed by 20 mg orally every 6 h vs ritodrine 50 µg/min administered by IV infusion, followed by 10 mg orally every 4–6 h if contractions stopped
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, GA at birth, SAEs, stillbirth, neonatal death before 28 d, neonatal death before 7 d, birth before 34 weeks, birth before 37 weeks, headache, hypotension, palpitations, perinatal death, nausea or vomiting, mean birthweight, birthweight < 2000 g, birthweight < 2500 g, respiratory morbidity, neurodevelopmental morbidity, cessation of treatment due to AEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women excluded post-randomisation as refused intervention (ritodrine arm) (< 10%). All other women included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Amorim 2009

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	54 women were randomised from 2 centres in Brazil between August 2003 and January 2004 Population: women with threatened preterm birth between 24+0 and 34+0 weeks and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 30 min and cervical change

Amorim 2009 *(Continued)*

	Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding), complications requiring immediate birth, maternal medical conditions (pre-eclampsia, diabetes), a fetus showing signs of non-reassuring well-being, malformation, demise, prior tocolytic use
Interventions	Nifedipine 10 mg sublingually, with an additional 10 mg in 30 min if required, followed by 20 mg every 6 h for 24 h after contractions stopped vs nitro-glycerine 10 mg administered transdermally, with an additional 10 mg in 6 h if required for 24 h for 24 h after contractions stopped
Outcomes	Delay in birth by 48 h, hypotension, tachycardia, nausea or vomiting, headache
Notes	If effective tocolysis was not achieved with any of the drugs within 12 h, the participants were administered 250 mg of terbutaline SC, as per the customary procedure. In cases of a recurrence of premature labour, the standard treatment with nifedipine was used at a dose of 10 mg sublingually, which could be repeated if the contractions did not disappear within 30 min, then 20 mg orally every 6 h. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomisation
Allocation concealment (selection bias)	Unclear risk	Unclear. Quote: "randomly assigned to receive tocolytic therapy with either transdermal nitroglycerin or nifedipine (orally sublingually), thus ensuring that the allocation was concealed."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. Quote: "both the participants and the doctors and researchers were aware of which medication was being used"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded. Quote: "both the participants and the doctors and researchers were aware of which medication was being used"
Incomplete outcome data (attrition bias) All outcomes	High risk	4 women were excluded from the analysis due to protocol violations or maternal medical conditions (3 in the nitroglycerin arm and 1 in the nifedipine arm), all other women were included in the analysis. > 10% in 1 arm
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Ara 2008

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	89 women were randomised across 2 centres in Bangladesh between January 2005 and December 2008 Population: women with threatened preterm birth between 30+0 and 34+0 weeks' gestation with a singleton pregnancy and intact membranes Definition of threatened preterm birth: at least 4 contractions in 30 min and cervical dilatation < 3 cm

Ara 2008 *(Continued)*

	Exclusion criteria: contraindications for tocolysis (severe vaginal bleeding or suspected intrauterine infection), severe pulmonary embolism, oligohydramnios, or a fetus showing signs of growth restriction. Women were screened for genital infection but no further details are reported.
Interventions	Nifedipine 20 mg administered orally and 10 mg sublingually followed by 20 mg every 4-6 h titrated to uterine contractions vs placebo
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, headache, birth before 37 weeks
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Lottery method was used
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Aramayo 1990

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	30 women were randomised from 1 centre in Mexico between March 1988 and November 1989 Population: women with threatened preterm birth between 28+0 and 36+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 3 contractions in 10 min with cervical dilation of at least 1-2 cm Exclusion criteria: maternal disease (cardiac) or medical conditions (pneumonia, arrhythmia, tachycardia, bradypnoea), a fetus showing signs of non-reassuring well-being, malformation, demise, ruptured membranes, cervical incompetence

Aramayo 1990 *(Continued)*

Interventions	Terbutaline 1.25 mg administered via IV infusion and titrated to contractions, followed by 5 mg orally 3 h after contractions had stopped, every 8 h. Magnesium sulphate 4 g administered IV bolus followed by 2 g/h titrated to contractions
Outcomes	Delay in birth by 48 h, birth before 37 weeks
Notes	Recurrences were treated with the same agent in each case and the treatment restarted from the beginning COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 woman was excluded for fetal distress, all other women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Unclear risk	Baseline characteristics NR. No other bias reported

Asgharnia 2002

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	120 women were randomised from 1 centre in Iran in June-December 2001 Population: women with threatened preterm birth between 24+0 to 32+0 weeks' gestation with intact membranes Definition of threatened preterm birth: contractions with cervical dilation of 2 cm Exclusion criteria: contraindication to tocolysis (severe vaginal bleeding), ruptured membranes, uterine or placental abnormalities, cervical dilation > 5 cm, allergy to study medications

Asgharnia 2002 *(Continued)*

Interventions	Indomethacin 25 mg administered orally every 6 h for 24 h vs magnesium sulphate 4 g administered by IV bolus followed by 2 g/h infusion until contractions ceased
Outcomes	Delay in birth by 48 h, SAEs, maternal infection, cessation of treatment due to AEs, maternal death, pulmonary oedema
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. Quote: "Of course, due to two types of treatments both patients and doctors were informed"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded. Quote: "Of course, due to two types of treatments both patients and doctors were informed" Quote: "Gynaecologist examined the mothers' side effects…. and paediatricians examined the babies' side effects"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Beall 1985

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	167 women were randomised from 1 centre in the USA between March 1983 and July 1984 Population: women with threatened preterm birth between 24+0 and 36+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: 1 contraction in 10 min Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), ruptured membranes, estimated fetal weight < 500 g or > 2500g, maternal medical conditions (hypertension, diabetes, hyperthyroidism, cervical dilation > 4 cm, a fetus showing signs of malformation or demise, complication requiring immediate birth, allergy to study medications, multiple pregnancy

Beall 1985 *(Continued)*

Interventions	Ritodrine 100 µg/min IV infusion and increased by 50% every 10 min and titrated to contraction and AEs with a maximum of 350 µg/min and maintained for 12 hours after contractions stopped followed by 2.5 mg terbutaline orally until 36 weeks' gestation vs terbutaline 20 µg/min IV infusion and increased by 50% every 10 min and titrated to contraction and AEs with a maximum of 70 µg/min and maintained for 12 hours after contractions stopped followed by 2.5 mg terbutaline orally until 36 weeks' gestation vs magnesium sulphate 4 g via IV bolus over 20 min and increased by 0.5 g/h every 30 min and titrated to uterine contractions or AEs with a maximum of 3.5 g/h and continued for 12 hours after contractions stopped followed by 2.5 mg terbutaline orally until 36 weeks' gestation
Outcomes	Delay in birth by 48 h, SAEs, maternal death, pulmonary oedema, perinatal death, stillbirth, neonatal death < 7 d
Notes	Women could receive rescue tocolysis in the event of failure. Women in ritodrine or terbutaline group would receive magnesium sulphate in the event of failure, women in the magnesium sulphate group were randomised (2nd randomisation) to either terbutaline or ritodrine in the event of treatment failure. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Administered by hospital pharmacist in a blinded fashion
Blinding of participants and personnel (performance bias) All outcomes	High risk	Magnesium sulphate was not blinded but ritodrine and terbutaline were blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Magnesium sulphate was not blinded but ritodrine and terbutaline were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	37 women were excluded (including 31 protocol violations in exclusion criteria and 6 in treatment protocol, 8 additional women were lost to follow-up). All other women were included in the per-protocol analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Besinger 1991

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	40 women were randomised from 2 centres in the USA between March 1987 and September 1988

Besinger 1991 *(Continued)*

	Population: women with threatened preterm birth between 23+0 and 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min or 8 in 60 min with cervical change > 2 cm dilation or > 75% effacement Exclusion criteria: ruptured membranes, cervical suture in place, cervical dilation > 4 cm. All women were screened for GBS, gonorrhoea, chlamydia and mycoplasma
Interventions	Ritodrine 100 µg-350 µg/min administered IV and titrated to uterine contractions for 8-12 h after contractions had stopped followed by 2.5-5.0 mg orally titrated to contractions and maternal AEs every 4-6 h until 35 weeks' gestation vs indomethacin 50 mg orally followed by 25-50 mg every 4 h until contractions stopped, followed by 25 mg every 4-6 h until 35 weeks' gestation
Outcomes	Delay in birth by 48 h, delay by 7 d, pregnancy prolongation, GA at birth, palpitations, perinatal death, nausea or vomiting, dyspnoea, SAEs, cessation of treatment due to AEs, headache, mean birthweight, neurodevelopmental morbidity, neonatal death before 28 d
Notes	Rescue tocolysis could be given if maximum drug dose given and progression of labour or intolerable AEs. Magnesium sulphate 4 g bolus IV followed by 2-4 g/h for 8-12 hours after contractions stopped (and the initial tocolytic stopped), if successful original oral maintenance therapy given. 12 women received magnesium sulphate - 6 in each arm received magnesium sulphate. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	3 women were excluded from the analysis (2 in ritodrine arm not followed as per protocol and 1 eliminated in indomethacin arm due to abruption) - all other women are included in the analysis. 10% in 1 arm
Selective reporting (reporting bias)	Unclear risk	The study protocol as unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Bisits 1998

Study characteristics

Bisits 1998 *(Continued)*

Methods	2-arm RCT, active-controlled
Participants	26 women were randomised from 1 centre in Australia (dates NR) Population: women with threatened preterm birth between 24+0 and 34+0 weeks' gestation with a singleton pregnancy Definition of threatened preterm birth: painful regular uterine contractions at least every 5 min Exclusion criteria: contraindications of tocolysis (suspected intrauterine infection or severe vaginal bleeding), rapidly progressing labour, multiple pregnancy, cervical dilation of ≥ 5 cm, maternal medical disease (hypotension, uncontrolled diabetes, cardiac disease), contraindications to study medications, a fetus showing signs of non-reassuring well-being
Interventions	Glyceryl trinitrate 10 mg administered transdermally for 12 h, followed by an additional patch in 1 h if contractions continued, patches replaced every 24 h if required. If uterine activity continued standard tocolytic treatment (IV albuterol) was commenced and patch removed vs albuterol 25 mcg/min administered by IV infusion and titrated to uterine contractions and AEs and reduced when contractions ceased
Outcomes	Birth < 37 weeks, palpitations, headache, dyspnoea, nausea or vomiting, cessation of treatment due to AEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Opaque sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Bisits 2004

Study characteristics

Bisits 2004 *(Continued)*

Methods	2-arm RCT, active-controlled
Participants	238 women were randomised across 4 tertiary obstetric hospitals in Singapore, Hong Kong and Australia between April 1997 and May 2000. Population: women with threatened preterm birth between 24+0 and 35+0 weeks' gestation with a singleton pregnancy Definition of threatened preterm birth: ≥ 2 uterine contractions in 10 min with a positive test for fFn or ruptured membranes Exclusion criteria: contraindications for tocolysis (suspected intrauterine infection), multiple pregnancy, cervical dilatation ≥ 5 cm or more, negative fFN test in the presence of intact membranes
Interventions	Salbutamol or ritodrine according to local practice vs glyceryl trinitrate 50 mg transdermally with an additional 50 mg patch in 1 h if contractions continued, patches remained on for 12 h. If the contractions continued after 2 h patches were removed and b2 sympathomimetic treatment commenced
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, neonatal death before 28 d, SAEs, cessation of treatment due to AEs, birth < 37 weeks, perinatal death, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity
Notes	COI: NR Funding from the Australian Council

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women were lost to follow-up, 1 in each arm (< 10%). All other women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Borna 2007

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	104 women were randomised from 1 centre in Iran between September 2003 and September 2004. Population: women with threatened preterm birth between 24+0 and 34+0 weeks' gestation with a singleton pregnancy and intact membranes Definition of threatened preterm birth: at least 4 uterine contractions in 20 min or eight in 60 min with cervical dilatation (< 4 cm) or cervical effacement Exclusion criteria comprised contraindication to tocolysis (suspected intrauterine infection), maternal medical complication such as renal or hepatic dysfunction, platelet or coagulation disorders, history of peptic ulcer disease, or the use of fluconazole, placenta or amniotic fluid abnormalities, cervical dilatation > 4 cm, a fetus showing signs of non-reassuring well-being or malformations
Interventions	Magnesium sulphate 4–6 g administered as an IV bolus followed by an infusion of 2–4 g/h for a maximum of 48 h vs celecoxib 100 mg administered orally twice day for a maximum of 48 h
Outcomes	Delay in birth by 48 h, GA at birth, mean birthweight, SAEs, hypotension, tachycardia, pulmonary oedema
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Low risk	Assigned by a third party
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "investigators and patients were blinded as to which preparation the patient was taking"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "investigators and patients were blinded as to which preparation the patient was taking"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Bracero 1991

Study characteristics

Bracero 1991 *(Continued)*

Methods	2-arm RCT, active-controlled
Participants	49 women were randomised across centres in the USA (number NR) between January 1987 and June 1988. Population: women with threatened preterm birth between 20+0 and 36+0 weeks' gestation with a singleton pregnancy and intact membranes Definition of threatened preterm birth: cervical dilatation of ≥ 2 cm, or effacement ≥ 80%, or regular uterine contractions of ≥ 2 in 10 min Exclusion criteria comprised contraindications to ritodrine or nifedipine, cervical dilation of > 4 cm, ruptured membranes, multiple pregnancy. Urinary tract infection was detected in 4 women (1 ritodrine group and 3 nifedipine group)
Interventions	Ritodrine 0.1 mg/min and increased by 0.05 mg/min every 10 min titrated to contractions with a maximum of 0.35 mg/min. The effective dose was maintained for 12 h, followed by 10 mg orally every 2 h for 24 h, then 10 mg every 4 h for 24 h, then 10-20 mg every 4 to 6 h vs nifedipine 30 mg administered orally followed by 20 mg every 6 h for 24 h, then every 8 h for 24 h, then every 8-12 h
Outcomes	Pregnancy prolongation, GA at birth, headache, nausea or vomiting, tachycardia, hypotension, palpitations, stillbirth, perinatal death, mean birthweight, respiratory morbidity, gastrointestinal morbidity, neonatal infection, neonatal death before 7 d, SAEs, dyspnoea, maternal infection, cessation of treatment due to AEs, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	7 women excluded from analyses dues to loss to follow-up, or discontinuation of treatment - remaining women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Cabar 2008

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	80 women were randomised from 1 centre in Brazil (dates NR). Population: women with threatened preterm birth with singleton pregnancy and intact membranes between 23+0 and 33+6 weeks' gestation Definition of threatened preterm birth: regular uterine contractions, cervical dilatation between 1-3 cm, cervical effacement > 50% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), any maternal, fetal or placental diseases, abnormal amniotic fluid volume or cervical incompetence, a fetus showing signs of growth restriction
Interventions	Atosiban 6.75 mg administered via IV bolus followed by 300 µg/min for 3 h, then 100 mcg/min for 3.5 h. If contractions persisted, 100 µg/min for 12 h with a total treatment time of up to 48 h vs terbutaline 20 mL/h administered by IV infusion. If contractions continued dose was increased by 20 mL/h until they stopped, this was maintained for 24 h
Outcomes	Birth before 34 weeks, stillbirth, perinatal death, birth before 37 weeks, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, tachycardia, dyspnoea, birth before 28 weeks, SAEs, pregnancy prolongation, neonatal death before 28 d, delay in birth by 7 d
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics are similar. No other bias reported

Canadian Preterm Labor Investigators 1992

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	708 women were randomised across 6 centres in Canada between December 1985 and June 1990 Population: women with threatened preterm birth between 20+0 and 35+0 weeks' gestation Definition of threatened preterm birth: ≥ 4 regular uterine contractions in 20 min or 6 in 60 min, or any contractions with cervical dilatation > 2 cm or effacement > 50% or ruptured membranes Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), serious maternal disease e.g. cardiovascular disease, hyperthyroidism, uncontrolled diabetes mellitus, asthma, severe pre-eclampsia, any maternal contraindication to study medication, any condition requiring immediate delivery, a fetus showing signs of non-reassuring well-being, malformations or demise
Interventions	Ritodrine 10-70 mL/h administered by IV infusion and titrated to contractions every 15 min with a maximal rate of 0.35 mg/min. The effective dose was maintained for 6 h and reduced followed by up to 12 x 10 mg tablets orally for 5 d vs placebo 10-70 mL/h administered by IV infusion titrated to contractions every 15 min and maintained for 6 h and decreased, followed by up to 12 placebo tablets/d orally for 5 d. Previous treatment was recommenced if required.
Outcomes	Palpitations, maternal death, birthweight < 2500 g, pulmonary oedema, neonatal infection, birth before 37 weeks, stillbirth, perinatal death, GA at birth, nausea or vomiting, neurodevelopmental morbidity, mean birthweight, headache, delay in birth by 48 h, respiratory morbidity, neonatal death before 7 d, arrhythmias, birth before 32 weeks, dyspnoea, pregnancy prolongation, neonatal death before 28 d, delay in birth by 7 d, cessation of treatment due to AEs
Notes	No COI Funding from the Canadian Medical Research Council

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "Patients, physicians, and nurses were blinded to the women's treatment allocation."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "All outcomes were ascertained by personnel blinded to the women's treatment assignment."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.

Canadian Preterm Labor Investigators 1992 *(Continued)*

Other bias	Unclear risk	Baseline characteristics NR. No other obvious bias reported

Cararach 2006

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	80 women were randomised across centres in Spain (number and dates NR) Population: women with threatened preterm birth between 22+0 and 35+0 weeks' gestation with a singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 2 uterine contractions in 10 min Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), cervix dilatation > 5 cm, polyhydramnios, contraindication to study medications or previous tocolysis use in current pregnancy, a fetus showing signs of non-reassuring fetal well-being, intrauterine growth restriction or malformations
Interventions	Nifedipine 30 mg (10 mg administered sublingually and 20 mg orally) followed by 20 mg every 6 h and discontinued if contractions ceased for 48 h vs ritodrine 50 µg every 20 min administered by IV infusion and titrated to contraction or AEs with a maximum dose of 350 µg/min. The effective dose was maintained for 2 d and followed by 10 mg every 6 h orally. Treatment was resumed if required.
Outcomes	Birthweight < 2500 g, neonatal infection, pulmonary oedema, stillbirth, birth before 37 weeks, perinatal death, GA at birth, hypotension, nausea or vomiting, neurodevelopmental morbidity, headache, mean birthweight, respiratory morbidity, neonatal death before 7 d, tachycardia, dyspnoea, SAEs, pregnancy prolongation, cessation of treatment due to AEs, neonatal death before 28 d, delay in birth by 7 d
Notes	No COI Funding from the Spanish Ministry of Health

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. Quote: "Clinicians were not blinded to the study group in which the women were allocated"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women lost to follow-up and excluded from analysis. All other women included

Cararach 2006 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Christensen 1980

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	30 women were randomised from 1 centre in Sweden between February 1977 and December 1978 Population: women with threatened preterm birth between 28+0 to 36+0 weeks' gestation with ruptured membranes and singleton pregnancy Definition of threatened preterm birth: preterm rupture of membranes Exclusion criteria comprised contraindications to tocolysis (suspected intrauterine infection), cervical dilation > 4 cm, multiple pregnancy. 3 women had urinary tract infections and were treated.
Interventions	Ritodrine 100 µg/min administered by IV infusion and titrated to uterine contractions at 10-min intervals by 50 µg/min, up to a maximum of 400 µg/min for 24 h, followed by oral ritodrine 20 mg 3 times/d until 35+6 weeks. Placebo administered by IV infusions for 24 h, followed by oral placebo 3 times/d until 35+6 weeks
Outcomes	Delay by 48 h, delay by 7 d, SAEs, maternal infection, neonatal death before 7 d, respiratory morbidity, neonatal infection
Notes	6 women were given a second infusion of ritodrine, as uterine contractions recurred during oral treatment. COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly numbered medication packs
Allocation concealment (selection bias)	Low risk	Coded medications allocated sequentially
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind - identical placebo used
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "The code key was not available to the investigators before completion of the study."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.

Christensen 1980 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Colon 2016

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	30 women were randomised from 2 tertiary centres in the USA Population: women between 24+0 and 34+0 weeks' gestation with threatened preterm birth Definition of threatened preterm birth: vaginal bleeding and uterine contractions or irritability Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), established preterm labour or premature rupture of membranes, maternal medical conditions such as coagulopathy, renal disease, myasthenia gravis, a fetus showing signs of non-reassuring well-being or malformations
Interventions	Magnesium sulphate 4 g administered by IV bolus followed by 2 g/h. Further 2-4 g could be administered at the discretion of the treating physician vs placebo
Outcomes	GA at birth, perinatal death, pulmonary oedema, neonatal infection, mean birthweight, headache, nausea or vomiting, delay in birth by 48 h, respiratory morbidity, neonatal death before 7 d, neonatal death before 28 d, pregnancy prolongation, SAEs, dyspnoea
Notes	No COI Funded by Stanford University

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Opaque, sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Woman's treating physician and nurse team were blinded to allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	NR but assumed blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis

Colon 2016 *(Continued)*

Selective reporting (reporting bias)	Low risk	The study report matches the study report that was registered prospectively: NCT00186069
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Cotton 1984

Study characteristics	
Methods	3-arm RCT, placebo-controlled
Participants	56 women were randomised from a centre in the USA (dates NR) Population: women between 26+0 and 34+0 weeks' gestation with threatened preterm birth Definition of threatened preterm birth: uterine contractions > 3 in 10 min and cervical examination revealing active labour Exclusion criteria were cervical dilatation > 4 cm
Interventions	Magnesium sulphate 4 g administered by IV bolus over 15 min followed by 2 g/h vs terbutaline 9.2 µg/min administered by IV infusion and increased by 5 µg titrated to contractions with a maximum of 25.3 µg/min vs placebo at 125 mL/h
Outcomes	Maternal death, mean birthweight, neonatal infection, pulmonary oedema, perinatal death, birth before 37 weeks, GA at birth, neurodevelopmental morbidity, gastrointestinal morbidity, birthweight < 2500 g, birthweight < 2000 g, delay in birth by 48 h, respiratory morbidity, tachycardia, arrhythmias, maternal infection, cessation of treatment due to AEs, pregnancy prolongation, neonatal death before 28 d, delay in birth by 7 d
Notes	No COI reported Funding from the National Institute of Health

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis

Cotton 1984 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Cox 1990

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	156 women were randomised from 1 centre in the USA between October 1987 and May 1989 Population: women between 24+0 and 34+0 weeks of gestation with threatened preterm birth and intact membranes Definition of threatened preterm birth: regular uterine contractions with cervical dilatation up to 5 cm Exclusion criteria: maternal or fetal complications requiring delivery
Interventions	Magnesium sulphate 4 g administered by IV bolus followed by 2 g/h for 24 h vs placebo at 80 mL/h for 24 h
Outcomes	Palpitations, GA at birth, perinatal death, mean birthweight, neurodevelopmental morbidity, gastrointestinal morbidity, delay in birth by 48 h, stillbirth, respiratory morbidity, arrhythmias, neonatal death before 28 d, cessation of treatment due to AEs, delay in birth by 7 d, pregnancy prolongation, birthweight < 2500 g, birthweight < 2000 g, birth before 37 weeks, neonatal infection, hypotension, nausea or vomiting, pulmonary oedema, headache, maternal death, birth before 34 weeks, tachycardia, neonatal death before 7 d, SAEs, dyspnoea, maternal infection, birth before 32 weeks
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Consecutively numbered, opaque, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis

Cox 1990 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

de Heus 2009

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	40 women were randomised from centres in the Netherlands (number NR) between October 2003 and June 2006 Population: women with threatened preterm birth between 25+0 and 33+0 weeks' gestation with singleton pregnancy Definition of threatened preterm birth: not defined Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection, severe vaginal bleeding), a fetus showing signs of malformation, previous tocolysis treatment
Interventions	Atosiban 6.75 mg administered via IV bolus, followed by 300 mg/min for 3 h, followed by 100 mg/min for 48 h vs nifedipine 10 mg every 15 min, followed 30 mg every 8 h for up to 48 h and gradually reduced
Outcomes	The study did not report any outcomes of interest
Notes	4 women received escape tocolysis within the first 24 h - no detail reported on what tocolysis was received No COI Funded by Ferring pharmaceuticals BV

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded. Quote: "the video tapes were analysed blindly and in a random order"
Incomplete outcome data (attrition bias) All outcomes	High risk	9 women were excluded after randomisation - 3 in atosiban arm and 6 in nifedipine arm due to escape tocolysis or rapid progress in to labour

de Heus 2009 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Funded by Ferring pharmaceuticals BV. No other bias reported

Ehsanipoor 2011

Study characteristics	
Methods	2 arm RCT, placebo-controlled
Participants	50 women were randomised across 2 centres in the USA Population: women between 24+0 and 31+6 weeks' gestation with threatened preterm birth, with a singleton pregnancy and ruptured membranes Definition of threatened preterm birth: confirmed ruptured membranes within 24 h Exclusion criteria: 6 uterine contractions in 1 h or cervical dilation > 3 cm, contraindication for tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical complications, multiple pregnancy, previous corticosteroid therapy, previous tocolysis use after rupture of membranes, a fetus showing signs of non-reassuring well-being, malformations, or maternal or fetal indication for delivery
Interventions	Indomethacin 50 mg administered rectally followed by 25 mg administered orally every 6 h for 48 h vs placebo administered rectally and orally every 6 h for 48 h
Outcomes	Delay in birth by 48 h, maternal infection, pregnancy prolongation, neonatal death before 28 d, delay in birth by 7 d, respiratory morbidity, gastrointestinal morbidity, neurodevelopmental morbidity , GA at birth, perinatal death, stillbirth, neonatal infection
Notes	COI: NR Funding from MemorialCare Foundation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Consecutively numbered, opaque, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "The subjects and all providers were blinded to which drug was given"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "The subjects and all providers were blinded to which drug was given"
Incomplete outcome data (attrition bias)	Low risk	2 women were lost to follow-up (1 in each arm), 1 woman did not receive the intervention, all others were included in the analysis

Ehsanipoor 2011 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

El Sayed 1999

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	31 women were randomised from 1 centre in the USA Population: women with threatened preterm birth before 35+0 weeks' gestation Definition of threatened preterm birth: ≥ 2 uterine contractions in 10 min, with cervical change or ruptured membranes Exclusion criteria: contraindications of tocolysis (severe vaginal bleeding), cervical dilation > 4 cm, placenta praevia, hypertension, a fetus showing signs of severe fetal growth restriction, non-reassuring fetal well-being or lethal malformations
Interventions	Magnesium sulphate 4 g administered as an IV bolus followed by infusion of 2 g/h titrated to contractions with a maximum of 4 g/h vs nitroglycerin 100 mg administered as an IV bolus followed by infusion of 1 mg/kg/min titrated to contractions with a maximum of 10 mg/kg/min
Outcomes	Cessation of treatment due to AEs, nausea or vomiting, palpitations, dyspnoea, headache, hypotension
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Third party
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	One woman was lost to follow-up. All other women were included in the analysis.

El Sayed 1999 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol provides very limited details - unable to clarify
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported.

European Atosiban Study 2001

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	245 women were randomised from 31 sites in the Czech Republic (9), Denmark (2), Sweden (8) and UK (12) between March 1994 and December 1996 Population: women between 23+0 and 33+0 weeks' gestation with threatened preterm birth and intact membranes Definition of threatened preterm birth: regular contractions of > 4 in 30 min lasting for > 30 s each and cervical dilation of ≤ 3 cm and effacement of > 50% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), triplets or more, ruptured membranes, NSAID use for tocolysis within previous 12 h, severe pre-eclampsia or hypertension or serious maternal medical disease, drug or alcohol misuse, urinary tract infection or retained intrauterine device, placental, amniotic fluid or uterine abnormalities, or a fetus showing signs of intrauterine growth restriction, non-reassuring well-being, demise or major malformations; contraindication to the use of terbutaline or any of the components of the study drugs; participation in a clinical trial of experimental drug within 30 d
Interventions	Atosiban IV bolus dose (6.75 mg in 0.9 mL normal saline), followed by an IV infusion of 300 mg/min atosiban in 5% dextrose for the first 3 h and then 100 mg/min atosiban in 5% dextrose for up to 18 h. Separately but simultaneously, a placebo IV infusion was administered. Both IV infusions were given for the same period of time. vs placebo administered as a single bolus injection followed by an IV infusion of placebo at a rate corresponding to the atosiban infusion (see above). Separately but simultaneously, terbutaline was given as an IV infusion in 5% dextrose at 10–25 mg/min. Both infusions ran for up to 18 h
Outcomes	Palpitations, neonatal infection, perinatal death, stillbirth, GA at birth, nausea or vomiting, hypotension, mean birthweight, headache, neurodevelopmental morbidity, delay in birth by 48 h, respiratory morbidity, tachycardia, dyspnoea, delay in birth by 7 d, birth before 28 weeks, neonatal death before 28 d, cessation of treatment due to AEs, SAEs
Notes	No COI This study was funded by Ferring Pharmaceuticals

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation stratified by GA < 28 weeks and > 28 weeks
Allocation concealment (selection bias)	Unclear risk	NR

European Atosiban Study 2001 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind. Quote: "Through the use of a double-blind, double-dummy technique, the utmost effort was made to keep the study blinded"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "Through the use of a double-blind, double-dummy technique, the utmost effort was made to keep the study blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 woman in the atosiban group was subsequently lost to follow-up (no delivery data available). 4 women in the terbutaline group did not receive treatment so were not analysed.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Ferguson 1984

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	50 women were randomised from 1 centre in the USA between August 1982 and January 1983 Population: women with threatened preterm birth before 36+0 weeks' gestation Definition of threatened preterm birth: regular uterine contractions and cervical change Exclusion criteria: instances where tocolysis would be detrimental to the mother or not beneficial to the fetus
Interventions	Ritodrine 50 µg/min and increased every 10-15 min and titrated to uterine contractions and AEs with a maximum of 350 µg/min plus magnesium sulphate 8.4 g/h in the 1st h followed by 4.8g/h I the 2nd h and 2.4 g/h in the following h followed by followed by oral ritodrine or terbutaline vs ritodrine 50 µg/min and increased every 10-15 min and titrated to uterine contractions and AEs with a maximum of 350 µg/min and placebo with the same regime as magnesium sulphate followed by oral ritodrine or terbutaline
Outcomes	Cessation of treatment due to AEs
Notes	No COI Funded by National Institute for Health grants

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Previously randomised file
Allocation concealment (selection bias)	Low risk	Sealed envelope

Ferguson 1984 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "both the magnesium sulphate and placebo solutions were labelled study solutions and were visually indistinguishable"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "both the magnesium sulphate and placebo solutions were labelled study solutions and were visually indistinguishable"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Ferguson 1990

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	66 women were randomised from 1 centre in the USA from July 1984-August 1987. Population: women with threatened preterm birth before 36+0 weeks' gestation Definition of threatened preterm birth: ≥ 8 uterine contraction in 1 h with cervical change Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (cardiac, hyperthyroidism, pre-eclampsia), multiple pregnancy, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, malformation or demise, cervical dilation > 4 cm, previous tocolytic use in the current pregnancy
Interventions	Nifedipine 10 mg administered orally followed by 20 mg every 20 min titrated to uterine contractions with a maximum of 40 mg in the first h, followed by 20 mg every 4-6 h vs ritodrine 50 µg/min administered by IV bolus and titrated to uterine contractions every 15-30 min with a maximum of 350 µg/min and decreased until 100 µg/min once contractions ceased followed by 10-20 mg/h every 4-6 h
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 37 weeks, neonatal death before 28 d, SAEs, cessation of treatment due to AEs, pulmonary oedema, palpitations, arrhythmias, perinatal death, stillbirth, neonatal death before 7 d, neurodevelopmental morbidity
Notes	If tocolysis failed or AEs were not tolerated women could receive the other study drug - 10 women were switched to the other study drug (5 in each arm) 2 women also received a single dose of IM terbutaline prior to enrolment (discovered after randomisation) - included in evaluation of tocolytic success and neonatal outcome analysis No COI Funded by National Institute for Health grants
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**

Ferguson 1990 *(Continued)*

Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 woman withdrew from study, 1 woman was withdrawn as she stopped taking maintenance tocolysis, women with ruptured membranes received tocolysis for 48 h and no longer and birth was initiated within 7 d. All the remaining women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Floyd 1992

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	90 women were randomised from 1 centre in the USA, study dates NR Population: women with threatened preterm birth between 20+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 1 contractions in 10 min, and cervical change with dilation > 2 cm Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), maternal medical condition or complication, multiple pregnancy, ruptured membranes, allergy to study drugs, previous tocolysis use in current pregnancy
Interventions	Nifedipine 30 mg orally followed by 20 mg every 8 h until contractions had stopped followed by 20 mg every 8 h until 37 weeks' gestation vs magnesium sulphate 4 g administered via IV bolus over 20 min followed by 4-6 g/h and titrated to uterine contractions and continued for 6 h after cessation followed by 2 g orally every 4 h until 37 weeks
Outcomes	Birthweight < 2500 g, birth before 34 weeks, stillbirth, perinatal death, hypotension, neonatal death before 7 d, SAEs, pregnancy prolongation, cessation of treatment due to AEs, neonatal death before 28 d
Notes	No COI reported. Funded by Vicksburg Hospital
Risk of bias	

Floyd 1992 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Fox 1993

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	90 women were randomised from 1 centre in the USA. Population: women aged 15-45 years between 34+0 and 36+6 weeks' gestation with threatened preterm birth Definition of threatened preterm birth: documented preterm labour with cervical change Exclusion criteria: NR
Interventions	Magnesium sulphate 4 g administered IV as a bolus, followed by 2-4 g/h until uterine contractions ceased, followed by oral magnesium gluconate until 37 weeks of gestation vs no treatment
Outcomes	Stillbirth, perinatal death, GA at birth, neurodevelopmental morbidity, mean birthweight, gastrointestinal morbidity, delay in birth by 48 h, respiratory morbidity, SAEs, pregnancy prolongation, cessation of treatment due to AEs, neonatal death before 28 d
Notes	No COI reported Funded by Vicksburg Hospital

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Fox 1993 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported.

Francioli 1988

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	24 women were randomised (number of centres, study country and dates NR) Population: women with threatened preterm birth between 28+0 and 36+0 weeks' gestation with intact membranes Definition of threatened preterm birth: not defined Exclusion criteria: cervical dilation > 2 cm, multiple pregnancy or cervical incompetence or suture
Interventions	Hexoprenaline sulphate administered IV (dose NR) vs hexoprenaline sulphate and magnesium hydrochloride administered IV infusion 40 mmol/500 mL, at the rate of 1-2 bottles/24 h for 3 d titrated to uterine contractions, followed by magnesium therapy 15 mmol and hexoprenaline sulphate (dose NR) orally according to contractions
Outcomes	Delay in birth by 7 d, mean birthweight, birthweight < 2000 g, birthweight < 2500 g, pregnancy prolongation, cessation of treatment due to AEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR

Francioli 1988 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

French and Australian Atosiban Investigators 2001

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	241 women were randomised across 31 centres in France and 5 centres in Australia (between February 1994 and February 1997). Population: women with threatened preterm birth between 23+0 and 33+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 uterine contractions in 30 min lasting for ≥ 30 s and cervical dilation of ≤ 3 cm and effacement of ≥ 50%. Exclusion criteria: triplets or more, ruptured amniotic membranes, major vaginal bleeding, previous tocolysis (use of NSAIDs within previous 12 h (Australia only), and use of beta-agonists within previous 30 min, and NSAIDs or calcium channel blockers within previous 24 h (France only)), severe pre-eclampsia or hypertension, fever > 37.5 °C, urinary tract infection, fetal/placental abnormalities (suspected chorioamnionitis, placental abruption, placenta praevia, intrauterine growth retardation, fetal distress/death, major congenital anomaly, hydramnios, retained intrauterine device), serious maternal disease (cardiovascular disease, symptomatic hyperthyroidism, uncontrolled diabetes mellitus, phaeochromocytoma, asthma), any contraindication to the use of salbutamol, alcohol or drug abuse, history of hypersensitivity to any of the components of the study drugs, participation in a clinical trial of an experimental drug within the previous month, significant renal impairment (Australia only)
Interventions	Atosiban 6.75 mg bolus administered IV, followed by IV infusion 300 µg/min for 3 h then 100 µg/min for up to 48 h in total vs salbutamol administered IV at 5-25 µg/min (France) or 2.5-45 µg/min (Australia) for up to 48 h, alongside placebo interventions corresponding to the atosiban regimen
Outcomes	Palpitations, pulmonary oedema, neonatal infection, stillbirth, perinatal death, GA at birth, hypotension, nausea or vomiting, neurodevelopmental morbidity, headache, mean birthweight, delay in birth by 48 h, respiratory morbidity, tachycardia, dyspnoea, SAEs, neonatal death before 28 d, delay in birth by 7 d

French and Australian Atosiban Investigators 2001 *(Continued)*

Notes	If re-treatment was required, the same agent was given unless they had failed or did not tolerate the initial agent. No COI Funded by Ferring Pharmaceuticals

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised using computer-generated randomisation lists and stratified by GA (≤ 28 weeks and > 28 weeks)
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind. Quote: "This multicenter, double-blind, 'double-placebo'… trial"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 woman was lost to follow-up in the salbutamol arm.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar except more twins in the salbutamol arm. No other obvious bias reported

Gamissans 1982

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	153 women were randomised from 1 centre in Barcelona between January 1977 and August 1980 Population: women with threatened preterm birth between 20+0 and 36+0 weeks' gestation with intact membranes (or 24+0 to 34+0 if ruptured membranes) with singleton pregnancy Definition of threatened preterm birth: contractions or cervical effacement and dilation up to 4 cm Exclusion criteria: maternal medical condition (pre-eclampsia, renal disease, hypertensive disease) rhesus immunisation, peptic ulcer
Interventions	Ritodrine 200 µg/min administered via IV infusion and titrated to uterine contractions for 24 h plus placebo administered rectally, followed by ritodrine 10 mg administered orally or IM very 3-6 h until 38 weeks vs ritodrine 200 µg/min administered via IV infusion and titrated to uterine contractions for 24 h plus indomethacin 50 mg administered rectally, followed by ritodrine 10 mg administered orally or IM very 3-6 h until 38 weeks if intact membranes or 35 weeks with ruptured membranes

Gamissans 1982 *(Continued)*

Outcomes	Birth before 37 weeks, birthweight < 2500 g, tachycardia, perinatal death
Notes	Treatment continued until 38 weeks if intact membranes or 35 weeks with ruptured membranes COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind. Quote: "Placebo and indomethacin were given as suppositories of identical appearance in a double blind manner"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "the code key was not available to investigators"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics were similar. Not all women received steroids, only those randomised in the first 2 years of recruitment; criteria demonstrated that 33 women in the ritodrine and placebo group and 34 women in the ritodrine and indomethacin group would have benefited from steroids. No other bias reported

Ganla 1999

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	100 women were randomised from 1 centre in India between March 1997 and March 1998. Population: women with threatened preterm birth between 26+0 and 36+0 weeks' gestation Definition of threatened preterm birth: ≥ 1 regular uterine contractions in 10 min for at least 30 min Exclusion criteria: contraindications of tocolysis (indication of intrauterine infection or severe vaginal bleeding), tocolysis within the last 7 d, maternal medical conditions (diabetes, hyperthyroidism, cardiac disease, severe pregnancy-induced hypertension, eclampsia), cervical dilation > 3 cm, a fetus showing signs of non-reassuring well-being, severe intrauterine growth restriction, malformations
Interventions	Nifedipine 5 mg administered sublingually, and repeated until uterine contractions ceased, up to a maximum dose of 40 mg in the first 2 h of treatment, then 10 mg orally, 3 h after the last sublingual

Ganla 1999 *(Continued)*

	dose, repeated every 8 h for 48 h, then 10-20 mg orally every 12 h until 36 weeks of gestation vs isoxsuprine 60 mg administered IV at a rate of 0.5 mg/min increased to 10 mg/min, for 12 h after cessation of uterine contractions, then 10 mg IM every 8 h for 48 h, then 10-20 mg orally every 8 h until 36 weeks of gestation
Outcomes	Pulmonary oedema, hypotension, nausea or vomiting, headache, delay in birth by 48 h, respiratory morbidity, tachycardia, SAEs, pregnancy prolongation, cessation of treatment due to AEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported.

Garcia-Velasco 1998

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	52 women were randomised from 1 centre in the USA between January 1993 and January 1996. Population: women with threatened preterm birth between 26+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 30 min and cervical changes Exclusion criteria: contraindications of tocolysis (suspected intrauterine infection or severe vaginal bleeding), previous tocolytic treatment, cervical dilation of ≥ 3 cm, maternal medical condition contraindicating tocolytic therapy
Interventions	Nifedipine 10 mg administered sublingually and 20 mg orally, followed by 10-20 mg (route NR) every 4-6 h depending on uterine contractions vs ritodrine administered IV at 0.05 mg/min infusion, increas-

Garcia-Velasco 1998 *(Continued)*

	ing by 0.05 mg every 20 min until uterine contractions ceased or maternal heart rate was ≥ 120 bpm, up to a maximum dose of 0.35 mg/min, maintained for 12 h, then ritodrine 5 mg administered orally every 3 h
Outcomes	Palpitations, birthweight < 2500 g, stillbirth, perinatal death, birth before 37 weeks, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, neonatal death before 7 d, SAEs, cessations of treatment due to AEs, pregnancy prolongation, neonatal death before 28 d
Notes	Retreatment given with same study drug if required. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerised random number table
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Garite 1987

Study characteristics

Methods	2-arm RCT
Participants	79 women were randomised from 1 centre in the USA between January 1983 and September 1986 Population: women with threatened preterm birth between 25+0 and 30+6 weeks' gestation with singleton pregnancy and ruptured membranes Definition of threatened preterm birth: ruptured membranes Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), maternal or fetal condition requiring immediate birth, maternal disease (cardiac), medical conditions (diabetes, thyrotoxicosis)

Garite 1987 *(Continued)*

Interventions	Ritodine 150 µg/min IV and increased by 50 µg every 10 min and titrated to contractions or AEs for a maximum of 350 µg/min in 24 h followed by 10 mg orally every 3 h until 31 weeks' gestation vs no treatment
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, maternal infection, respiratory morbidity, neonatal infection, perinatal death, stillbirth, neonatal death
Notes	Women in the tocolysis group only received tocolysis if contractions commenced at ≥ 3 contractions in 20 min (23 women). No COI reported Funded by Long Beach Memorial Center

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Unclear risk	Baseline characteristics were similar. Tocolysis was only given when contractions started (59% of the tocolysis group). No other bias reported

George 1991

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	25 women were randomised from 1 centre in India (dates NR but conducted over a period of 10 months) Population: women with threatened preterm birth between 28+0 and 36+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 1 uterine contractions in 10 min lasting for ≥ 30 s and cervical dilation of < 2 cm

George 1991 *(Continued)*

	Exclusion criteria: contraindications to tocolysis (signs of intrauterine infection), maternal complication, premature rupture of membranes or polyhydramnios, signs of fetal malformation
Interventions	Nifedipine 30 mg administered orally, followed by 20 mg orally every 8 h for 48 h vs isoxuprine 40 mg administered IV over 4 h, followed by 30 mg IM every 24 h for 48 h
Outcomes	Delay in birth by 48 h, tachycardia, hypotension, birth before 37 weeks, respiratory morbidity, perinatal death
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Glock 1993

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	100 women were randomised from 1 tertiary care centre in the USA between January 1991 and February 1992 Population: women with threatened preterm birth between 20+0 weeks and 33+6 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 1 regular uterine contractions in 10 min with cervical change or cervical dilatation of ≥ 2 cm with regular uterine activity Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), maternal medical disease (diabetes, hyperthyroidism, cardiac disease, pre-eclampsia, renal

Glock 1993 *(Continued)*

	failure), previous tocolytic drug use in current pregnancy, hydramnios, cervical dilation of ≥ 4 cm, a fetus showing signs of non-reassuring well-being, growth restriction or malformation
Interventions	Nifedipine 10 mg administered sublingually, followed by 10 mg every 20 min, up to a maximal dose of 40 mg during the 1st h until uterine contractions ceased, followed by 20 mg orally, starting 4 h after the last sublingual dose, repeated every 4 h for 48 h, then 10 mg administered orally every 8 h until 34 weeks of gestation vs magnesium sulphate 6 g administered IV over 30 min, followed by an infusion of 2 g/h, increasing to a maximum rate of 4 g/h as needed to arrest labour for 24 h, then dose weaned by 0.5 g/h every 4-6 h, terbutaline 5 mg administered orally when magnesium sulphate infusion rate was 0.5 g/h and continued every 6 h until 34 weeks of gestation
Outcomes	Birth before 34 weeks, pulmonary oedema, stillbirth, birth before 37 weeks, perinatal death, GA at birth, headache, nausea or vomiting, hypotension, mean birthweight, delay in birth by 48 h, birth before 28 weeks, SAEs, cessation of treatment due to AEs, neonatal death before 28 d
Notes	If tocolytic agent was not suppressing cervical dilation then a second agent was substituted. 4 women receiving magnesium sulphate also received indomethacin. One woman receiving indomethacin received magnesium sulphate. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	20 women were excluded post-randomisation as they did not meet inclusion criteria, and were also excluded from the ITT analysis. Numbers were similar across both arms.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Goodwin 1994

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	120 women were randomised across 5 centres in the USA between February 1990 and January 1991

Goodwin 1994 *(Continued)*

	Population: women with threatened preterm birth between 20+0 to 36+6 weeks' gestation. Inclusion criteria differed slightly between the 5 sites. Definition of threatened preterm birth: ≥ 6 contractions in 1 h or > 4 contractions in 30 min with cervical dilatation up to 3 cm and no cervical change during observation period of > 1 h Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), ruptured membranes, a fetus showing signs of non-reassuring well-being, malformations or demise. 1 centre excluded multiple gestations.
Interventions	Atosiban administered IV, 300 µg/min continuously for 2 h vs placebo administered IV continuously for 2 h
Outcomes	Delay in birth by 48 h, GA at birth, mean birthweight, respiratory morbidity, headache, nausea or vomiting, SAEs
Notes	The same agent could be repeated if required. No COI Funded by RW. Johnson Pharmaceutical research

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation schedule with block size of 4
Allocation concealment (selection bias)	Low risk	Sequentially numbered, opaque, sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "The treatment assignment was not revealed to other people and the individual preparing the drug was not involved in the patient care"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "The treatment assignment was not revealed to other people"
Incomplete outcome data (attrition bias) All outcomes	Low risk	8 women (4 in each treatment group) were excluded post-randomisation as they did not meet inclusion criteria, withdrew their consent or did not receive treatment at the discretion of the investigator. All 8 were excluded from the efficacy analysis. 1 woman from each arm was excluded from the safety analysis (withdrew consent or did not receive the treatment as per her medical team)
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics were similar. No other obvious bias reported

Goodwin 1996

Study characteristics

Methods	5-arm RCT, active-controlled

Goodwin 1996 *(Continued)*

Participants	302 women were randomised across 15 centres in the USA Population: women with threatened preterm birth between 20+0 and 34+6 weeks' gestation with singleton pregnancy Definition of threatened preterm birth: ≥ 4 uterine contractions in 30 min and progressive cervical change (1 cm dilation or ≥ 50% cervical effacement under observation), 1-3 cm cervical dilation with ≥ 75% effacement or 3 cm dilation with ≥ 50% effacement also qualified as threatened preterm birth when accompanied by regular uterine activity Exclusion criteria: prior enrolment in the study, cervix dilated > 3 cm, multiple gestation, previously undiagnosed pre-eclampsia or blood pressure > 150/100 mm Hg, > 1 prior preterm labour episode for this pregnancy, prior tocolytic therapy within 72 h, temperature exceeding 100 °F (37.78 °C), urinary tract infection, trauma, fetal anomaly, retained intrauterine device, hydramnios, current alcohol or drug abuse, serious maternal disease (including those conditions listed on the package insert as contraindications to ritodrine), and any contraindication to tocolysis (e.g. suspected chorioamnionitis, placental abruption, bleeding praevia, fetal growth restriction, fetal distress, fetal death)
Interventions	Atosiban 0-6.5 mg bolus administered IV, followed by 30-300 µg/min infusion, continuing 6 h after the woman's last contraction for a maximum of 12 h vs ritodrine administered by IV infusion starting at 0.1 mg/min, increased every 10 min to a maximum rate of 0.35 mg/min until the cessation of uterine activity, the failure of therapy, or the occurrence of unacceptable AEs, or in 1 centre, by continuous infusion starting at 0.05 mg/min, increased every 10 min to a maximum rate of 0.35 mg/min until the cessation of uterine activity, the failure of therapy, or the occurrence of unacceptable AEs
Outcomes	Delay in birth by 48 h, cessation of treatment due to AEs, headache, nausea or vomiting, tachycardia, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity, neonatal infection, birthweight < 2500 g
Notes	2-arm active-controlled randomised trial (5-arm trial extracted as 2-arm trial as 4 arms received atosiban. Data from these arms have been combined in to a single arm). Study authors were employed by the pharmaceutical company that developed the trial drug.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation schedule, stratified by institution
Allocation concealment (selection bias)	Low risk	Sealed, opaque envelope
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study was double-blinded, except for the ritodrine arm. Quote: "Subject assignments were maintained in sealed, opaque envelopes in the pharmacy at each site."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All women were included in the analysis. Some loss to follow-up for neonatal outcomes; 61 babies did not have cranial ultrasound for IVH outcome, 8 babies did not have delivery information available, 10 babies did not have neonatal morbidity information

Goodwin 1996 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics NR Study authors were employed by the pharmaceutical company that developed the trial drug.

Guinn 1997

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	179 women were randomised from 1 centre in the USA (between September 1993 and May 1995) Population: women with threatened preterm birth between 20+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 3 contractions in 30 min and cervical dilation of ≤ 1 cm and cervical effacement < 80% Exclusion criteria comprised contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), severe maternal disease (diabetes, pre-eclampsia, cardiac arrhythmias, pulmonary oedema, severe hypertension), placenta praevia or oligohydramnios, a fetus showing signs of non-reassuring well-being, severe growth restriction, malformations, demise
Interventions	Terbutaline 0.25 mg administered SC vs placebo or no treatment
Outcomes	Pregnancy prolongation, GA at birth, birth before 34 weeks
Notes	2-arm, placebo-controlled trial (3-arm trial extracted as 2-arm trial as 1 arm received saline and 1 arm received no treatment. Data from these arms have been combined in to a single arm). COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias)	Low risk	All women included in the analysis

Guinn 1997 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias noted

Haghighi 1999

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	74 women were randomised from 1 centre in Iran (study conducted over 18 months; dates NR) Population: women with threatened preterm birth between 23+0 and 35+6 weeks' gestation with singleton pregnancy Definition of threatened preterm birth: ≥ 1 regular uterine contractions in 10 min Exclusion criteria: NR
Interventions	Nifedipine 10 mg administered sublingually, repeated every 20 min, up to a maximal dose of 40 mg during the 1st h until uterine contractions ceased, followed by 20 mg orally, starting 6 h after the last sublingual dose, given every 6 h during the first 24 h, then every 8 h for the next 24 h vs magnesium sulphate 6 g bolus administered IV over 15 min, followed by an infusion of 2 g/h increasing to 4 g/h as needed to stop uterine contractions, continued for 12 h after uterine contractions had ceased, up to 48 h, then followed by terbutaline 5 mg administered orally every 6 h
Outcomes	Delay in birth by 48 h, cessation of treatment due to AEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.

Haghighi 1999 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics NR; brief communication only

Haghighi 2005

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	156 women were randomised from 1 centre in Iran between October 2001 and December 2002. Population: women with threatened preterm birth between 33+0 and 35+6 weeks' gestation with singleton pregnancy Definition of threatened preterm birth: > 8 uterine contractions/h, lasting > 30 s and cervical dilatation > 1 cm during a 3.5 h observation Exclusion criteria: NR
Interventions	Isosorbide dinitrate 5 mg administered sublingually, repeated every 30 min up to a maximum of 40 mg until uterine contractions ceased; if uterine contractions ceased then isosorbide dinitrate 10 mg was administered orally, 1 h after the last sublingual dose, and repeated every 6 h for 48 h vs placebo 5 mg administered sublingually, repeated every 30 min up to a maximum of 40 mg until uterine contractions ceased; if uterine contractions ceased then placebo 10 mg was administered orally, 1 h after the last sublingual dose, and repeated every 6 h for 48 h
Outcomes	Birth before 37 weeks, headache, tachycardia, hypotension
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sequentially numbered, opaque, sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The study was single-blinded (not explicitly stated). Quote: "to receive either Isosorbide dinitrate or placebo (which was identical in presentation to Isosorbide dinitrate)". Unclear whether personnel blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 women in isosorbide dinitrate group (7.4%) excluded from analysis post-randomisation because of hypotension

Haghighi 2005 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Unclear risk	Baseline characteristics NR; brief communication only

Hatjis 1987

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	74 women were randomised from 1 tertiary care centre in the USA between October 1982 and July 1984. Population: women with threatened preterm birth between 20+0 to 35+0 weeks' gestation and premature rupture of membranes Definition of threatened preterm birth: persistent contractions at least every 5-7 min and contractions associated with an increase in the pelvic score (modified Bishop Pelvic Score) Exclusion criteria: NR
Interventions	Ritodrine 50 µg/min administered by IV infusion and titrated to uterine contractions for 8-10 h followed by oral ritodrine or terbutaline until 37 weeks of gestation vs magnesium sulphate 4 g administered by IV infusion over 20-30 min and maintained at 2-3 g/h for variable periods plus ritodrine 50 µg/min IV infusion and titrated to uterine contractions before being tapered over 10-12 h and followed by oral ritodrine or terbutaline until 37 weeks of gestation
Outcomes	Birthweight < 2500 g, pulmonary oedema, stillbirth, perinatal death, delay in birth by 48 h, respiratory morbidity, tachycardia, SAEs, cessation of treatment due to AEs, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	10 women were excluded from the analysis after randomisation.

Hatjis 1987 *(Continued)*

		Quote: "Ten patients did not complete treatment: 4 patients in arm 1 (ritodrine only) [2 because of chest pain/maternal tachycardia, 1 because of mature amniotic fluid lecithin-sphingomyelin ratio"
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias identified

Hawkins 2019

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	90 women were randomised across 2 centres in the USA between May 2014 and November 2017. Population: women with threatened preterm birth between 28+0 to 33+6 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: uterine activity and cervical dilation of 2-4 cm Exclusion criteria: contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical complications (hypertension), placenta praevia, enrolment in progesterone studies, a fetus showing signs of non-reassuring well-being, malformations or demise
Interventions	Nifedipine 20 mg administered orally followed by 20 mg 90 min later if contractions persisted followed by 20 mg every 4 h for a total of 48 h vs placebo for the same regime
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 37 weeks, perinatal death, cessation of treatment due to AEs, neonatal death before 28 d
Notes	No COI No information on funding reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random block number table
Allocation concealment (selection bias)	Low risk	Drug allocation using a 3rd person
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias)	Low risk	2 women withdrew consent, the remaining women are included in the analyses.

Hawkins 2019 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	The outcomes reported match the study protocol that was registered prospectively (NCT02132533).
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

He 2002

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	60 women were randomised from 2 centres in China between January 1998 and Septmeber 1999 Population: women with threatened preterm birth between 28+0 to 37+0 weeks and intact membranes Definition of threatened preterm birth: ≥ 1 contractions in 10 min with cervical dilation > 2 cm Exclusion criteria: ruptured membranes, imminent birth
Interventions	Nitroglycerin 5 mg administered transdermally for 24 h with additional patches if required up to 25 mg, patches changed every 24 h vs magnesium sulphate plus salbutamol (details NR)
Outcomes	Delay in birth by 7 d, pregnancy prolongation, headache, cessation of treatment due to AEs
Notes	1 woman was switched over to other arm (from nitroglycerin patch to magnesium sulphate plus salbutamol). COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomisation
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.

He 2002 *(Continued)*

Other bias	Unclear risk	Baseline characteristics NR

Hollander 1987

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	70 women were randomised from 1 centre in the USA from August 1984 to December 1985. Population: women with threatened preterm birth between 20+0 and 35+0 weeks' gestation with intact membranes and a singleton pregnancy Definition of threatened preterm birth: ≥ 2 contractions in 10 min with cervical dilation of ≥ 2 cm of effacement of ≥ 80% Exclusion criteria: women requiring immediate birth due to maternal or fetal complications, cervical dilation of ≥ 4 cm, multiple pregnancy, ruptured membranes
Interventions	Ritodrine 100 µg/min administered via IV infusion and titrated to contractions or maternal AEs with a maximum of 350 µg/min continued for 12 h after tocolysis followed by 10 mg orally every 2 h for 12 h followed by 10-20 mg every 2 h until 37 weeks vs magnesium sulphate 4 g administered as IV bolus followed by 2 g/h infusion titrated to uterine contractions or AEs and continued for 12 h after tocolysis followed by 10 mg orally every 2 h for 12 h followed by 10-20 mg every 2 h until 37 weeks
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, maternal infection, cessation of treatment due to AEs, GA at birth, tachycardia, nausea or vomiting, mean birthweight
Notes	Women were crossed over to the other arm if contractions persisted or AEs were intolerable. No other drugs were given for tocolysis if both treatments were unsuccessful. 6 women in the ritodrine arm also received magnesium sulphate, 3 women in the magnesium sulphate arm also received ritodrine. Some women in both groups received terbutaline 5 mg administered orally until 37 weeks instead of ritodrine as a maintenance. COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias)	Low risk	All women are included in the analysis

Hollander 1987 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	The study protocol was not available for verification
Other bias	Low risk	Baseline characteristics were similar.

How 1998

Study characteristics		
Methods	2-arm RCT	
Participants	145 women were randomised from 2 centres in the USA between August 1992 and November 1995. Population: women with threatened preterm birth between 24+0 and 34+0 weeks' gestation with premature rupture of membranes. Definition of threatened preterm birth: not defined Exclusion criteria: contraindications of tocolysis (suspected intrauterine infection or severe vaginal bleeding), complications requiring delivery, cervical dilation of > 3 cm, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, malformations	
Interventions	Magnesium sulphate 6 g administered by IV bolus, followed by 2 g/h and increased by 1 g/h every h to a maximum of 5 g/h and titrated to contraction. This dose was maintained for 4 h, gradually decreased by 1–2 g/h, and maintained for 6–8 h before it was discontinued. vs no treatment	
Outcomes	Birth before 32 weeks, perinatal death, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity, mean birthweight	
Notes	COI and funding information: NR	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Table of random numbers
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis

How 1998 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics were similar despite higher previous preterm birth in the no tocolysis group

How 2006

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	54 women were randomised from 1 university hospital in the USA between August 2002 and July 2004. Population: women with threatened preterm birth between 32+0 and 34+6 weeks' gestation with a singleton pregnancy and intact membranes and cervical dilation < 4 cm Definition of threatened preterm birth: ≥ 6 uterine contractions in 60 min with cervical dilation or effacement Exclusion criteria: contraindications to tocolysis (indication of intrauterine infection or severe vaginal bleeding), cervical dilation > 4 cm, multiple pregnancy, a fetus showing signs of non-reassuring well-being or malformations, maternal conditions (pre-eclampsia, HIV), preterm premature rupture of membranes
Interventions	Magnesium sulphate 6 g administered IV over 30 min, followed by 2-5 g/h infusion. After 24 h, nifedipine 10-20 mg administered orally every 4-6 h until 36+6 weeks of gestation, or delivery vs no treatment
Outcomes	Perinatal death, delay in birth by 48 h, delay in birth by 7 d, mean birthweight, pregnancy prolongation, neonatal death before 7 d, neonatal death before 28 d, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number
Allocation concealment (selection bias)	Low risk	Sealed, opaque, sequentially numbered envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	This study was not blinded. Quote: "One limitation of our study is the lack of placebo. Although there is the potential for biased treatment by managing physicians, all physicians provided a standard management protocol with the same home care instructions"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.

How 2006 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Low risk	Baseline characteristics were similar.

Howard 1982

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	51 women were randomised from 1 centre in the USA between January 1978 and July 1979. Population: women between 24+0 to 36+0 weeks' gestation with threatened preterm birth with intact membranes Definition of threatened preterm birth: ≥ 2 contractions in 10 min and cervical dilation or effacement Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding), placenta praevia, cervical dilation > 4 cm, maternal medical condition (arrhythmias, hyperthyroidism, diabetes), ruptured membranes
Interventions	Terbutaline 10 µg/min for 50-60 min IV and repeated 3 times if required, followed by 0.25 mg SC every 2-4 h for 24 h, followed by 2.5 mg orally every 2-4 h until 36 weeks' gestation or fetal weight > 2500 g vs placebo in the same regime
Outcomes	Pregnancy prolongation, mean birthweight, respiratory morbidity, neonatal death before 7 d, tachycardia, arrhythmias
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Dispensing pharmacist knew the identify of the study drug
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinded. Quote: "only the dispensing pharmacist knew the identity of the study drug"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded. Quote: "only the dispensing pharmacist knew the identity of the study drug"
Incomplete outcome data (attrition bias) All outcomes	High risk	Per-protocol analysis performed: only 33 women included in the analysis, 18 women were removed after randomisation (2 removed consent, 2 lost to follow-up, 1 fetal malformation, 1 termination of pregnancy, 5 born at < 36 weeks' gestation, 1 > 4 cm dilated, 3 placental abruptions - not stated which arm)

Howard 1982 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was not available for verification.
Other bias	Low risk	Baseline characteristics were similar.

Ingemarsson 1976

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	30 women were randomised from 1 centre in Sweden from February 1973-November 1974. Population: women between 28+0 to 36+0 weeks' gestation with threatened preterm birth with singleton pregnancy and intact membranes Definition of threatened preterm birth: at least 1 contraction in 10 min for 30 min with cervical effacement and dilation of ≥ 1 cm Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), ruptured membranes, multiple pregnancy, uterine malformations or cervical dilation > 4 cm
Interventions	Terbutaline 10 µg /min administered by IV infusion and increased by 25 µg/min after 10 min and titrated to uterine contractions and gradually reduced for a total time of 8 h, followed by 250 µg administered SC 4 times/d for 3 d and 15 mg orally until 36 weeks' gestation vs placebo of the same regime
Outcomes	Birth before 34 weeks, birthweight < 2500 g, neonatal death before 7 d, hypotension, perinatal death, tachycardia
Notes	Received diazepam before intervention COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly numbered ampoules
Allocation concealment (selection bias)	Low risk	Coded ampoules
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind. Quote: "two groups were treated in a double-blind manner"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "The code key was not available to the investigator"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are included in the analysis.

Ingemarsson 1976 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Low risk	Baseline characteristics are similar. No other bias

Jaju 2011

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	120 women were randomised from 1 centre in India between October 2006 and September 2008. Population: women with threatened preterm birth between 28+0 and 36+0 weeks' gestation with vertex presentation of a singleton pregnancy with intact membranes Definition of threatened preterm birth: ≥ 4 uterine contractions in 20 min with cervical dilation > 1 cm and cervical effacement of ≥ 80% Exclusion criteria: contraindication for tocolysis (indication of intrauterine infection or severe vaginal bleeding), cervical dilation > 3 cm, maternal conditions (pregnancy-induced hypertension, bronchial asthma, severe anaemia), maternal disease (diabetes mellitus, cardiovascular diseases), a fetus showing signs of intrauterine growth restriction, malformations or hydramnios
Interventions	Nifedipine 30 mg administered orally; if uterine contractions persisted after 90 min another 20 mg orally, followed by 20 mg orally every 8 h until 37 weeks of gestation or delivery, whichever was earlier vs ritodrine 100 mg administered IV starting at a rate of 50 µg/min and increased by 50 µg every 15 min until uterine contractions ceased, up to maximum rate of 350 µg/min, and infusion continued for 24 h after the cessation of uterine contractions, then 10 mg orally 30 min before stopping infusion and continued every 6 h till 37 weeks of gestation or delivery, whichever was earlier
Outcomes	Palpitations, pulmonary oedema, birth before 37 weeks, perinatal death, nausea or vomiting, headache, delay in birth by 48 h, respiratory morbidity, dyspnoea, SAEs, cessation of treatment due to AEs, delay in birth by 7 d
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear. Quote: "Simple randomisation technique"
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR

Jaju 2011 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Low risk	Baseline characteristics were similar.

Janky 1990

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	62 women were randomised from 1 centre in France between June 1987 to June 1988. Population: women with threatened preterm birth between 28+0 to 36+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 2 uterine contractions in 10 min with cervical change Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (cardiac, high blood pressure, glaucoma, diabetes), ruptured membranes after 34 weeks, a fetus showing signs of non-reassuring well-being or demise cervical dilation of > 4 cm. 11 women had urinary tract infections, these were equal across both arms, it does not report if these were treated
Interventions	Nifedipine 20 mg administered orally every 8 h for 7 d vs ritodrine 0.20-0.30 mg/min administered IV and titrated to uterine contractions for 24 h followed by 20 mg orally every 4 h followed by 20 mg every 6 h for 7 d
Outcomes	Palpitations, neonatal infection, stillbirth, perinatal death, GA at birth, hypotension, headache, mean birthweight, neonatal death before 7 d, cessation of treatment due to AEs, tachycardia, pregnancy prolongation, neonatal death before 28 d
Notes	In the case of failure, the first treatment was combined with other tocolytic medication with a different effect. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded

Janky 1990 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The protocol was unavailable for verification
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Jannet 1997

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	90 women were randomised from 1 centre in France between January 1993 and December 1994. Population: women with threatened preterm birth between 25+0 and 35+3 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: cervical dilation of ≥ 2 cm and > 3 uterine contractions in 30 min Exclusion criteria: maternal and fetal contraindications to tocolysis, maternal medical conditions (cardiac disease, cardiac arrhythmia, diabetes, hypokalaemia), multiple gestation, premature rupture of membranes, contraindication to study drug
Interventions	Nicardipine administered IV at a rate of 3 mg/h, increased as required after 2 h to a rate of 6 mg/h, for 48 h in total. If uterine contractions had not ceased at 48 h then the IV infusion was continued. If uterine contractions had ceased at 48 h, followed by 60 mg orally every d until 37 weeks' gestation vs salbutamol administered IV at a rate of 0.15 mg/h, increased as required after 2 h to a rate of 3 mg/h, for 48 h in total. If uterine contractions had not ceased at 48 h then the IV infusion was continued. If uterine contractions had ceased at 48 h, salbutamol 8 mg administered orally every d and 2 mg administered rectally every day until 37 weeks' gestation
Outcomes	Birth before 34 weeks, birth before 37 weeks, GA at birth, mean birthweight, SAEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	The investigators were not blinded. It is unclear whether the participants were blinded. Quote "This randomised study was not double-blind because of the well-known side effects of both treatments"

Jannet 1997 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	The investigators were not blinded. Quote "This randomised study was not double-blind because of the well-known side effects of both treatments."
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women in the nicardipine arm were lost to follow-up rapidly and data on their pregnancy and delivery were unavailable. 2 women in the salbutamol arm excluded post-randomisation because they had twin pregnancies
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Low risk	Baseline characteristics were similar.

Kara 2009

Study characteristics	
Methods	2-arm active RCT
Participants	77 women were randomised from 1 centre in Turkey between March and November 2002. Population: women with threatened preterm birth between 20+0 and 36+0 weeks with singleton pregnancy Definition of threatened preterm birth: ≥ 1 uterine contractions in 10 min with or without cervical dilatation and effacement Exclusion criteria: with pre-eclampsia, eclampsia, placental abruption, placenta praevia, cervical dilatation > 4 cm, premature rupture of membranes, chorioamnionitis, fetal death, fetal distress, major fetal anomalies, intrauterine growth restriction, diabetes mellitus, hyperthyroidism, cardiovascular diseases, multiple pregnancy and polyhydramnios
Interventions	Magnesium sulphate 6 g administered via IV bolus over 20 min followed 2-4 g/h and titrated to stopped or maternal AEs for 24 h after the contractions stopped followed by oral terbutaline 5 mg every 4-6 h until 36 weeks vs nifedipine 10 mg administered sublingually with additional 10 mg in 20 min if the uterine contractions persisted, followed by sublingual nifedipine 10 mg administered every 20 min till the uterine contractions subsided followed by 20 mg every 4 h administered after cessation of uterine contractions and maintained additional 48 h followed by 10 mg orally every 8 h until 36 weeks
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, pregnancy prolongation, birth before 37 weeks, GA at birth, mean birthweight, headache, nausea or vomiting
Notes	If women were considered resistant to nifedipine they could be switched to another treatment modality if the uterine contractions had not subsided. COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR

Kara 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Kashanian 2005

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	80 women were randomised from 1 secondary centre in Iran. Population: women with threatened preterm birth between 26+0 and 34+0 weeks' gestation Definition of threatened preterm birth: ≥ 4 uterine contractions in 20 min or 8 contractions in 60 min and cervical dilatation of ≥ 1 cm and cervical effacement of ≥ 50% Exclusion criteria: contraindication to tocolysis (severe vaginal bleeding), rupture of membranes, cervical dilatation > 3 cm, maternal medical disorders (hypotension or systemic disorders) or uterine anomaly, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction or demise
Interventions	Atosiban administered IV at 300 µg/min until uterine contractions have ceased and for 6 h afterwards, up to a maximum of 12 h vs nifedipine 20 mg administered orally every 6 h for 24 h, then every 8 h for the following 24 h, then 10 mg every 8 h for the last 24 h
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, pregnancy prolongation, palpitations, headache, tachycardia, hypotension
Notes	COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	4-part, ABCD, block-random allocation
Allocation concealment (selection bias)	Unclear risk	NR

Kashanian 2005 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	This study was not blinded. Quote: "Because the two drugs are completely different in shape and form a blind study was not an option"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

Kashanian 2011

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	82 women were randomised from 1 secondary centre in Iran between May 2008 and March 2009. Population: women with threatened preterm birth between 26+0 and 33+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 uterine contractions in 20 min or ≥ 8 contractions in 60 min, cervical dilation of ≥ 1 cm, and cervical effacement of ≥ 50% Exclusion criteria: contraindication for tocolysis (indication of intrauterine infection or severe vaginal bleeding), multiple pregnancy, rupture of membranes, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction or demise, cervical dilation ≥ 4 cm, maternal disease or disorder (systemic disorders, pre-eclampsia, hypotension), uterine anomalies, poly- or oligohydramnios, use of tocolysis, smoking, or drug misuse
Interventions	Nifedipine 10 mg administered orally every 20 min up to a maximum of 4 doses. In women whose uterine contractions ceased, 20 mg orally given every 6 h for 24 h, then every 8 h for the next 24 h, then 10 mg every 8 h for the next 24 h (total duration of treatment 3 d) vs indomethacin 100 mg administered rectally, and repeated 1 h later if uterine contractions continued (total duration of treatment 2 h)
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, SAEs, cessation of treatment due to AEs, palpitations, headache, tachycardia, hypotension, GA at birth, perinatal death
Notes	No COI Funded by Iran University

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "4-part, block random approach using sealed, sequentially distributed envelopes to which the letters A, B, C and D had been allocated. Letters A and

Kashanian 2011 *(Continued)*

		C responded to the Nifedipine group, and letter B and D corresponded to the Indomethacin group."
Allocation concealment (selection bias)	Unclear risk	Sealed, sequentially distributed envelopes to which the letters A, B, C and D had been allocated.
Blinding of participants and personnel (performance bias) All outcomes	High risk	This study was not blinded. Quote "Because the shape and route of administration of the 2 drugs were different, the study could not be performed blind, but the investigators assessing the outcome were blind to group assignment."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded. Quote "Because the shape and route of administration of the 2 drugs were different, the study could not be performed blind, but the investigators assessing the outcome were blind to group assignment."
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women in the nifedipine arm were excluded post-randomisation, because nifedipine was discontinued due to hypotension. These women were not included in the analysis. Data missing for 1 woman in the indomethacin arm but no explanation of loss to follow-up
Selective reporting (reporting bias)	Unclear risk	Protocol registered retrospectively
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

Kashanian 2014

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	120 women were randomised from 1 centre in Iran between June 2010 and March 2011. Population: women with threatened preterm birth between 26+0 to 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min or 8 in 60 min with cervical dilation of ≥ 1 cm and effacement of ≥ 50% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), ruptured membranes, maternal or fetal conditions requiring immediate birth, cervical dilation > 5 cm, increased or reduced liquor volume, systemic disorders, smoking, drug use, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, malformation or demise, sensitivity to study drugs
Interventions	Nitroglycerin 10 mg administered transdermally with an additional 10 mg if contractions continued vs nifedipine 10 mg administered orally every 20 min and titrated to contractions with a maximum of 4 doses, followed by 20 mg every 6 h up to 24 h, followed by 20 mg every 8 h for the second 24 h and finally 10 mg every 8 h for the next 24 h
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, GA at birth, cessation of treatment due to AEs, headache, hypotension, mean birthweight
Notes	If contractions remained 2 h after the beginning of tocolysis, it was considered as failure of treatment and an alternative tocolytic was started. Recurrent episodes of contractions and preterm labour were managed with alternative tocolytic - no details on alternative tocolysis reported No COI

Kashanian 2014 *(Continued)*

Funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear - randomly grouped by a colleague for block randomisation in 4 parts
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. Quote: "Because the shapes of the two medicines were totally different, blinding was not performed'
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded. Quote: "those assessing the outcomes, were blinded to group assignment'
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 women were lost to follow-up 5 in the nitroglycerin group and 2 in the nifedipine group - 2 women in the nifedipine group were also excluded from the analysis because of treatment discontinuation
Selective reporting (reporting bias)	Unclear risk	The study protocol matches the outcomes reported. The protocol was registered retrospectively (IRCT201108262624N8).
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Kashanian 2020

Study characteristics

Methods	3-arm RCT, active-controlled
Participants	152 women were randomised from 1 centre in Iran from May 2016-March 2018. Population: women with threatened preterm birth between 26+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: 4 contractions in 20 min or 1 cm cervical dilation and ≥ 50% effacement Exclusion criteria: contraindication for tocolysis (severe vaginal bleeding), maternal or fetal distress requiring immediate birth, maternal medical condition (pre-eclampsia, eclampsia), polyhydramnios, cervical dilation > 5 cm, multiple pregnancy, ruptured membranes, a fetus showing signs of non-reassuring well-being, malformation, demise, tocolytic use within 24 h
Interventions	Indomethacin 100 mg administered rectally with oral placebo, followed by 25 mg orally in 2 h, followed by 25 mg every 4 h plus placebo (as per the nifedipine regime). The maximum daily dosage of indomethacin was 200 mg/d and the maximum duration of administration was 48 h vs nifedipine 20 mg administered orally with rectal placebo, followed by 20 mg after 90 min, followed by 20 mg every 4 h for 48 h, with a maximum dose of 180 mg/d. Placebo was given similarly to the indomethacin group vs indomethacin 100 mg administered rectally with nifedipine 20 mg administered orally, followed by indomethacin 25 mg orally in 2 h, followed by 25 mg every 4 h plus nifedipine 20 mg 90 min later followed

Kashanian 2020 *(Continued)*

	by 20 mg every 4 h for 48 h. The maximum daily dosage of indomethacin was 200 mg/d and the maximum dose of nifedipine was 180 mg/d
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, GA at birth, birth before 37 weeks, mean birthweight, hypotension
Notes	Intervention duration in the protocol is different from the study write-up. Uterine contractions were monitored for the first 2 h after administration of the tocolysis. If the contractions were the same as those before the drug administration, it was considered as a failure of treatment and another tocolytic was started - these were removed from the analysis. No COI Funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomisation
Allocation concealment (selection bias)	Low risk	Software allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind. Quote: "The participants and the investigators did not know how the patients were allocated to the three groups. The groups were named as A, B and C and placebo were used to blind them."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "The participants and the investigators did not know how the patients were allocated to the three groups. The groups were named as A, B and C and placebo were used to blind them."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Women were excluded from the analysis if they did not respond to randomised treatment after 2 h and required additional tocolysis.
Selective reporting (reporting bias)	Unclear risk	The outcomes reported match the study protocol that was retrospectively registered (IRCT20091023002624N26).
Other bias	Low risk	Baseline characteristics were similar.

Klauser 2014

Study characteristics

Methods	3-arm RCT, active-controlled
Participants	301 women were randomised from 1 centre in the USA. Population: women with threatened preterm birth between 20+0 and 32+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 1 regular uterine contractions in 5 min and cervical dilation 1-6 cm

Klauser 2014 *(Continued)*

	Exclusion criteria: contraindication for tocolysis (indication of intrauterine infection or severe vaginal bleeding), severe pre-eclampsia, a fetus showing signs of intrauterine growth restriction, non-reassuring well-being, malformation
Interventions	Magnesium sulphate 6 g administered IV over 20 min, then given at 4-6 g/h until uterine contractions were < 6/h vs nifedipine 30 mg administered orally followed by 20-30 mg every 4-6 h until uterine contractions ceased vs indomethacin 100 mg administered as a rectal suppository, repeated if necessary 2 h after the initial dose, then 50 mg orally every 6 h until uterine contractions ceased for at least 1-2 h, for a maximum of 48 h
Outcomes	Maternal death, birth before 34 weeks, neonatal infection, pulmonary oedema, stillbirth, birth before 37 weeks, perinatal death, GA at birth, hypotension, nausea or vomiting, neurodevelopmental morbidity, gastrointestinal morbidity, mean birthweight, delay in birth by 48 h, delay in birth by 7 d, SAEs, cessation of treatment due to AEs, dyspnoea, tachycardia, hypotension, pregnancy prolongation, respiratory morbidity, neonatal death before 28 d
Notes	No COI Funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence by 3rd party - no further details reported
Allocation concealment (selection bias)	Low risk	Sealed opaque envelope
Blinding of participants and personnel (performance bias) All outcomes	High risk	This study was not blinded. Quote: "The tocolytic's were not blinded to the care providers nor patients since they were given by different routes and had different appearances"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded. Quote "those assessing outcomes were not privy to group assignment as they were not involved in their clinical care"
Incomplete outcome data (attrition bias) All outcomes	Low risk	25 women in total were excluded post-randomisation (< 10%): 10 women from indomethacin arm, 5 women from magnesium sulphate arm, 10 women from nifedipine arm. Reasons for exclusion were > 32 weeks' gestation, no medication available, lethal fetal anomaly
Selective reporting (reporting bias)	Low risk	The study report matches the study protocol that was registered prospectively (NCT00811057).
Other bias	Unclear risk	Baseline characteristics were similar. No other bias reported

Koks 1998

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	102 women were randomised from 1 regional hospital with a neonatal intensive care referral centre in the Netherlands between 1992 and 1995.

Koks 1998 *(Continued)*

	Population: women with threatened preterm birth between 24+0 and 34+0 weeks' gestation with singleton or twin pregnancy Definition of threatened preterm birth: ≥ 6 uterine contractions lasting > 30 seconds in 60 min with or without cervical dilation and effacement. Women transferred from another hospital who were already receiving betamimetic drugs were also included Exclusion criteria: contraindications of tocolysis (suspected intrauterine infection or severe vaginal bleeding), triplets or greater, polyhydramnios, maternal medical condition contraindicating the use of study drug, a fetus showing signs of non-reassuring well-being
Interventions	Nifedipine 30 mg administered sublingually, then 20-40 mg orally 2-4 times daily. (From February 1993, the maximum dose increased from 20 mg 2-4 times daily to 40 mg every 8 h according to the protocol of another Dutch nifedipine study (Papatsonis 1997), hoping to further improve results). If a woman had already been treated with a betasympathicomimetic drug, the dose was halved and she was started on an oral dose of 20 mg nifedipine. After 12 h, the other tocolytic drug was stopped and the normal dosage of nifedipine was continued. Tocolytic medication stopped at 34 weeks of gestation and earlier if possible, the dosage of nifedipine was gradually reduced with a minimal dosage of 20 mg 3 times/d vs ritodrine administered IV starting at a rate of 200 µg/min until tocolysis achieved, then dosage decreased to least possible dose to obtain tocolysis, the maximum dose was 400 µg/min. For women already receiving betasympathicomimetic drugs, the dose was continued. Tocolytic medication stopped at 34 weeks of gestation and earlier if possible, oral ritodrine retard (80 mg 3 times/d) was used as a tapering-off scheme
Outcomes	Palpitations, birth before 34 weeks, stillbirth, perinatal death, GA at birth, mean birthweight, delay in birth by 48 h, delay in birth by 7 d, neonatal death before 7 d, cessation of treatment due to AEs, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelopes with a random assignment
Blinding of participants and personnel (performance bias) All outcomes	High risk	This study was not blinded. Quote "Because the two medications were administered differently, one orally and the other by infusion therapy, we decided not to mask the women."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women included in the analysis
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Unclear risk	Baseline characteristics were similar. No other bias reported

Kose 1995

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	73 women were randomised from 1 centre in Turkey (dates NR). Population: women with threatened preterm birth between 22+0 and 36+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 3 contractions in 20 min with cervical dilation and effacement Exclusion criteria: cervical dilation > 4 cm, no uterine contractions, contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (pre-eclampsia, eclampsia, diabetes, hypertension, heart conditions), a fetus showing signs of intrauterine growth restriction, malformation, demise, multiple pregnancy, ruptured membranes, previous tocolysis
Interventions	Nifedipine 30 mg administered orally, followed by 10 mg in 2 h if contractions reduced but still continued, followed by 4 x 20 mg/d maintenance 6 h later or if no contraction in first 24 h after initial maintenance dose then dose reduced to 3 x 20 mg in 3 d, followed by 4 x 10 mg to 37/40 vs ritodrine 0.2 µg/mL (0.05 mg/min) administered IV and increased every 15 min 0.05 mg/min with a maximum of 0.35 mg/min and titrated to uterine contraction or AEs and kept at effective dose for 12 h followed by 10 mg orally before end of IV infusion then 10 mg every 6 h until 37 weeks
Outcomes	Delay by 48 h, delay by 7 d, neonatal death before 28 d, pregnancy prolongation, tachycardia, neonatal death before 7 d, mean birthweight, headache, nausea or vomiting, hypotension, GA at birth, perinatal death, palpitations, pulmonary oedema, birthweight < 2500 g, neonatal infection
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Women were excluded if tocolysis was ineffective or was stopped due to AEs.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Kramer 1999

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	20 women were randomised from 1 centre in the USA. Population: women with threatened preterm birth between 24+0 and 35+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min or 8 in 60 min with cervical dilatation ≥ 2 cm, effacement ≥ 80%, or documented cervical change Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), maternal illness or ruptured membranes
Interventions	Sulindac 200 mg administered orally every 12 h for 6 doses vs terbutaline 5 mg orally every 4 h for 72 h
Outcomes	Neonatal infection, pulmonary oedema, stillbirth, perinatal death, birth before 37 weeks, hypotension, neurodevelopmental morbidity, nausea or vomiting, headache, gastrointestinal morbidity, neonatal death before 7 d, tachycardia, dyspnoea, SAEs, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random table
Allocation concealment (selection bias)	Low risk	Identical opaque capsules by the pharmacy
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Both the principal investigator and the woman were unaware of the type of medication given
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Both the principal investigator and the woman were unaware of the type of medication given
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Kupferminc 1993

Study characteristics

Kupferminc 1993 *(Continued)*

Methods	2-arm RCT, active-controlled
Participants	71 women were randomised from 1 centre in Israel between June 1988 and December 1992. Population: women with threatened preterm birth between 26+0 and 34+0 weeks' gestation, with singleton or twin pregnancies and intact membranes Definition of threatened preterm birth: ≥ 1 regular uterine contractions in 6 min with cervical change Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), maternal medical condition contraindicating tocolysis, polyhydramnios, hypertension, or cervical dilation of ≥ 4 cm
Interventions	Nifedipine 30 mg administered orally, then if uterine contractions persisted after 90 min another 20 mg orally, then 20 mg administered orally every 8 h until 34-35 weeks of gestation vs ritodrine administered IV at an initial rate of 50 µg/min, increased by 15 µg every 15 min until contractions ceased, up to a maximum rate of 300 µg/min, and the effective tocolytic rate maintained for 12 h, then 10 mg orally every 3 h until 34-35 weeks of gestation
Outcomes	Palpitations, perinatal death, stillbirth, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, delay in birth by 7 d, neonatal death before 7 d, cessation of treatment due to AEs, neonatal death before 28 d
Notes	Nifedipine was discontinued if severe AEs occurred or the uterine contractions did not stop within the 2 h period after the 4th dose of nifedipine. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Only singleton pregnancies included in statistical analysis. Quote "Due to the small number of twin pregnancies in each group, results of tocolysis for twins are presented separately, without statistical analysis."
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Unclear risk	Baseline characteristics were reported to be similar but no baseline characteristics table. No other obvious bias

Kurki 1991b

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	660 women were randomised across 2 secondary centres in Finland between May 1987 and September 1990. Population: women with threatened preterm birth between 25+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 1 uterine contractions in 10 min, cervical dilation of 2-4 cm and Bishop score of 1-9 Exclusion criteria: contraindications to tocolysis (signs of intrauterine infection or placenta praevia), maternal medical disease, abnormal amniotic fluid volume, fetus showing signs of non-reassuring well-being, growth restriction or malformations, multiple pregnancy, ruptured membranes, cervical dilation of ≥ 4 cm, previous tocolytic use in current pregnancy. 2 women in the indomethacin group had GBS at admission.
Interventions	Indomethacin 100 mg administered rectally, then 50 mg orally every 8 h for the first day, then 50 mg 3 times/d for the 2nd and 3rd days, until cessation of uterine contractions or for a maximum of 3 d vs nylidrin administered IV at an initial rate of 50 µg/min, increased within 30 min to a rate of 100-150 µg/min, until cessation of uterine contractions or for a maximum of 3 d
Outcomes	Perinatal death, delay in birth by 48 h, pregnancy prolongation, palpitations, nausea or vomiting, GA at birth, mean birthweight, neonatal death before 7 d, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity, neonatal infection, pulmonary oedema, birth before 37 weeks, hypotension, headache, tachycardia, arrhythmias, dyspnoea, SAEs, neonatal death before 28 d
Notes	No COI Funded by Helsinki University and Foundation for paediatric research

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Subjects were treated in randomised order (choice by a sealed envelope)"
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The study was double-blind. Quote: "Women treated with Indomethacin also received an IV infusion of physiologic saline, and those treated with Nylidrin received a placebo rectal suppository and placebo oral capsules."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women included in the analysis
Selective reporting (reporting bias)	Unclear risk	Protocol was not available for verification

Kurki 1991b *(Continued)*

Other bias	Unclear risk	Baseline characteristics were reported to be similar but no baseline characteristics table. No other obvious bias

Laohapojanart 2007

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	40 women were randomised from 1 centre in Thailand (dates NR). Population: women with threatened preterm birth between 24+0 to 36+0 weeks' gestation with a singleton pregnancy Definition of threatened preterm birth: ≥ 4 uterine contractions in 20 min, cervical dilation 1-4 cm and cervical effacement Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal disease (cardiac, renal, hypertension, pre-eclampsia, diabetes, thyrotoxicosis) multiple pregnancy
Interventions	Nifedipine 10 mg administered orally every 20 min up to maximum dose of 40 mg within the 1st h of treatment, then 20 mg orally every 4-6 h for 72 h vs terbutaline administered IV at an initial rate of 10 µg/min, increased by 5 µg every 10 min until a rate 25 µg/min achieved, and the uterine contraction-inhibiting rate maintained for 2-6 h after cessation of uterine contractions, then 0.25 mg SC every 4 h for 24 h
Outcomes	Birthweight < 2500 g, pulmonary oedema, stillbirth, birth before 37 weeks, perinatal death, GA at birth, hypotension, nausea or vomiting, neurodevelopmental morbidity, headache, mean birthweight, delay in birth by 48 h, respiratory morbidity, neonatal death before 7 d, tachycardia, SAEs, cessation of treatment due to AEs, neonatal death before 28 d, delay in birth by 7 d
Notes	No COI Funded by Prince of Songkla University

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear. Quote: "The blocks of size 4, 6, and 8 were used to randomise the patients in order to get the balance number of patients in both arms at any time of enrolment"
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear "all outcomes were determined by the responsible obstetricians" - not stated whether these obstetricians were blinded or not

Laohapojanart 2007 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	1 woman in the nifedipine arm stopped treatment after 1 h and delivered 2 h later, and is excluded from the analysis. 4 women in the terbutaline arm lost to follow-up, and excluded from the analysis
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Low risk	Baseline characteristics similar

Larmon 1999

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	122 women were randomised from 1 secondary centre in the USA between March 1996-June 1997. Population: women aged ≥ 13 years with threatened preterm birth between 24+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 uterine contractions/h for at least 1 h and cervical change Exclusion criteria: contraindications of tocolysis (indication of intrauterine infection or severe vaginal bleeding), urgent indication for delivery, maternal medical conditions (renal insufficiency, hepatic insufficiency, myasthenia gravis, pre-eclampsia, hypotension), use of tocolytic agents during the pregnancy, cervical incompetence or dilation of ≥ 4 cm, contraindication to use of the study drug, medications, a fetus showing signs of non-reassuring fetal well-being, intrauterine growth restriction, malformations
Interventions	Magnesium sulphate 6 g administered IV as a loading dose, then infusion given at a rate of 2 g/h, and increased until uterine contractions ceased up to a maximum rate of 4 g/h, then after preterm labour was arrested and 1 h before discontinuation of the IV infusion, magnesium lactate administered orally as 4 Mag-Tab tablets every 12 h, continued until 37 weeks of gestation or delivery vs nicardipine 40 mg administered orally, then 20 mg given every 2 h until uterine contractions had ceased up to a maximum total dose of 80 mg nicardipine, then 2 h later nicardipine 45 mg administered orally every 12 h until 37 weeks of gestation or delivery
Outcomes	Stillbirth, perinatal death, GA at birth, hypotension, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, pregnancy prolongation, cessation of treatment due to AEs, neonatal death before 28 d
Notes	No COI reported Funded by Vicksburg Hospital

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Numbered, opaque, sealed envelopes

Larmon 1999 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	This study was not blinded. Quote "Because of the different administration routes for nicardipine and magnesium sulphate, neither patients nor physicians were blinded to treatment allocation."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear - physicians were blinded and it's likely that they were also outcome assessors but this is not stated explicitly.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Low risk	Baseline characteristics are similar. No other obvious bias

Larsen 1980

Study characteristics	
Methods	4-arm RCT, placebo-controlled
Participants	199 women were randomised from 1 centre in Denmark (dates NR). Population: women with preterm labour between 20+0 and 36+0 weeks of gestation, and women who were in labour and had a fetus that was thought to weigh < 2500 g Definition of threatened preterm birth: regular contractions or contractions accompanied by cervical effacement and/or dilation Exclusion criteria: antepartum haemorrhage, placental abruption, rhesus-negative women with previously affected babies or a history of ABO incompatibility, women with cardiac disease, ruptured membranes, cervical dilation ≥ 5 cm, signs of intrauterine infection, eclampsia or severe pre-eclampsia, diabetes mellitus, and multiple gestation
Interventions	Ritodrine 100 µg/min administered IV, increasing by 50 µg every 5-10 min up to a maximum dose of 350 µg/min as needed, then IV infusion continued for 30 min to 24 h after uterine contractions have ceased, or ritodrine 10 mg administered IM every 4 h for 12 h, then every 6 h for 12 h, both followed by ritodrine 10 mg administered orally 4 times/d, increased to 12 times/d if needed, up until 37 weeks' gestation or delivery vs placebo and bed rest. This is a 4-arm trial, 3 arms contribute to a single arm: 1. ritodrine administered IV at 100 µg/min, increasing by 50 µg every 5-10 min up to a maximum dose of 350 µg/min as needed, then IV infusion continued for 24 h, and 30 min before discontinuing the infusion ritodrine 10 mg administered orally 4 times/d, increased to 12 times/d if needed, up until 37 weeks' gestation or delivery 2. ritodrine administered IV at 100 µg/min, increasing by 50 µg every 5-10 min up to a maximum dose of 350 µg/min as needed, discontinued 30 min after cessation of uterine contractions, and 30 min before discontinuing the infusion ritodrine 10 mg administered orally 4 times/d, increased to 12 times/d if needed, up until 37 weeks' gestation or delivery 3. ritodrine 10 mg administered IM every 4 h for 12 h, then every 6 h for 12 h, and 3 h after the last IM injection, ritodrine 10 mg administered orally 4 times/d, increased to 12 times/d if needed, up until 37 weeks' gestation or delivery

Larsen 1980 *(Continued)*

Outcomes	Delay in birth by 48 h, perinatal death, birthweight < 2500 g, respiratory morbidity, stillbirth, neonatal death < 28 d, neonatal death before 7 d, cessation of treatment due to AEs, palpitations, tachycardia, headache
Notes	2-arm placebo controlled randomised trial (4-arm trial that has been extracted as a 2-arm trial. In 3 of the arms women received a different ritodrine regime, the data have been combined and presented in 1 arm). COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	23 women excluded post-randomisation because they met exclusion criteria, 19 from the ritodrine arms and 4 from the placebo arm
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Unclear risk	Baseline characteristics were similar.

Larsen 1986

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	99 women were randomised across 7 centres in Denmark (dates NR). Population: women with threatened preterm birth between 20+0 to 36+0 weeks' gestation with a singleton pregnancy and intact membranes. Definition of threatened preterm birth: 1 uterine contraction/5 min for 30 min or 6 for 30 min and a Bishop's score of > 4 and < 9 Exclusion criteria: contraindication for tocolysis (indication of intrauterine infection or severe vaginal bleeding), other tocolytic or beta-blocker administration, multiple pregnancy, ruptured membranes, placental anomalities, serious maternal complications or serious medical conditions, placental or am-

Larsen 1986 *(Continued)*

	niotic abnormalities, rhesus or ABO immunisation, indication of non-reassuring fetal well-being, fetal demise or malformations, maternal or fetal complications requiring delivery
Interventions	Ritodrine 10 mg administered by IM injections followed by 10 mg every 6 h for 24 h, plus an additional 10 mg if required, followed by 5-15 mg every 6 h plus 10-20 mg at night administered orally and titrated to uterine contractions with the lowest dose possible used vs placebo administered IM every 6 h for 24 h, followed by every 6 h orally (as with ritodrine protocol)
Outcomes	Delay in birth by 48 h, pregnancy prolongation, gestation at birth, stillbirth, mean birthweight, birthweight < 2500 g, birth < 37 weeks, neonatal death before 7 d, neonatal death before 28 d, perinatal death, SAEs, respiratory morbidity
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed by a 3rd party by numbered boxes
Allocation concealment (selection bias)	Low risk	Numbered boxes selected by clinicians
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "clinicians did not know which boxes contained ritodrine"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "clinicians did not know which boxes contained ritodrine"
Incomplete outcome data (attrition bias) All outcomes	High risk	26 post-randomisation exclusions
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

Leake 1983

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	35 women were randomised from 1 centre in the USA between March 1973-January 1974. Population: women with threatened preterm birth between 24+0 and 36+0 weeks' gestation Definition of threatened preterm birth: regular contractions with progressive cervical dilation or effacement or ruptured membranes.

Leake 1983 *(Continued)*

	Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disorders (chronic hypertension, cardiac disease), cervical dilation > 4 cm
Interventions	Ritodrine hydrochloride administered IV at 100 µg/min and titrated to contractions every 10 min 50 µg/min until a maximum of 350 µg/min for 12 h (in labour) OR ritodrine 30 mg (SROM but not labour) followed by ritodrine 20 mg administered orally every 4 h vs placebo administered IV for 12 h followed by placebo administered orally every 4 h
Outcomes	GA at birth, mean birthweight
Notes	Funding from N.V. Philips-Duphar, Amsterdam - pharmaceuticals company

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind but no further details reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind but no further details reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Only women who were maintained on oral therapy for a minimum for 12 h and who were within 6 h of their last dose of oral therapy were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Protocol unavailable for verification
Other bias	Unclear risk	Baseline characteristics were similar. Funding from N.V. Philips-Duphar, Amsterdam - pharmaceuticals company

Lees 1999

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	245 women were randomised across 20 centres in the UK (14), Italy (3), Germany (1), Thailand (1) and Indonesia (1) between December 1994 and August 1996. Population: women with threatened preterm birth between 24+0 and 36+0 weeks' gestation and intact membranes Definition of threatened preterm birth: ≥ 2 contractions in 10 min for > 1 h with or without cervical change

Lees 1999 *(Continued)*

	Exclusion criteria: contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (hypotension), placenta praevia, urinary tract infection, ruptured membranes, tocolytic or anti-inflammatory therapy in pregnancy, sensitivity to trial medications, a fetus showing signs of non-reassuring well-being
Interventions	GTN 10 mg administered transdermally (with an additional 10 mg if required) for 24 h vs ritodrine administered via IV infusion according to local policy or RCOG guidelines, commencing at a rate of 50 pico g/min and titrated to uterine contractions and maternal AEs for 24 h
Outcomes	Delay in birth by 7 d, SAEs, birth before 32 weeks, birth before 37 weeks, pregnancy prolongation, stillbirth, perinatal death, neonatal death before 28 d, pulmonary oedema, dyspnoea, palpitations, birth before 34 weeks, nausea or vomiting, tachycardia, headache
Notes	Funding from Schwarz Pharma research grant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation by random permuted block from a centrally prepared random number list, stratified by centre
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Only blinded in centres that did not routinely use tocolysis. Blinding not performed in other centres
Blinding of outcome assessment (detection bias) All outcomes	High risk	Only blinded in centres that did not routinely use tocolysis. Blinding not performed in other centres
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 women were excluded post-randomisation due to poor record keeping. 12 women were lost to follow-up similar in both arms. All other women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics were similar. The study was part funded by Schwarz Pharma. UK centres recruited women between GA of 24+0 to 31+6 other centres recruited women between 24+0 to 36+0

Leveno 1986

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	106 women were randomised from 1 centre in the USA. Population: women with threatened preterm birth between 24+0 to 33+0 weeks' gestation with intact membranes

Leveno 1986 *(Continued)*

	Definition of threatened preterm birth: regular uterine contractions with cervical dilatation of ≥ 1 cm but < 4 cm Exclusion criteria: contraindications to tocolysis (signs of intrauterine infection or severe vaginal bleeding), maternal medical disorders or pregnancy or fetal complications, previous caesarean section, cervical dilation > 4 cm, a fetus showing signs of intrauterine growth restriction
Interventions	Ritodrine 100 µg/min administered by IV infusion increased every 10 min by 50 µg/min (with a maximum dose of 350 µg/min) until contractions ceased and continued for 24 h, followed by 10 mg orally 30 min before IV was discontinued, followed by 20 mg every 3 h until 36 weeks' gestation vs placebo administered by IV infusion to parallel the volume of ritodrine
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 32 weeks, birthweight < 2000 g, pulmonary oedema, cessation of treatment due to AEs, hypotension, dyspnoea, palpitations, birthweight < 2500 g, perinatal death, gastrointestinal morbidity, neurodevelopmental morbidity, neonatal death before 7 d, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Unclear. Quote: "This volume of saline infused per hour for the control group was selected to parallel the volume administered during ritodrine infusion"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics are reported as similar but no baseline characteristics table provided. No other obvious bias

Lin 2009

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	45 women were randomised from 1 centre in Taiwan.

Lin 2009 *(Continued)*

	Population: women aged ≥ 18 years with threatened preterm birth between 24+0 to 33+0 weeks' gestation and intact membranes Definition of threatened preterm birth: ≥ 4 uterine contractions in 30 min lasting for > 30 seconds with cervical dilation of ≤ 3 cm and effacement of ≥ 50% Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or signs of intrauterine infection), maternal medical disorders or severe complications, ruptured membranes, higher order multiple pregnancy, drug or alcohol abuse, urinary tract infection, placental or amniotic abnormalities, a fetus showing signs of growth restriction or malformations, contraindications to the study treatment, exposure to NSAIDs for tocolysis within 12 h, previous trial participation within 1 month
Interventions	Atosiban 6.75 mg administered by an IV bolus, followed by 18 mg/h for 3 h followed by 6 mg/h for 15 h for a maximum of 18 h vs ritodrine 20 mL/h administered by IV infusion and titrated to uterine contractions by increasing by 10 mL/h every 10-30 min for a maximum of 18 h
Outcomes	Maternal death, stillbirth, perinatal death, GA at birth, mean birthweight, delay in birth by 48 h, respiratory morbidity, tachycardia, SAEs, neonatal death before 28 d, delay in birth by 7 d
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomised
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	Protocol unavailable for verification
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

Lyell 2007a

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	196 women were randomised across 2 centres in the USA.

Lyell 2007a *(Continued)*

	Population: women with threatened preterm birth between 24+0 weeks to 33+6 weeks of gestation Definition of threatened preterm birth: at least 2 uterine contractions/10 min and the presence of cervical change or ruptured membranes, or ≥ 2 cm cervical dilation and 80% effacement Exclusion criteria: contraindications for tocolysis (severe vaginal bleeding, intrauterine infection), maternal medical disease, placenta praevia or a fetus showing signs of non-reassuring well-being or intrauterine growth restriction
Interventions	Magnesium sulphate 4 g bolus followed by 2-4 g/h administered by an IV infusion titrated to uterine contractions (additional 2 g bolus was allowed) vs nifedipine 10 mg administered sublingually every 20 min for 3 doses, followed by 20 mg administered orally every 4-6 h titrated to uterine contractions. Both treatments were continued for 48 h or at least 12 h of 6 or fewer contractions/h
Outcomes	Palpitations, birthweight < 2500 g, neonatal infection, pulmonary oedema, stillbirth, birth before 37 weeks, perinatal death, GA at birth, hypotension, nausea or vomiting, neurodevelopmental morbidity, headache, mean birthweight, gastrointestinal morbidity, delay in birth by 48 h, respiratory morbidity, neonatal death before 7 d, birth before 32 weeks, dyspnoea, SAEs, neonatal death before 28 d
Notes	No COI reported Funded by Stanford University

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table was used
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 women were excluded following randomisation as they did not meet the inclusion criteria.
Selective reporting (reporting bias)	Unclear risk	The study report matches the study protocol that was registered retrospectively (NCT00185900).
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

Matsuda 1993

Study characteristics

Methods	2-arm RCT, placebo-controlled

Matsuda 1993 *(Continued)*

Participants	81 women were randomised from 1 centre in Japan between April 1987 and March 1990. Population: women with threatened preterm birth between 23+0 and 34+6 weeks' gestation and ruptured membranes Definition of threatened preterm birth: ruptured membranes Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), maternal medical conditions (diabetes, pregnancy-induced hypertension), advanced preterm labour with regular uterine contractions, a fetus showing signs of non-reassuring well-being. Women were screened for GBS and gonorrhoea and excluded if positive.
Interventions	Ritodrine 50-100 µg/min administered via IV bolus and titrated to uterine contractions by increasing by 50 µg/min every 10-20 min with a maximum rate of 250 µg/min vs placebo
Outcomes	Delay in birth by 48 h, delay by 7 d, neonatal death within 28 d, neonatal infection, perinatal death, pulmonary oedema, arrhythmia, GA at birth, maternal infection, mean birthweight, pregnancy prolongation, respiratory morbidity
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Unclear risk	Baseline characteristics were similar. Data set is from 2 publications with different denominators

Mawaldi 2008

Study characteristics

Methods	2-arm RCT, active-controlled

Mawaldi 2008 *(Continued)*

Participants	174 women were randomised from 1 centre in Saudia Arabia. Population: women with threatened preterm birth between 24+0 to 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≤ 3 uterine contractions/10 min in 60 min and cervical dilation ≤ 3 cm and < 50% effacement Exclusion criteria: contraindication to tocolysis (signs of intrauterine infection or severe vaginal bleeding), triplet or higher pregnancies, rupture of membranes, maternal medical disorders, hypotension, a fetus showing signs of non-reassuring well-being or malformations
Interventions	Terbutaline 0.25 mg administered SC followed by a further 0.25 mg every 45 min and titrated to uterine contractions and AEs vs nifedipine 30 mg administered orally, followed by 20 mg after 90 min, followed by a further 20 mg every 8 h for 48 h
Outcomes	Delay in birth by 48 h, headache, palpitations, hypotension, nausea or vomiting, SAEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Simple randomisation process
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. Quote" "Because one drug was administered orally and the other subcutaneously, blinding was not attempted"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded. Quote: "Because one drug was administered orally and the other subcutaneously, blinding was not attempted"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

McWhorter 2004

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	214 women were randomised from 1 high-risk obstetric centre in the USA between December 1999 and December 2002.

McWhorter 2004 *(Continued)*

	Population: women with threatened preterm birth between 22+0 to 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: progressive cervical dilatation or effacement with regular uterine contractions Exclusion criteria: contraindications to tocolysis, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction or fetal malformations, cervical dilation > 4 cm, allergy to trial medications. All women were treated with antibiotics until a negative urogenital culture returned, positive cultures were similar across arms.
Interventions	Magnesium sulphate 4–6 g administered by IV bolus followed by 2–4 g/h for a maximum of 48 h vs rofecoxib 50 mg administered orally once a day for a maximum of 48 h
Outcomes	Delay in birth by 48 h, GA at birth, mean birthweight, neonatal death before 7 d, neonatal death before 28 d, neonatal infection, perinatal death, gastrointestinal morbidity, neurodevelopmental morbidity, respiratory morbidity, nausea or vomiting, dyspnoea, headache, arrhythmias, cessation of treatment due to AEs, maternal infection, SAEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Allocated by hospital pharmacist
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "investigators and patients were blinded as to which preparation the patient was taking"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "At no time before data analysis did any clinical investigator have access to or knowledge of the identity of assigned drug."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Unclear risk	Baseline characteristics were reported as similar, but no baseline characteristics table provided. No other obvious bias

Meyer 1990

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	58 women were randomised from 1 centre in the USA.

Meyer 1990 *(Continued)*

	Population: women with threatened preterm labour between 22+0 to 35+0 weeks with intact membranes and singleton pregnancy Threatened preterm labour was defined as ≥ 6 contractions in 30 min or progressive cervical change Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding) or other maternal medical conditions contraindicating tocolysis use
Interventions	Terbutaline 5 mg oral and 250 µg SC followed by nifedipine orally 30 mg followed by 20 mg every 6 h for 24 h, followed by 20 mg every 8 h for another 24 h, followed by 10 mg every 8 h vs terbutaline 5 mg oral and 250 µg SC followed by ritodrine 50 µg/min titrated to uterine contractions or AEs for 12 h with a maximum of 350 µg/min followed by terbutaline 5 mg every 6 h
Outcomes	Delay in birth by 48 h, maternal infection, cessation of treatment due to AEs, neonatal death before 28 d, mean birthweight, birthweight < 2500 g, pregnancy prolongation, perinatal death
Notes	if tocolysis failed (after 2 h from the start of the nifedipine or ritodrine if contractions remained or AEs were intolerable) magnesium sulphate could be given 6 g IV bolus followed by 2 g/h COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Miller 1982

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	29 women were randomised from 1 centre in the USA between October 1979 and September 1980. Population: women with threatened preterm birth before 37+0 weeks with intact membranes

Miller 1982 *(Continued)*

	Definition of threatened preterm birth: 2 contractions in 10 min for > 1 h with cervical dilation < 5 cm and estimated fetal weight < 2500 g Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (cardiac, renal, insulin-dependent diabetes), uterine malformation, cervical dilation > 5 cm, ruptured membranes, fetal weight > 2500g
Interventions	Magnesium sulphate 4 g administered via IV bolus over 5 min followed 10 mL/h (2%) for 2 h then 1% for 22 h at a rate of 125 mL/h followed by terbutaline 5 mg orally vs terbutaline 0.25 mg administered by IV bolus over 5 min followed by 10 µg/min and titrated to uterine contractions to a maximum of 25 µg/min followed 5 mg orally
Outcomes	Cessation of treatment due to AEs, birth before 37 weeks, nausea or vomiting, hypotension, dyspnoea, SAEs
Notes	If treatment was deemed a failure then women could be switched to the other arm. 2 women in the magnesium sulphate group also received terbutaline for treatment failure, 1 woman in terbutaline arm switched to magnesium sulphate due to AEs COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are reported in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Low risk	Baseline characteristics were similar.

Morales 1989

Study characteristics	
Methods	2-arm-RCT, active-controlled
Participants	106 women were randomised from 1 centre in the USA between July 1987 and June 1988.

Morales 1989 *(Continued)*

	Population: women with threatened preterm birth < 32 weeks with intact membranes Definition of threatened preterm birth: ≥ 4 regular contractions in 20 min with cervical effacement or dilation Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), maternal medical conditions, a fetus showing signs of growth restriction or malformation, cervical dilation > 4 cm
Interventions	Ritodrine 50 µg/min administered IV and titrated to uterine contractions with a maximum of 350 µg/min followed by terbutaline (dose or duration NR) orally vs indomethacin 100 mg rectally with an addition 100 mg rectally 1-2 h if contractions persisted followed by 25 mg orally every 4 h for 48 h, followed by terbutaline orally
Outcomes	Perinatal death, delay in birth by 48 h, delay in birth by 7 d, arrhythmias, tachycardia, hypotension, cessation of treatment due to AEs, mean birthweight, respiratory morbidity, neurodevelopmental morbidity, stillbirth, neonatal death before 28 d, SAEs
Notes	If randomised treatment was ineffective or intolerable, magnesium sulphate 5 mg administered by IV bolus followed by 2-4 g/h and titrated to uterine contractions COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Moutquin 2000

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	252 women were randomised across 13 sites in Canada and Israel.

Moutquin 2000 *(Continued)*

	Population: women with threatened preterm birth between 23+0 to 33+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 regular uterine contractions in 30 min with cervical dilatation of ≤ 3 cm and cervical effacement of ≥ 50% Exclusion criteria: contraindications of tocolysis (severe vaginal bleeding or intrauterine infection), serious maternal disease or pregnancy complications, alcohol or drug misuse, multiple pregnancies of triplets or more, ruptured membranes, placental abnormalities, a fetus showing signs of intrauterine growth restriction, non-reassuring well-being, malformations or fetal death, contraindications to study drugs, use of NSAIDs for tocolysis within last 12 h or previous trial participation within 1 month. Women with urinary tract infection were excluded.
Interventions	Atosiban 6.75 mg administered by IV bolus, followed by 300 µg/min by IV infusion for 3 h, followed by 100 µg/min up to 18 h vs ritodrine 0.10-0.35 mg/min administered by IV infusion and titrated to uterine contractions until contractions ceased (in Israel ≤ 4 contractions/h) for up to 18 h
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, GA at birth, mean birthweight, birthweight < 2500 g, pulmonary oedema, dyspnoea, palpitations, arrhythmias, headache, hypotension, nausea or vomiting, cessation of treatment due to AEs, respiratory morbidity, neurodevelopmental morbidity, neonatal infection, neonatal death before 28 d, SAEs, stillbirth
Notes	Supported by Ferring Pharmaceuticals A/S, Copenhagen, Denmark and Ferring Pharmaceuticals participated in the study processes.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated block randomisation stratified by GA ≤ 28 weeks and > 28 weeks
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 women excluded post-randomisation, all others included in analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias.

Neri 2009

Study characteristics

Neri 2009 *(Continued)*

Methods	2-arm RCT, active-controlled
Participants	62 women were randomised across 1 centre in Italy between October 2005 and September 2007. Population: women with threatened preterm birth between 26+0 to 33+0 weeks' gestation intact membranes and singleton pregnancy Definition of threatened preterm birth: > 6 contractions in 1 h with cervical dilation or effacement Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disorders (pre-eclampsia, hypertension), a fetus showing signs of reduced amniotic fluid volume, growth restriction, placental insufficiency
Interventions	Atosiban 6.75 mg administered by IV bolus followed by 37.5 mg in 250 mL at 24 mL/h for 3 h then 8 mL/h for up to 48 h vs ritodrine 100-350 µg/min and titrated to uterine contractions or maternal AEs
Outcomes	Neonatal infection, GA at birth
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	8 women were withdrawn: 4 women were lost to follow-up (2 in each arm), 4 women gave birth before the nonstress test was conducted. All other women are included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Niebyl 1980

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	32 women were randomised from 1 hospital in the USA between June 1976 and June 1978.

Niebyl 1980 *(Continued)*

	Population: women with threatened preterm birth between 24+0 and 35+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 2 uterine contractions in 10 min or cervical dilation ≥ 2 cm of 75% effaced Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection), ruptured membranes, a fetus showing signs of intrauterine growth restriction, allergy to study medications, peptic ulcer
Interventions	Indomethacin 50 mg orally followed by 25 mg every 4 h for 24 h vs placebo of the same regime
Outcomes	Delay in birth by 48 h, GA at birth, mean birthweight, neonatal infection, stillbirth, respiratory morbidity, gastrointestinal morbidity, neonatal death before 7 d, neonatal death before 28 d, SAEs, maternal infection, perinatal death
Notes	If contraction re-occurred, treatment was recommenced as randomised. If progressive cervical dilation > 4 cm 2 h after 1st dose then treatment was stopped and an alternative treatment given; 2 women in placebo group received isoxsuprine and 1 received alcohol; 0 women in the indomethacin group received additional rescue tocolysis that was not indomethacin. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	2 women were removed from the analysis due to issues with trial medication (2 in indomethacin arm)
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Nijman 2016

Study characteristics

Methods	2-arm RCT, placebo-controlled

Nijman 2016 *(Continued)*

Participants	50 women were randomised across 8 perinatal centres with NICU facilities in the Netherlands. Population: women with threatened preterm labour between 24+0 and 33+6 weeks of gestation and ruptured membranes Definition of threatened preterm birth: preterm pre-labour rupture of membranes without signs of active labour Exclusion criteria: ≥ 3 uterine contractions/10 min, previous treatment with tocolysis in the last 7 d (tocolysis for < 6 h for transportation was allowed), symptoms justifying start of tocolysis, ruptured membranes > 72 h, signs of chorioamnionitis or intrauterine infection, signs of fetal distress, fetal major congenital anomaly, contraindication for the use of nifedipine, maternal disease as reason for delivery (hypertension, HELLP syndrome or pre-eclampsia)
Interventions	Nifedipine 20 mg administered orally every 6 h, until the start of active labour, for a maximum of 18 d or until 34+0 weeks' gestation vs placebo 20 mg administered orally every 6 h, until the start of active labour, for a maximum of 18 d or until 34+0 weeks' gestation Cointerventions: antenatal corticosteroids, prophylactic antibiotic therapy and magnesium sulphate administered according to local policy
Outcomes	Perinatal death, delay in birth by 48 h, delay in birth by 7 d, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity, neonatal infection, mean birthweight, GA at birth, pregnancy prolongation, SAEs, cessation of treatment due to AEs
Notes	No COI No funding received

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Web-based computerised randomisation program in a 1:1 ratio, using permuted blocks of 4
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "research staff, clinicians and participants were blinded for treatment allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded. Quote: "research staff, clinicians and participants were blinded for treatment allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Low risk	The study report matches the study protocol that was registered prospectively (NTR3363; Dutch Trial Registry).
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

Nonnenmacher 2009

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	105 women were randomised from 1 centre in Germany. Population: women with threatened preterm birth between 24+0 and 33+6 weeks' gestation Definition of threatened preterm birth: ≥ 4 uterine contractions with cervical changes Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (cardiac, hyperthyroidism), maternal drug or alcohol misuse, allergy to trial medications, a fetus showing signs of non-reassuring well-being, growth restriction or demise
Interventions	Atosiban 6.75 mg administered by IV bolus, followed by 18 mg/h over 3 h, then 6 mg/h for up to 45 h vs fenoterol 1.5-2.0 µg/min administered IV and titrated to uterine contractions with a maximum 3.5 µg/min in 30 min if required and titrated to contractions then reduced accordingly
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, cessation of drug due to AEs, GA at birth, mean birthweight
Notes	5 women were changed from fenotol to atosiban due to AEs. COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics are similar. No other bias

Padovani 2015

Study characteristics

Padovani 2015 *(Continued)*

Methods	2-arm RCT, active-controlled
Participants	66 women were randomised from 3 centres in Brazil between August 2010 and March 2012. Population: women with threatened preterm birth between 24+0 to 33+6 weeks' gestation with a singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min, cervical dilatation < 3 cm, effacement of ≥ 50% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding) maternal medical conditions (asthma, diabetes, cardiovascular disease, severe anaemia, pregnancy-induced hypertension, hypotension), a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, previous tocolysis use in current pregnancy
Interventions	Terbutaline 2.5 µg/min by IV infusion followed 2.5 µg/min increase every 15 min and titrated to uterine contraction for 24 h with a maximum of 20 µg/min vs nifedipine 20 mg orally, if contractions did not cease after 30 min, a second dose of 20 mg was given followed by 20 mg every 8 h for a period of 48 h. The total dose administered during 48 h was 120 mg.
Outcomes	The outcomes reported were: delay in birth by 48 h, pregnancy prolongation, headache, nausea or vomiting, gastrointestinal morbidity, neonatal infection, neurodevelopmental morbidity, neonatal death before 7 d, hypotension, tachycardia, mean birthweight, birth before 34 weeks, birth before 37 weeks, cessation of treatment due to AEs, SAEs, perinatal death, neonatal death before 28 d
Notes	Other tocolytic agents were not permitted concomitantly unless, after at least 1 h of observation during treatment, there was an increase or no change in the frequency of the contractions, or an increase in cervical dilatation of ≥ 1 cm

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Pharmacist informed the attending physician of allocation (those enrolling women were unaware of the arm to which they would be allocated)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. Quote: "The doctors and nurses were not blind to allocation. Data were collected by a physician in training, and outcome were adjudicated by one of two physicians blind to group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded. Quote: "Data were collected by a physician in training, and outcome were adjudicated by one of two physicians blind to group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	States that protocol is registered but unavailable for verification
Other bias	Low risk	Baseline characteristics were similar. No COI

Padovani 2015 *(Continued)*

	No funding received

Papatsonis 1997

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	185 women were randomised from 3 centres in the Netherlands between February 1992 and February 1995. Population: women with threatened preterm birth between 20+0 to 33+4 weeks' gestation with singleton pregnancy Definition of threatened preterm birth: at least 1 contraction in 10 min for 1 h or rupture of membranes Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (diabetes, cardiac, hyperthyroidism, pre-eclampsia), multiple pregnancy, a fetus showing signs of intrauterine growth restriction, malformation
Interventions	Ritodrine 386 µg/min administered by IV bolus then reduced to 97 µg/min and titrated to uterine contraction or maternal AEs for 3 d then reduced followed by 40 mg orally every 8 h until 34 weeks' gestation vs nifedipine 10 mg sublingually with a further 10 mg in 15 min if contractions persisted with a further 20 mg given if required at 15-min intervals followed by 60-160 mg daily for 3 d followed by 20 mg 3 times a d until 34 weeks
Outcomes	Birth before 34 weeks, neonatal infection, stillbirth, birth before 37 weeks, perinatal death, GA at birth, neurodevelopmental morbidity, mean birthweight, gastrointestinal morbidity, delay in birth by 48 h, neonatal death before 7 d, SAEs, cessation of treatment due to AEs, neonatal death before 28 d, delay in birth by 7 d
Notes	Indomethacin could be given if contractions did not respond to randomised treatment: 20 women in the ritodrine group and 26 in the nifedipine group. Women who stopped tocolysis due to AEs were removed from the maternal analysis (ritodrine 12 women). COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation by pharmacist with stratification by gestation and membrane status
Allocation concealment (selection bias)	Low risk	Sealed opaque envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR

Papatsonis 1997 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Per protocol analysis was done rather than ITT as women who received treatment in the other arm due to AEs of initial treatment randomisation were removed from the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Parilla 1997

Study characteristics		
Methods	2-arm RCT, active-controlled	
Participants	12 women were randomised from 1 centre in the USA. Population: women with threatened preterm birth < 30 weeks' gestation with intact membranes Definition of threatened preterm birth: regular uterine contractions and progressive cervical dilatation and effacement Exclusion criteria comprised contraindications to tocolysis (signs of intrauterine infection or severe vaginal bleeding), pre-eclampsia, ruptured membranes, a fetus showing signs of intrauterine growth restriction, non-reassuring well-being	
Interventions	Magnesium sulphate 8 g administered by IV bolus over 1 h, followed by 4 g over 1 h, followed by 2.5 g/h for 12 h after contraction cessation vs indomethacin 50-100 mg administered orally or rectally, followed by 25-50 mg orally every 4-6 h for 24-48 h	
Outcomes	GA at birth, perinatal death, mean birthweight, respiratory morbidity, gastrointestinal morbidity, neurodevelopmental morbidity, neonatal death before 28 d	
Notes	COI and funding information: NR	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated series of random numbers
Allocation concealment (selection bias)	Low risk	Sealed, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias)	Low risk	All women were included in the analysis.

Parilla 1997 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics were similar.

Parsons 1987

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	52 women were randomised from 1 centre in the USA between September 1983 and July 1984. Population: women with threatened preterm birth between 25+0 to 34+0 weeks' gestation with threatened preterm birth and intact membranes. Definition of threatened preterm birth: not defined Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection), ruptured membranes, antibiotic treatment or tocolytic treatment time < 12 h
Interventions	Terbutaline 0.25 mg administered by IV infusion, followed by 10 µg/min that was increased by 5 µg/min every 10 min and titrated to uterine contractions or AEs and continued for 12 h after contractions vs magnesium sulphate 4 g via IV bolus followed by 2 g/h and increased by 0.5 g/h every 30 min and titrated to uterine contractions with a max 3 g/h and continued for 12 h after contractions
Outcomes	Outcomes of interest: NR
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.

Parsons 1987 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Pezzati 2001

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	54 women were randomised from 1 centre in Italy. Population: women with threatened preterm birth between 24+0 to 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: regular uterine contractions and cervical dilatation of ≥ 1 cm Exclusion criteria: cervical dilatation > 5 cm, significant maternal complications including pre-eclampsia or eclampsia, or other maternal or fetal complications requiring delivery, or a fetus showing signs of intrauterine growth restriction, non-reassuring well-being or malformations, infants with infection, anaemia, polycythaemia or patent ductus arteriosus
Interventions	Magnesium sulphate 4 g in 20–30 min administered by IV infusion followed by 2 g/h vs ritodrine 50 mg/min administered by IV infusion, titrated to uterine contraction or maternal AEs, with a maximum dosage of 250 mg/min. Co-interventions: antenatal corticosteroids
Outcomes	Perinatal death, GA at birth, neurodevelopmental morbidity, mean birthweight, gastrointestinal morbidity, respiratory morbidity, neonatal death before 7 d, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.

Pezzati 2001 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias

Raymajhi 2003

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	62 women were randomised from centres in Nepal (number of centres NR). Population: women with threatened preterm birth between 28+0 to 36+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 1 uterine contractions/10 min with cervical effacement or dilatation ≤ 3 cm Exclusion criteria comprised contraindications to tocolysis (severe vaginal bleeding or signs of intrauterine infection), maternal medical complications or disease (severe pre-eclampsia and eclampsia, cardiac disease, thyroid disorder) and advanced labour, a fetus showing signs of intrauterine growth restriction, fetal demise, oligoamnios, or malformations
Interventions	Nifedipine 10 mg administered sublingually plus 500 mL of crystalloid solution infused over 30–45 min, followed by 20 mg every 20 min for up to 4 doses, followed by 10-20 mg in 4-6 h after the last dose, followed by 10–20 mg orally every 6–8 h for up to 7 d vs isoxsuprine 40 mg in 500 mL Ringer lactate at 0.08 mg/min administered by IV bolus titrated to uterine contractions and AEs with a maximum of 0.24 mg/min, followed by 10 mg administered orally every 8 h for up to 7 d
Outcomes	Palpitations, pulmonary oedema, stillbirth, birth before 37 weeks, perinatal death, GA at birth, hypotension, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, neonatal death before 7 d, tachycardia, SAEs, pregnancy prolongation, cessation of treatment due to AEs, neonatal death before 28 d, delay in birth by 7 d
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR

Raymajhi 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baselline characteristics were matched but not clearly reported to assess comparability.

Read 1986

Study characteristics	
Methods	3-arm RCT, placebo-controlled
Participants	60 women were randomised from 1 centre in the UK (dates NR). Population: women between 20+0 and 35+0 weeks' gestation with threatened preterm birth with singleton pregnancies and intact fetal membranes. Definition of threatened preterm birth: ≥ 1 uterine contraction every 10 min Exclusion criteria: contraindications to tocolysis (signs of intrauterine infection or severe vaginal bleeding), multiple pregnancy, ruptured membranes, previous cervical surgery, mid-trimester pregnancy loss or preterm birth, maternal medical conditions contraindicating study drug use, a fetus showing signs of non-reassuring well-being or polyhydramnios, or cervical dilation > 4 cm dilated
Interventions	Nifedipine 30 mg orally followed by 20 mg at 8 h intervals for 3 d vs ritodrine IV 50 µg/min rising by 50 µg every 10 min to a maximum of 300 µg/min or until contractions ceased vs no treatment
Outcomes	SAEs, pregnancy prolongation, neonatal death before 28 d, neonatal death before 7 d, mean birthweight, delay in birth 48 h, still birth, perinatal death
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR

Read 1986 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Richter 2005

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	40 women were randomised from 1 centre in Germany. Population: women with threatened preterm birth between 18+0 to 24+0 weeks of gestation Definition of threatened preterm birth: regular uterine contractions of 4 in 30 min, cervical effacement > 50%, cervical dilatation up to 3 cm Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), serious maternal disease, preterm rupture of the membranes, oligohydramnios or polyhydramnios, a fetus showing signs of malformations, growth restriction or demise, multiple pregnancy, alcohol and drug abuse, hypersensitivity to study drug or study participation within the last 6 months
Interventions	Atosiban IV bolus injection (approximately 1 min, 6.75 mg of atosiban in 0.9 mL of sodium chloride) followed immediately by high-dosage saturation infusion with atosiban in 0.9% sodium chloride for 3 h (300 micro g/ min) followed by a low-dosage continuous infusion with atosiban in 0.9% sodium chloride for up to 45 h (100 micro g/min) vs placebo via IV infusion
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, stillbirth, cessation of treatment due to AEs
Notes	COI and funding information: NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR

Richter 2005 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Romero 2000

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	531 women were randomised across 37 centres in the USA (dates NR). Population: women with threatened preterm birth between 20+0 to 33+6 weeks' gestation with intact membranes. Definition of threatened preterm birth: ≥ 4 contractions in 30 min with cervical dilation of 1-3 cm and ≥ 50% effacement Exclusion criteria: contraindications of tocolysis (intrauterine infection), urinary tract infection, maternal complications requiring delivery, placental abnormalities, a fetus showing signs of non-reassuring well-being or malformation or substance misuse
Interventions	Atosiban 6.75 mg administered IV as a bolus over 1 min, followed by 300 µg/min infusion over 3 h, then 100 µg/min infusion for up to 45 h until uterine contractions ceased, then 30 µg/min SC until the end of the 36th week of gestation or delivery vs placebo bolus administered over 1 min, followed by 300 µg/min infusion over 3 h, then 100 µg/min infusion for up to 45 h until uterine contractions ceased, then 0.004 mL/min SC until the end of the 36th week of gestation or delivery
Outcomes	Maternal death, stillbirth, birth before 37 weeks, perinatal death, neurodevelopmental morbidity, mean birthweight, gastrointestinal morbidity, delay in birth by 48 h, respiratory morbidity, neonatal death before 7 d, tachycardia, birth before 32 weeks, SAEs, neonatal death before 28 d, delay in birth by 7 d
Notes	Funded by RW Johnson Pharmaceutical research institute

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation schedule, stratified by centre
Allocation concealment (selection bias)	Low risk	Sequentially numbered envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded. Quote: "Investigators, study personnel and monitors remained blinded throughout the study"
Blinding of outcome assessment (detection bias)	Low risk	Blinded. Quote: "Investigators, study personnel and monitors remained blinded throughout the study".

Romero 2000 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	30 women (15 in each arm) were excluded post-randomisation because they did not meet the inclusion criteria. They are included in the ITT analysis but the results of the ITT analysis of both populations led to the same conclusion as the analysis for women as per protocol analysis.
Selective reporting (reporting bias)	Unclear risk	Protocol not available for verification
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Saade 2021

Study characteristics	
Methods	2-arm active RCT
Participants	23 women were randomised across 46 centres in UK, USA, Italy, Japan and Canada between February 2016 and July 2017. Population: women with threatened preterm birth between 24+0 to 33+6 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: ≥ 4 contractions in 30 min and cervical dilation > 1 cm and effacement of > 25% Exclusion criteria: women requiring immediate birth for maternal or fetal reasons, contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (cardiac or liver disease, diabetes, hypertension), drug use, allergy to study drugs, current tocolysis use, polyhydramnios, oligohydramnios, ruptured membranes, a fetus showing signs of non-reassuring well-being, growth restriction, malformation
Interventions	Retosiban 6 mg administered as IV bolus over 5 min followed by a 6-mg/h infusion 48 h followed by an additional 6 mg/h if there was an inadequate response after the first h of treatment, followed by at 12 mg/h vs placebo in the same regime
Outcomes	GA at birth, mean birthweight, birth before 37 weeks, neonatal death before 28 d, maternal death, SAEs
Notes	Rescue tocolysis was permitted. 1 woman in the retosiban group received ketorolac, 2 women in the placebo group received magnesium sulphate, 1 received nifedipine, 1 received terbutaline. No other tocolytics were permitted. Women who received tocolysis before trial entry ceased tocolysis. Funded by GlaxoSmithKline

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Infusions and matching placebos were prepared by unblinded pharmacists/qualified individuals

Saade 2021 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind. Quote: "Participants were blinded for the study duration"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "All other personnel were blinded for the study duration"
Incomplete outcome data (attrition bias) All outcomes	High risk	2 women in the retosiban group became ineligible after randomisation and were excluded from the analysis, all women are included in the analyses.
Selective reporting (reporting bias)	Low risk	The outcomes reported match the outcomes reported in the study protocol that was registered prospectively (NCT02377466).
Other bias	Unclear risk	Baseline characteristics were similar. Funded by GlaxoSmithKline.

Sakamoto 1985

Study characteristics	
Methods	2-arm placebo RCT
Participants	291 women were randomised from 31 centres in Japan between May 1982 and July 1983. Population: women with threatened preterm birth between 24+0 and 37+0 weeks' gestation Definition of threatened preterm birth: contractions with cervical dilation < 4 cm and effacement < 80% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal disease (cardiac, liver), maternal medical conditions (hyperthyroidism, diabetes, kidney malfunction), a fetus showing signs of non-reassuring well-being, malformation, demise, multiple pregnancy, ruptured membranes
Interventions	Ritodrine 5 mg administered orally 3 times a d for 2 weeks or until 37 weeks vs placebo orally 3 times a d for 2 weeks or until 37 weeks
Outcomes	Neonatal death before 28 d, tachycardia, palpitations, nausea or vomiting, birthweight < 2500 g
Notes	Women could receive rescue tocolysis if the randomised treatment was ineffective. 11 women in the ritodrine arm and 27 women in the placebo arm received rescue tocolysis. Birthweight < 2500 g and birth before 37 weeks excluded women who received rescue tocolysis COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Allocation by the controller who kept the key code until the end of the study

Sakamoto 1985 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	15 women were excluded from the analysis: 7 in the ritodrine group and 8 in the control group due to ineligibility after randomisation. 2 women in the ritodrine group and 1 in the placebo group were partially included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Low risk	Baseline characteristics were similar

Salim 2012

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	149 women were randomised from 1 centre in Israel between January 2008 and December 2011. Population: women with threatened preterm birth between 24+0 and 33+6 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 30 min lasting ≥ 30 s, and cervical effacement ≥ 50% and cervical dilation up to 4 cm. Exclusion criteria: contraindication for tocolysis (indication of intrauterine infection or severe vaginal bleeding), rupture of membranes, maternal disease (severe pre-eclampsia, cardiovascular, liver, hypotension) uterine malformation, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, malformations or demise), triplets or greater
Interventions	Atosiban 6.75 mg administered IV as a bolus, followed by 3000 µg/min infusion for 3 h, then 100 µg/min infusion for 45 h vs Nifedipine 20 mg administered orally, followed by another 2 doses of 20 mg 20-30 min apart as needed, then after 6 h 20-40 mg administered orally 4 times a d for 48 h
Outcomes	Palpitations, birth before 34 weeks, birthweight < 2500 g, neonatal infection, birth before 37 weeks, perinatal death, GA at birth, hypotension, nausea or vomiting, neurodevelopmental morbidity, headache, mean birthweight, gastrointestinal morbidity, delay in birth by 48 h, respiratory morbidity, tachycardia, birth before 28 weeks, pregnancy prolongation, cessation of treatment due to AEs, neonatal death before 28 d, delay in birth by 7 d
Notes	No COI Funded by Emek medical centre

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomisation sequence generation program, in blocks of 10

Salim 2012 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	This study was not blinded as study drugs were administered by different roots
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 women were excluded post-randomisation (2 from each arm) because of cervical dilation progression or withdrawal of consent. There were similar numbers of women in both arms.
Selective reporting (reporting bias)	Low risk	Study report matches the study protocol that was registered prospectively (NCT00599898).
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Schleussner 2003

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	50 women were randomised in 2 specialised centres in Germany between June 1999 and May 2000. Population: women with threatened preterm birth between 27+0 and 35+0 weeks' gestation Definition of threatened preterm birth: ≥ 3 contractions in 30 min with a Bishop score of ≥ 3 Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or signs of intrauterine infection), multiple pregnancy, preterm rupture of membrane, contraindication to study drugs or participation in another study
Interventions	Transdermal nitroglycerin therapy (2 patches of Nitroderm TTS 10 at an initial dosage of 0.8 mg/h nitroglycerin) vs continuous IV fenoterol at 120 mg/h along with magnesium sulphate 1.2 g/h and verapamil 1.2 mg/h
Outcomes	Mean birthweight, headaches, palpations, SAEs
Notes	COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Women were randomised according to the study identification number in each centre following a random list.
Allocation concealment (selection bias)	Unclear risk	NR

Schleussner 2003 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	6 women dropped out of the study. However, ITT analysis was conducted on the data of all women, including those who dropped out.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Schorr 1998

Study characteristics	
Methods	2-arm active RCT
Participants	88 women were randomised from 1 centre in the USA (dates NR). Population: women with threatened preterm birth between 20+0 to 32+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 12 contractions in 1 h and ≥ 2 cm cervical dilation or effacement > 50% Exclusion criteria: contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (peptic ulcer, asthma, thrombocytopenia), sensitivity to study medication, cervical dilation > 4 cm, ruptured membranes, oligohydramnios, a fetus showing signs of growth restriction, malformation, non-reassuring well-being
Interventions	Magnesium sulphate 6 g administered by IV bolus over 20 min followed by 2-6 g/h titrated to uterine contractions and continued for up to 4 h after contractions ceased followed by 2 g orally every 4 h until 37 weeks vs ketorolac 60 mg administered IM followed by 30 mg every 6 h until contractions ceased followed by magnesium sulphate 2 g orally every 4 h until 37 weeks
Outcomes	Birth before 37 weeks, GA at birth, neurodevelopmental morbidity, birthweight < 2000 g, birth before 32 weeks, maternal infection, SAEs, cessation of treatment due to AEs, neonatal death before 28 d
Notes	No COI reported Funded by Vicksburg Hospital

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Pharmacy personnel no other details reported

Schorr 1998 *(Continued)*

Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics are similar

Shim 2006

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	128 women were randomised across 6 centres in South Korea. Population: women aged ≥ 18 years with threatened preterm birth between 24+0 weeks and 33+6 weeks of gestation with a singleton pregnancy Definition of threatened preterm birth: at least 4 regular uterine contractions/30 min plus cervical dilatation of < 3 cm and cervical effacement of > 50% Exclusion criteria: contraindications for tocolysis (severe vaginal bleeding or intrauterine infection), serious maternal disease e.g. cardiovascular disease, severe pre-eclampsia or hypertension, fever, urinary tract infection, multiple pregnancy, ruptured membranes, placental or amniotic fluid abnormalities, or a fetus with malformations, any contraindication to the use of beta-adrenergic agonists or hypersensitivity to components of the study drugs, alcohol or drug abuse, previous exposure to NSAIDs for tocolysis within 12 h of study entry, or participation in a clinical trial within 1 month
Interventions	Atosiban 6.75 mg administered by an IV bolus, followed by 300 mg/min for the 1st 3 h and then 100 mg/min for up to 48 h vs ritodrine 0.1–0.35 mg/min administered by IV infusion for up to 48 h, with 0.05 mg/min increments/10 min as required with a maximum of 0.35 mg/min titrated to contractions. After 12 h of continuous infusion at the maximally effective dose or when contractions ceased, the dose was decreased every 30 min by 0.05 mg/min
Outcomes	Palpitations, perinatal death, GA at birth, pulmonary oedema, stillbirth, neonatal infection, mean birthweight, headache, nausea or vomiting, hypotension, neurodevelopmental morbidity, delay in birth by 48 h, respiratory morbidity, tachycardia, delay in birth by 7 d, pregnancy prolongation, neonatal death before 28 d, cessation of treatment due to AEs, SAEs, dyspnoea
Notes	Supported by Ferring pharmaceuticals
Risk of bias	

Shim 2006 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation stratified by GA < 28 and > 28 weeks at study entry
Allocation concealment (selection bias)	Low risk	An independent company used computer-generated randomisation lists to randomly assign women.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The study was single-blinded. Quote: "All infusates were prepared by assigned nurses and administered by a piggy-back method" no further details are reported.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessors were reported to be blinded. Quote: "Infusates were administered using a piggy-back method and we maintained the investigator-blinded methods in assessing outcomes".
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women were excluded post-randomisation due to not fulfilling the inclusion criteria so were not included in the ITT analysis, all other women were included in the analysis. All women were included in the safety analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Smith 1999

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	33 women were randomised from 1 tertiary centre in Canada. Population: women between 24+0 and 34+0 weeks of gestation with threatened preterm birth in singleton and twins pregnancies with intact membranes Definition of threatened preterm birth: evidence of cervical change Exclusion criteria included: rupture of membranes; any maternal condition such as significant antepartum haemorrhage or fetal condition necessitating immediate delivery; suspicion of lethal anomalies or intrauterine fetal death; multiple gestation greater than twins; cervical dilatation > 4 cm; treatment with another tocolytic agent within 24 h; previous randomisation in this trial; known sensitivity to nitroglycerin; or failure to give consent
Interventions	Nitroglycerin patch (replaced every 24 h for 48 h) vs placebo patch (replaced every 24 h for 48 h)
Outcomes	Perinatal death, GA at birth, prolongation of pregnancy, mean birthweight, respiratory morbidity, delay in birth by 48 h, gastrointestinal morbidity, neurodevelopmental morbidity
Notes	COI and funding information: NR
Risk of bias	

Bias	Authors' judgement	Support for judgement

Smith 1999 *(Continued)*

Random sequence generation (selection bias)	Low risk	Randomisation with stratification in blocks of 2 by a 3rd party
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered opaque envelopes prepared by 3rd party
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Yes. Quote: "The investigators, attending physicians and study patients were blinded to the randomisation process"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Yes. Quote: "The investigators, attending physicians and study patients were blinded to the randomisation process"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Smith 2007

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	158 women were randomised from multiple centres in Canada. Population: women between 24+0 and 32+0 weeks of gestation with threatened preterm birth in singleton pregnancies with intact membranes Definition of threatened preterm birth: > 4 painful uterine contractions/20 min and evidence of cervical change (change in Bishop score or Bishop score > 6) Exclusion criteria: any maternal or fetal condition necessitating delivery, multiple gestations, preterm labour rupture of the membranes preterm, intrauterine fetal demise or suspected lethal fetal anomalies, cervix dilated > 5 cm, treatment with tocolysis within 24 h, previous enrolment in the trial, known sensitivity to GTN, failure to consent
Interventions	Transdermal GTN patch 0.4 mg/h vs placebo patch
Outcomes	Respiratory morbidity, gastrointestinal morbidity, neurodevelopmental morbidity, perinatal death, delay in birth by 48 h, birth before 28 weeks, birth before 34 weeks, birth before 37 weeks, serious adverse events, prolongation of pregnancy, GA at birth, hypotension, stillbirth, headache, neonatal death before 28 d
Notes	No COI Funded by Canadian Institutues for Health Research
Risk of bias	

Smith 2007 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomisation and stratification by centre and GA
Allocation concealment (selection bias)	Low risk	Sealed opaque study envelopes prepared by 3rd party
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Yes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Yes
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis
Selective reporting (reporting bias)	Unclear risk	The trial was registered retrospectively (ISRCTN 20129681).
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Spellacy 1979

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	29 women were randomised from 1 centre in the USA (study dates NR). Population: women with threatened preterm birth between 20+0 to 36+0 weeks of gestation with an estimated fetal weight < 2500 g Definition of threatened preterm birth: ≥ 1 contractions every 10 min with cervical change Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), cervical dilation > 5 cm, severe maternal or fetal diseases (no examples given)
Interventions	Ritodrine 100 µg/min administered by IV infusion and titrated to uterine contractions or AEs for 12 h with a maximum of 350 µg/min, followed by 5-10 mg IM every 3-8 h titrated to uterine contractions for 24 h followed by 10-20 mg orally 3-8 times/d (maximum 120 mg/daily) until 38 weeks' gestation vs placebo following the same regime
Outcomes	Palpitations, perinatal death, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, neonatal death before 28 d, delay in birth by 7 d
Notes	Funded by pharmaceutical company (Philips-Duphar)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Spellacy 1979 *(Continued)*

Random sequence generation (selection bias)	Low risk	Random numbering of treatment packs
Allocation concealment (selection bias)	Low risk	Random number-assigned treatment pack, the contents of which were concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind. Quote: "none of the healthcare professionals knew the identify of the drug until after th pregnancy was completed."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "none of the healthcare professionals knew the identify of the drug until after th pregnancy was completed."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification
Other bias	Unclear risk	Funded by pharmaceutical company (Philips-Duphar)

Surichamorn 2001

Study characteristics	
Methods	3-arm active RCT
Participants	96 women were randomised from 1 centre in Thailand. Population: adult women between 28+0 and 35+0 weeks of gestation of a singleton pregnancy with threatened preterm birth Definition of threatened preterm birth: regular painful contractions occurring at intervals of < 10 min, observed for at least 30 min, the cervix effaced or almost effaced and dilatated not more than 3 cm Exclusion criteria: fever, placenta praevia, placental abruption, fetal abnormality, hydramnios, incompetent cervix, premature rupture of membranes, maternal arrhythmias, hypertension, hyperthyroidism, diabetes mellitus, received prior tocolytic agent or absolute contraindication to terbutaline or magnesium sulphate
Interventions	Magnesium sulphate loading dose 4 g IV over 20 min, followed by an infusion of 2 g/h increasing to a maximum rate of 4 g/h as needed to arrest labour for 24 h, followed by 2.5 mg terbutaline every 6 h until 36 weeks' gestation vs terbutaline 0.25 mg administered by IV bolus followed by 10 µg/min and titrated to uterine contractions with a maximum of 25 µg/min, followed by 0.25 mg SC every 4 h for 24 h, followed by 2.5 mg orally every 6 h until 36 weeks' gestation
Outcomes	Stillbirth, perinatal death, birth before 37 weeks, GA at birth, hypotension, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, neonatal death before 7 d, cessation of treatment due to AEs, neonatal death before 28 d, delay in birth by 7 d
Notes	COI and funding information: NR
Risk of bias	

Surichamorn 2001 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	25 women excluded post-randomisation. All other women were included in the analysis. Exclusions were similar across arms.
Selective reporting (reporting bias)	Unclear risk	The protocol was not available for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Szulc 2000

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	60 women were randomised from 1 centre in Poland between January and December 1998. Population: women with threatened preterm birth between 23+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min with cervical dilation up to 3 cm or effacement of ≥ 60% Exclusion criteria: contraindication to tocolysis, ruptured membranes, multiple pregnancy
Interventions	Nitroglycerin 10 mg administered transdermally with an additional 5 mg in 1 h if required and retained for 24 h, and repeated in 24 h vs fenoterol 1 mg administered via IV infusion and titrated to uterine contractions followed by 5 mg orally every 6-8 h
Outcomes	Headache, tachycardia, nausea or vomiting
Notes	COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Random coding - no other details reported

Szulc 2000 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Taherian 2006

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	120 women were randomised from 2 centres in Iran between December 2005 and September 2006. Population: women between 26+0 and 36+0 weeks of gestation with threatened preterm birth and intact fetal membranes Definition of threatened preterm birth: progressive cervical dilatation and effacement associated with ≥ 4 uterine contractions in 10 min Exclusion criteria were contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), cervical dilatation > 5 cm or obstetrical contraindication for tocolysis use e.g. severe pre-eclampsia, lethal fetal anomalies, maternal cardiac or liver diseases
Interventions	Nifedipine 10 mg orally then every 20 min (max dose of 40 mg in first h). If contractions subsided then 10-20 mg every 6 h vs IV magnesium sulphate loading dose of 4 g over 15 min then a maintenance dose of 2-3 g/h IV infusion
Outcomes	Birth before 37 weeks, GA at birth, hypotension, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, birth before 32 weeks
Notes	COI and funding information: NR
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Table of random numbers

Taherian 2006 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Tchilinguirian 1984

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	77 women were randomised from 1 centre in the USA between April 1981 and March 1983. Population: women with threatened birth between 24+0 to 36+0 weeks' gestation Definition of threatened preterm birth: uterine contractions with or without ruptured membranes Exclusion criteria were rupture of membranes for > 24 h, cervical dilation > 4 cm
Interventions	Ritodrine (dose and duration NR) followed by oral ritodrine vs magnesium sulphate 4 g administered by IV bolus and titrated to uterine contractions for 12 h after contractions stopped followed by oral ritodrine
Outcomes	Delay in birth by 48 h
Notes	COI and funding information: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	Unclear risk	NR

Tchilinguirian 1984 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Thornton 2009

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	163 women were randomised from 21 sites in Belgium (4), Czech Republic (5), Finland (3), Lithuania (2), Poland (4), and Romania (3) between November 2003 and July 2007. Population: women between 34+0 and 35+6 weeks' gestation with threatened preterm birth with intact membranes Definition of threatened preterm birth: > 6 uterine contractions lasting ≥ 30 s in 30 min, cervical length of 15 mm and cervical dilatation > 1 cm and < 4 cm Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding), maternal disease (diabetes; existing or gestational, eclampsia, severe pre-eclampsia, haemoglobinopathies) or thromboembolic disorders or coagulation deficiency, previous major uterine surgery or abnormality, large leiomyomas, retained intrauterine contraceptive device or cervical cerclage, multiple pregnancy, ruptured membranes, oligo- or polyhydramnios, a fetus showing signs of non-reassuring well-being, growth restriction or malformations, alcohol or drug misuse in 12 months, hypersensitivity to study drug, treatment with anticoagulants or fibrinolytic or other tocolysis
Interventions	Single IV bolus dose (1 mL) of 1 of the following treatments: 0.3, 1, 3, or 10 mg barusiban vs placebo
Outcomes	Neonatal death before 28 d, cessation of treatment due to AEs, birth before 37 weeks, perinatal death, stillbirth, neonatal death before 7 d, SAEs, respiratory morbidity
Notes	Supported by Ferring Pharmaceuticals A/S, Copenhagen, Denmark

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation was computer-generated for each participating site by an independent statistician from Ferring Pharmaceuticals
Allocation concealment (selection bias)	Low risk	All participants and study personnel, including those assessing the outcomes,were blinded to treatment assignment for the duration of the study.

Thornton 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	All participants and study personnel, including those assessing the outcomes,were blinded to treatment assignment for the duration of the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All participants and study personnel, including those assessing the outcomes,were blinded to treatment assignment for the duration of the study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in analysis
Selective reporting (reporting bias)	Unclear risk	The protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics: NR

Thornton 2015

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	64 women were randomised across 58 centres in the USA, Argentina, Bulgaria, Columbia, France, Republic of Korea, Lithuania, Puerto Rico, Singapore, Spain, UK. Population: women with threatened preterm birth between 30+0 and 35+6 weeks' gestation with intact membranes and a singleton pregnancy Definition of threatened preterm birth: ≥ 6 contractions/h with cervical dilatation ≥ 1 cm Exclusion criteria comprised contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal or fetal conditions requiring immediate birth, cervical dilation > 4 cm, ruptured membranes, maternal medical conditions (pre-eclampsia, hypertension, diabetes or substance abuse) or a fetus showing signs of non-reassuring well-being
Interventions	Retosiban 6 mg administered via IV bolus followed by 6 mg/h for 48 h, after 1 h infusion rate could be increased to 12 mg/h if required vs placebo of the same regime
Outcomes	Delay in birth by 7 d, mean birthweight, headache, nausea or vomiting
Notes	Women who did not respond to the dose increase could discontinue study medication and receive an alternative rescue tocolytic at the discretion of the investigator. 10 women received rescue tocolysis, 3 (10%) in the retosiban group and 7 (21%) in the placebo group. Rescue tocolysis included magnesium sulphate (n = 6), nifedipine (n = 3), fenoterol (n = 2), ritodrine (n = 1), atosiban (n = 1) and salbutamol (n = 1). Around 1/4 women received tocolysis prior to randomisation, this was even across the arms, tocolysis was given in the current pregnancy but previously, no women were receiving additional tocolysis at the time of randomisation. Funded by GlaxoSmithKline

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Thornton 2015 *(Continued)*

Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Quote: "assigned to treatment in accordance with randomisation schedule"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women are included in the analyses.
Selective reporting (reporting bias)	Low risk	The outcomes reported match the protocol that was registered prospectively (NCT00404768).
Other bias	Low risk	Baseline characteristics were similar.

Tohoku 1984

Study characteristics	
Methods	2-arm RCT, placebo-controlled
Participants	47 women were randomised from 10 centres in Japan between June 1981 and January 1982. Population: women with threatened preterm birth between 24+0 and 36+0 weeks' gestation with estimated fetal weight < 2500 g and intact membranes Definition of threatened preterm birth: ≥ 2 regular contractions in 40 min Exclusion criteria comprised contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), cervical dilation of ≤ 5 cm, maternal medical condition (kidney, heart or liver disease, hyperthyroidism, a fetus showing signs of non-reassuring well-being, malformation or demise
Interventions	Ritorine hydrochloride 100 µg/min administered by IV infusion and titrated to uterine contractions and AEs every 30 min to a maximum of 200 µg/min (40 drops/min) for a total of 2 h vs placebo administered IV at the same rate with 20 drops/min titrated to contraction for a total of 2 h. After 60 min with no effect other appropriate measures could be substituted.
Outcomes	Palpitations
Notes	If no tocolytic effects had been observed after 60 min had passed since commencement, then it was determined that under the judgment of the doctor, other appropriate measures could be substituted. Other tocolytics were avoided during the 2-h period of 'evaluation' but treatment was freely allowed after the evaluation period. No details on what was given and how many received it. COI and funding information: NR
Risk of bias	

Tohoku 1984 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics are similar. No other bias

Trabelsi 2008

Study characteristics	
Methods	2-arm active RCT
Participants	48 women were randomised from 1 centre in Tunisia between January and July 2005. Population: women with threatened preterm birth between 28+0 and 35+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 2 contractions in 10 min with ≥ 50% cervical effacement Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (pre-eclampsia, hypertension, cardiopathy, diabetes), oligohydramnios, placenta praevia, cervical dilation of > 3 cm, a fetus showing signs of growth restriction, malformation, contraindications to study drugs, tocolysis use before study admission
Interventions	Nicardapine 2 mg/min administered IV and increased every 30 min and titrated to uterine contractions or AEs with a maximum of 4 mg/h for 48 h followed by 2 tablets/d orally (dose NR) until 37 weeks vs salbutamol 0.125 mg/h for 48 h followed by 2 oral tablets or rectal suppositories of 1 g/d until 37 weeks
Outcomes	GA at birth, hypotension, headache, mean birthweight, delay in birth by 48 h, tachycardia, cessation of treatment due to AEs
Notes	if tocolysis failed with nicardipine then salbutamol was given. 6 women in salbutamol arm were changed to nicardipine due to AEs. COI and funding information: NR

Trabelsi 2008 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study was not double-blind due to the well-known AEs.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 women were lost to follow-up; all other women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Valdes 2012

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	153 women were randomised across 2 centres in Chile. Population: women with threatened preterm birth between 23+0 to 34+0 weeks' gestation with a singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 1 uterine contractions/10 min for 1 h despite hydration and rest, with or without cervical dilation or effacement Exclusion criteria comprised contraindication to tocolysis (signs of intrauterine infection or severe vaginal bleeding), maternal medical disease (diabetes mellitus, cardiovascular disease, hyperthyroidism), ruptured membranes, a fetus showing signs of severe intrauterine growth restriction or malformations, contraindications to the use of study medications
Interventions	Nifedipine 20 mg administered orally, followed by a further 20 mg or 40 mg if contractions persisted, with a maximum dose of 60 mg in 1 h, followed by 20 mg every 6 h then gradually reduced to a minimum of 10-mg every 6 h then stopped vs fenoterol 1 µg/min administered by IV infusion increased every 30 min and titrated to uterine contractions or AEs and maintained for 12 h, with a maximum dose of 4 µg/min, then gradually reduced to 0.5–1 µg/min for 48 h and then stopped
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 34 weeks, birth before 37 weeks, GA at birth, mean birthweight, hypotension, respiratory morbidity, SAEs, cessation of treatment due to AEs, pregnancy prolongation

Valdes 2012 *(Continued)*

Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Permuted-block design centrally prepared by the principal investigator
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear. Quote: "the collaborators in the participating centres were unaware of enrolment order"
Incomplete outcome data (attrition bias) All outcomes	High risk	21 women were withdrawn from the study due to inadequate randomisation or missing data. Incomplete data for d 7 follow-up. Different numbers reported in text and table
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Van De Water 2008

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	93 women were randomised across 4 centres in the Netherlands. Population: women with threatened preterm labour between 24+0 and 34+0 weeks' gestation with a singleton pregnancy Definition of threatened preterm birth: ≥ 1 uterine contraction/10 min for 60 min Exclusion criteria comprised contraindications to tocolysis (severe vaginal bleeding or intrauterine infection), multiple pregnancy, serious maternal disease (e.g. diabetes mellitus, cardiovascular diseases, hyperthyroidism, pre-eclampsia), a fetus with malformations
Interventions	Nifedipine 20 mg administered orally, an additional 20 mg given if tocolysis not achieved within 30 min, followed by 90-120 mg/d titrated to uterine contractions for 48 h, followed by 90 mg once/d for 7 d vs ritodrine 200 mg/min administered IV and increased by 50 mg/min every 30 min until tocolysis achieved, maintained for 48 h then decreased to 50 mg/min then stopped, followed by 80 mg administered orally 3 times a d for 7 d
Outcomes	Neonatal infection, perinatal death, GA at birth, neurodevelopmental morbidity, gastrointestinal morbidity, mean birthweight, delay in birth by 48 h, respiratory morbidity, birth before 34 weeks, SAEs, still-

Van De Water 2008 *(Continued)*

	birth, cessation of treatment due to AEs, delay in birth by 7 d, pregnancy prolongation, neonatal death before 7 d, birth before 28 weeks, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Van Vliet 2016

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	510 women were randomised across 19 centres (10 tertiary care centres with a NICU facility and 9 secondary centres) in the Netherlands and Belgium between July 2011 and July 2014. Population: women aged ≥ 18 years with threatened preterm birth between 25+0 weeks and 34+0 weeks' gestation Definition of threatened preterm birth: at least 3 uterine contractions in 30 min and presence of 1 of the following: cervical length of ≤ 10 mm, both a cervical length of 11–30 mm and a positive fFN test, or presence of ruptured amniotic membranes Exclusion criteria: contraindications for tocolysis (severe vaginal bleeding or signs of intrauterine infection), maternal medical disease or conditions (hypertension, current antihypertensive treatment, history of myocardial infarction, angina) cerclage, cervical dilatation > 5 cm, tocolytic treatment for > 6 h before arrival in a participating centre, or a previous episode of tocolytic treatment, a fetus showing signs of non-reassuring well-being or malformations
Interventions	Nifedipine 20 mg administered orally, followed by 20 mg every 6 h for the next 47 h vs atosiban 6.75 mg by an IV bolus over 1 min followed by 18 mg/h for the first 3 h, followed by 6 mg/h for 45 h

Van Vliet 2016 *(Continued)*

Outcomes	Neonatal infection, perinatal death, GA at birth, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity, mean birthweight, delay in birth by 48 h, SAEs, cessation of treatment due to AEs, pregnancy prolongation, delay in birth by 7 d, maternal death, pulmonary oedema, hypotension, birth before 32 weeks, maternal infection
Notes	Study authors received payments to attend research institute. Funded by Netherlands Organisation for Health Research

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated 1:1 randomisation in permuted block sizes of 4 stratified by centre
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study was not blinded. Quote: "Because of the nature of the interventions, clinical staff or women were not masked"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women were lost to follow-up, 1 in each arm. 5 women in the nifedipine arm withdrew consent after randomisation and were not included in the analysis.
Selective reporting (reporting bias)	Low risk	The study report matches the study protocol that was registered prospectively (Trial NL2806 (NTR2947)).
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Vis 2014

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	73 women were randomised from 10 tertiary centres in the Netherlands between December 2009 and August 2012. Population: women between 24+0 and 34+0 weeks' gestation with threatened preterm birth and intact fetal membranes Definition of threatened preterm birth: symptoms of preterm labour, intact membranes, cervical length 10-30 mm with negative fFN test Exclusion criteria: contraindication for tocolysis (indication of intrauterine infection or severe vaginal bleeding), tocolysis within the previous 7 d (unless a single dose of tocolytic treatment required for transport from a secondary hospital), ruptured membranes, a fetus showing signs of non-reassuring well-being, malformation

Vis 2014 *(Continued)*

Interventions	Nifedipine 20 mg 4 times/d administered orally vs placebo
Outcomes	Birth before 34 weeks, neonatal infection, perinatal death, birth before 37 weeks, GA at birth, neurodevelopmental morbidity, nausea or vomiting, headache, gastrointestinal morbidity, mean birthweight, respiratory morbidity, cessation of treatment due to AEs, delay in birth by 7 d
Notes	4 women did not complete 48 h of medication. No COI Funded by Netherlands Organisation for Health Research

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Blocked randomisation scheme, stratified for centre, via a secure website
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR although placebo used
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis
Selective reporting (reporting bias)	Low risk	The study report matches the study report that was registered prospectively (NTR 1857).
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Walters 1977

Study characteristics

Methods	2-arm RCT, placebo-controlled
Participants	48 women were randomised from 1 centre in Australia (dates NR). Population: women with threatened preterm birth between 28+0 to 32+0 weeks' gestation Definition of threatened preterm birth: cervical dilation of ≥ 1 cm Exclusion criteria: any pregnancy complication
Interventions	Ritodrine 10 mg every 6 h until the end of 37 weeks vs placebo of identical size and appearance every 6 h until the end of 37 weeks

Walters 1977 *(Continued)*

Outcomes	GA at birth, mean birthweight, pregnancy prolongation, birthweight < 2500 g, palpitations, nausea or vomiting, headache, stillbirth
Notes	The administration of other drugs was avoided. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	High risk	Women were excluded after randomisation for inaccurate estimation of pregnancy or failure to take the study drugs, this was 3 women in the ritodrine group and 6 women in the placebo group (> 10%).
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Wang 2000

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	71 women were randomised from 1 centre in China between November 1998 to August 1999. Population: women with threatened preterm birth between 28+0 to 36+0 weeks' gestation Definition of threatened preterm birth: not defined Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), maternal medical disease (heart, diabetes), contraindications to the use of β2-receptor
Interventions	Ritodrine 50 μg/min administered via IV infusion and titrated to contractions and AEs and increasing by 50 μg every 10-30 min until effective then gradually reduced to 50 μg/mL followed by 10 mg orally 30 min before end of IV infusion, then every 4-6 h, and after 3 d it was changed to 10 mg, once every 8-12 h, then stopped at 36 weeks of gestation or above vs 10-20 mL/h IV magnesium sulphate followed by 60-80 mL

Wang 2000 *(Continued)*

Outcomes	Pregnancy prolongation, cessation of treatment due to AEs
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	High risk	The outcomes of only 57 women are reported yet 71 are randomised - no detail on the remaining 14 women (> 10%).
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar.

Wani 2004

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	132 women were randomised from 1 centre in United Arab Emirates between September 1996-July 1998. Population: women with threatened preterm birth between 23+0 to 34+0 weeks' gestation with a singleton pregnancy and intact membranes Definition of threatened preterm birth: painful, regular uterine contractions for > 20 h and ≥ 2 cm cervical dilatation Exclusion criteria: contraindications to tocolysis (none specified) or previous tocolytic use in the current pregnancy
Interventions	GTN 10 mg transdermally followed by an additional patch in 1 h if contractions continued. Patches were replaced after 24 h and continued for up to 5 d vs ritodrine 150-350 mg/min administered IV titrated to uterine contractions, followed by a minimal dose to maintain suppression and continued for at least 24 h for a maximum of 3 d. Treatment was recommenced if uterine contractions resumed

Wani 2004 *(Continued)*

Outcomes	Palpitations, birth before 34 weeks, birthweight < 2500 g, birth before 37 weeks, perinatal death, nausea or vomiting, headache, mean birthweight, delay in birth by 48 h, tachycardia, SAEs, pregnancy prolongation, cessation of treatment due to AEs, delay in birth by 7 d
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. Quote: "We do not believe the absence of blinding could have effected clinical management due to obvious morbidity associated with ritodrine"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded. Quote: "We do not believe the absence of blinding could have effected clinical management due to obvious morbidity associated with ritodrine"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics NR. No other bias reported

Weerakul 2002

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	89 women were randomised from 1 centre in Thailand between June 1999 and July 2000. Population: women with threatened preterm birth between 28+0 to 34+0 weeks' gestation Definition of threatened preterm birth: NR Exclusion criteria: NR
Interventions	Nifedipine 10-40 mg administered sublingually over 60 min titrated to uterine contractions, followed by 60-120 mg once/d, titrated to uterine contractions for 3 d vs terbutaline 0.25 mg administered by IV bolus followed by 5-15 g/min titrated to uterine contractions and maintained for 2 h, followed by 0.25 mg administered by SC injection every 4 h for 24 h. IV infusion was recommenced if uterine contractions resumed.
Outcomes	Birth before 34 weeks, neonatal infection, stillbirth, birth before 37 weeks, perinatal death, GA at birth, neurodevelopmental morbidity, mean birthweight, gastrointestinal morbidity, delay in birth by 48 h,

Weerakul 2002 *(Continued)*

	neonatal death before 7 d, SAEs, pregnancy prolongation, cessation of treatment due to AEs, neonatal death before 28 d
Notes	COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerised random number table
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other obvious bias reported

Wilkins 1988

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	120 women were randomised from 1 centre in the USA between June 1985 and April 1987. Population: women with threatened preterm birth between 25+0 to 36+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 2 contractions in 10 min with cervical effacement of > 50% or dilation of ≥ 2 cm Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding), ruptured membranes, maternal medical conditions (pre-eclampsia), cervical dilation > 4 cm, a fetus showing signs of non-reassuring well-being, growth restriction or malformation
Interventions	Ritodrine 0.1 mg/min via IV infusion and increased by 0.05 mg/min and titrated to uterine contractions or AEs with a maximum of 0.35 mg/min and continued for 12 h after contractions stopped followed by ritodrine 20 mg orally every 2-4 h until 37 weeks vs magnesium sulphate 4 g via IV bolus over 15 min followed by 2 g/h and titrated to contractions and AEs for 24 h followed by ritodrine 20 mg orally every 2-4 h until 37 weeks

Wilkins 1988 *(Continued)*

Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 37 weeks, pulmonary oedema, dyspnoea
Notes	Women could switch arms and receive other drug if the drug randomised to was ineffective. 10 women in ritodrine arm required magnesium sulphate, 20 women in magnesium sulphate arm required ritodrine. COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	Low risk	Sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Zhang 2002

Study characteristics

Methods	3-arm RCT
Participants	84 women were randomised from 1 centre in China between June 2000-May 2001. Population: women with threatened preterm birth between 28+0 to 35+0 weeks' gestation Definition of threatened preterm birth: ≥ 1 contraction in 10 min or cervical dilation between 1-2 cm Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical condition (pre-eclampsia), a fetus showing signs of intrauterine growth restriction, malformation, cervical dilation > 3 cm, contraindication to study drugs
Interventions	Nifedipine 10 or 20 mg orally, with an additional 10 or 20 mg if contractions persisted after 15 min, with a maximum dosage of 40 mg in the 1st h, followed by 10 mg every 8 h vs no tocolysis
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 37 weeks

Zhang 2002 *(Continued)*

Notes	2-arm RCT (3-arm trial extracted as 2-arm trial. 2 arms used different doses of nifedipine, these 2 arms have been combined as a single arm) COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Unclear risk	Baseline characteristics are NR. No other bias reported

Zhu 1996

Study characteristics

Methods	2-arm RCT, active-controlled
Participants	126 women were randomised from 1 centre in China (over a 3-month period; dates NR). Population: women with threatened preterm birth between 28+0 and 36+0 weeks' gestation Definition of threatened preterm birth: not defined Exclusion criteria: contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), a fetus showing signs of distress or imminent birth
Interventions	Ritodrine administered via IV bolus 0.05 mg/min followed by 0.1 mg/min after 10 min then and titrated to contraction and AEs 0.05-0.1 mg/min every 10 min and titrated to contraction and AEs with a maximum of 4 mL/min, 150 mg/1500 mL vs magnesium sulphate 30 g/1500 mL via IV bolus then 1.5-2 g/h and titrated to uterine contraction until contraction reduced for ≥ 2 h
Outcomes	Birth before 37 weeks
Notes	COI and funding information: NR

Zhu 1996 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

Zuckerman 1984

Study characteristics	
Methods	2-arm RCT, active-controlled
Participants	36 women were randomised from 1 centre in Israel (dates NR). Population: women with threatened preterm birth between 25+0 and 35+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: ≥ 2 contractions in 10 min with cervical effacement and/or dilation of at least 1-2 cm Exclusion criteria comprised contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disorders (cardiac, diabetes, pre-eclampsia), a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, cervical dilation > 4 cm
Interventions	Indomethacin 100 mg administered rectally with a further 100 mg if contractions persisted, then 25 mg orally 4 times a d for 24 h vs placebo
Outcomes	Delay in birth by 48 h, delay by 7 d, birth before 37 weeks, birthweight < 2500 g, birthweight < 2000 g, tachycardia, perinatal death, mean birthweight, GA at birth, nausea or vomiting, neonatal death before 28 d, cessation of treatment due to AEs, hypotension, SAEs
Notes	If cervical dilation progressed after 2 h then other therapy for contraction cessation was administered. 8 women received additional tocolysis (ritodrine).

Zuckerman 1984 *(Continued)*

COI and funding information: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear. Quote: "allocated at random"
Allocation concealment (selection bias)	Low risk	Envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind. Quote: "the key code was not available to investigators before completion of the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable for verification.
Other bias	Low risk	Baseline characteristics were similar. No other bias reported

AE: adverse effect; **bpm:** beats per minute; **COI:** conflict of interest; **fFN:** fetal fibronectin; **GA:** gestational age; **GBS:** group B streptococcus;**GTN:** glyceryl trinitrate; **IM:** intramuscular(ly); **ITT:** intention-to-treat; **IV:** intravenous(ly); **IVH:** intraventricular haemorrhage; **NICU:** neonatal intensive care unit; **NR:** not reported; **NSAID:** non-steroidal anti-inflammatory drug; **RCOG:** Royal College of Obstetricians and Gynaecologists; **RCT:** randomised controlled trial; **SAE:** serious adverse effect; **SC:** subcutaneous(ly); **SROM:** spontaneous rupture of membranes

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
ACTRN12616000748415	Only maintenance tocolysis
ACTRN12617001639314	Not tocolysis
Alavi 2015a	Only maintenance tocolysis
Alavi 2015b	Only maintenance tocolysis
Al Omari 2006	Not RCT
Anonymous 2004	Not RCT
Arda 2008	Abstract - insufficient information
Arikan 1997	Ineligible patient population

Study	Reason for exclusion
Barden 1990	Ineligible comparator (not placebo/no treatment/other tocolytic)
Bedoya 1972	Unclear intervention
Bivins 1993	Only maintenance tocolysis
Briscoe 1966	Not RCT
Brown 1981	Only maintenance tocolysis
Bulgay Moerschel 2008	Abstract - insufficient information
Caballero 1979	Abstract - insufficient information
Cabero 1988	Same tocolytic class comparator
Calder 1985	Randomisation inadequate
Caritis 1982	Ineligible comparator (not placebo/no treatment/other tocolytic)
Carr 1999	Only maintenance tocolysis
Castillo 1988	Abstract with insufficient information
Castren 1975	Not RCT
Cavalle-Garrido 1997	Abstract with insufficient information
Chau 1992	Not RCT
Chawanpaiboon 2009	Ineligible comparator (not placebo/no treatment/other tocolytic)
Chhabra 1998	Same tocolytic class comparator
Cifuentes 1994	Not RCT
Clavin 1996	Abstract with insufficient information
Csapo 1977	Not RCT
Danti 2014	Ineligible patient population
Das 1969	Not RCT
Decavalas 1994	Abstract with insufficient information
Dubay 1992	Abstract with insufficient information
Dunstan Boone 1990	Randomisation inadequate
EUCTR2013-002561-19-AT	Trial terminated - no results
Freeman 2008	Abstract with insufficient information
Fuchs 1976	Ineligible comparator (not placebo/no treatment/other tocolytic)

Study	Reason for exclusion
Goodwin 2003	Abstract with insufficient information
Goyal 2020	Randomisation inadequate
Groom 2000	Not RCT
Groom 2005	Ineligible patient population
Guinn 1998	Only maintenance tocolysis
Gummerus 1985	Only maintenance tocolysis
Gummerus 1987	Ineligible patient population
Hallak 1992	Ineligible patient population
Hallak 1993	Abstract with insufficient information
Hobel 1990	Personal communication dated 1990, insufficient information
Hogberg 1998	Abstract with insufficient information
Holleboom 1996	Same tocolytic class comparator
Horton 2012	Ineligible intervention (not tocolytic)
Horton 2015	Ineligible indication (not tocolysis)
How 1994	Only maintenance tocolysis
How 1995	Only maintenance tocolysis
Husslein 2007	Ineligible comparator (not placebo/no treatment/other tocolytic)
Illia 1993	Not RCT
IRCT20120215009014N	Ineligible comparator (not placebo/no treatment/other tocolytic)
IRCT201204232967N	Randomisation inadequate
IRCT201301281760N	No published data - authors contacted
IRCT2013062613777N1	No published data - authors contacted
Jain 2006	Abstract with insufficient information
Jones 1995	Ineligible intervention (not tocolytic)
Junejo 2008	Not RCT
Jung 2020	Abstract with insufficient information
Kashanian 2008	Abstract with insufficient information
Kashanian 2015	Abstract with insufficient information

Study	Reason for exclusion
Katz 1983	Not RCT
Kawagoe 2011	Same tocolytic class comparator
Khuteta 1988	Ineligible intervention (not tocolytic)
Kim 1983	Not RCT
Kosasa 1985	Randomisation inadequate
Kullander 1985	Same tocolytic class comparator
Kurki 1991a	Not RCT
Lauersen 1977	Ineligible intervention (not tocolytic)
Leake 1980a	Abstract with insufficient information
Leake 1980b	Not RCT
Lenzen 2012	Abstract with insufficient information
Levy 1985	Inadequate randomisation
Lewis 1996	Only maintenance tocolysis
Lorzadeh 2007	Ineligible comparator (not placebo/no treatment/other tocolytic)
Lumme 1991	Abstract with insufficient information
Lyell 2007b	Only maintenance tocolysis
Lyell 2008	Only maintenance tocolysis
Lyell 2009	Abstract with insufficient information
Ma 1992	Inadequate randomisation
Maitra 2007	Inadequate randomisation
Malik 2007	Inadequate randomisation
Mariona 1980	Personal communication from 1980, insufficient information
Martin 1990	Ineligible patient population
Martin 1992	Ineligible patient population
Martinez 1994	Abstract with insufficient information
Mathew 1997	Abstract with insufficient information
Mathews 1967	Ineligible patient population
Matijevic 2006	Only maintenance tocolysis

Study	Reason for exclusion
Merkatz 1980	Control is unclear
Mittendorf 1997	Abstract with insufficient information
Mittendorf 2002	Ineligible patient population
Morales 1993	Ineligible comparison
Motazedian 2010	Same tocolytic class comparator
Moutquin 1997	Abstract with insufficient information
Na Nan 2018	Abstract with insufficient information
NCT00116623	Trial terminated - no results
NCT00463736	Trial terminated - no results
NCT00525486	Maintanence only
NCT00620724	Maintanence only
NCT00641784	Trial terminated - no results
NCT01314859	Trial withdrawn - no participants
NCT01360034	Not threatened preterm birth
NCT01577121	Not tocolysis
NCT01796522	Maintanence only
NCT01985594	Ineligible comparator (not placebo/no treatment/other tocolytic)
NCT02438371	Same class tocolytic comparator
NCT02583633	No results - pending quality review last updated 2015
NCT03040752	No results available
Nelson 1985	Ineligible comparator (not placebo/no treatment/other tocolytic)
Neri 2008	Abstract with insufficient information
Nevils 1994	Abstract with insufficient information
Newton 1991	Only maintenance tocolysis
OConnor 1979	Ineligible patient population
Panter 1999	Prior tocolysis
Papadopoulos 1997	Abstract - insufficient information
Papatsonis 1997a	Abstract with insufficient information

Study	Reason for exclusion
Parilla 1993	Only maintenance tocolysis
Park 1982	Not RCT
Parry 2014	Same tocolytic class comparator
Parsons 1988	Ineligible intervention (not tocolytic)
Pasargiklian 1983	Ineligible comparator (not placebo/no treatment/other tocolytic)
Poppiti 2009	Ineligible patient population
Purwaka 2004	Ineligible comparator (not placebo/no treatment/other tocolytic)
Rashid 2018	Abstract with insufficient information
Rath 2006	Abstract with insufficient information
Rezk 2015	Same tocolytic class comparator
Ricci 1990	Only maintenance tocolysis
Ridgway 1990	Only maintenance tocolysis
Rios Anez 2001	Same tocolytic class comparator
Roos 2013	Only maintenance tocolysis
Roy 2006	Same tocolytic class comparator
Rust 1996	Prior tocolysis
Ryden 1977	Same tocolytic class comparator
Sanchez Ramos 1997	Only maintenance tocolysis
Sauve 1991	Abstract with insufficient information
Sayin 2004	Only maintenance tocolysis
Sciscione 1993	Abstract with insufficient information
Sharma 2000	Abstract with insufficient information
Shrivastava 2008	Abstract with insufficient information
Silver 1997	Abstract with insufficient information
Singh 2011	Not RCT
Sirohiwal 2001	Not RCT
Smit 1983	Ineligible indication (not tocolysis)
Smith 1993	Inadequate randomisation

Study	Reason for exclusion
Snyder 1989	Personal communication from 1989, insufficient information
Sofat 1994	Abstract with insufficient information
Spatling 1989	Same tocolytic class comparator
Spearing 1979	Abstract with insufficient information
Stika 2002	Same tocolytic class comparator
Thornton 2017	Same tocolytic class comparator
Uma 2012	Same tocolytic class comparator
Valenzuela 2000	Only maintenance tocolysis
Verspyck 2017	Only maintenance tocolysis
Verspyck 2018	Ineligible indication (not tocolysis)
Vis 2009	Not RCT
Von Oeyen 1990	Same tocolytic class comparator
Wani 1999	Abstract with insufficient information
Weiner 1988	Unclear intervention
Weisbach 1986	Only maintenance tocolysis
Wenstrom 1997	Only maintenance tocolysis
Wesselius De Casparis 1971	Randomisation by episode not participant
Woodland 1990	Abstract with insufficient information
Yi 1991	Abstract with insufficient information
Zarcone 1994	Ineligible patient population
Zygmunt 2003	Same tocolytic class comparator

RCT: randomised controlled trial

Characteristics of studies awaiting classification *[ordered by study ID]*

Akhtar 2018

Methods	2-arm active randomised trial
Participants	72 women were randomised from 1 centre in Pakistan between March 2017-March 2017. Population: women with threatened preterm birth (GA range included NR) with singleton pregnancy Definition of threatened preterm birth: not defined

Akhtar 2018 *(Continued)*

	Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding), multiple pregnancy, a fetus showing signs of malformation or demise, allergy to study drugs
Interventions	Nifedipine administered orally (1st dose NR) followed by 20 mg after 30 min, then 20 mg after another 30 min if required, with a maximum 160 mg vs GTN 10 mg administered transdermally with another patch in 1 h if required, maximum dose of 20 mg
Outcomes	Delay by 48 h
Notes	

Ali 2013

Methods	2-arm active RCT
Participants	160 women were randomised from 1 centre in Pakistan between July 2009 and January 2010. Population: women with threatened preterm birth between 24+0 and 37+0 weeks' gestation with singleton pregnancy and intact membranes. Definition of threatened preterm birth: not defined Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding) cervical dilation > 4 cm, ruptured membranes
Interventions	Ritodrine 0.05 mg/min via IV infusion and increased 0.15 mg/min every 15 min and titrated to uterine contractions or AEs followed by 10 mg orally 6 h before end of infusion vs nifedipine 20 mg orally followed by 20 mg every 6 h until uterine contractions subsided
Outcomes	Delay by 48 h
Notes	

Al Jawady 2020

Methods	2-arm active RCT
Participants	200 women were randomised from 1 centre in Iraq between January 2009-March 2010. Population: women with threatened preterm labour between 24+0 and 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 1 h, cervical dilation up to 3 cm and cervical effacement of up to 50% Exclusion criteria: maternal complications requiring birth, maternal medical condition (diabetes), ruptured membranes, cervical dilation > 3 cm, a fetus showing signs of non-reassuring well-being, allergy to study drugs
Interventions	Salbutamol (dose NR) administered by IV infusion and reduced by 50% every 6 h up to 48 h vs atosiban 6.75 mg administered by IV bolus followed by 18 mg/h for 3 h, followed by 6 mg/h for up to 48 h
Outcomes	Delay by 48 h, delay by 7 d, tachycardia, dyspnoea, respiratory morbidity, neonatal infection, neurodevelopmental morbidity

Al Jawady 2020 *(Continued)*

Notes	

Aziz 2018

Methods	2-arm active RCT
Participants	182 women were randomised from 1 centre in Pakistan between January 2018-June 2018. Population: women with threatened preterm birth between 28+0 and 36+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: not defined Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (liver, cardiac), maternal medical disorder (pre-eclampsia, hypotension), maternal age < 16 years or > 35 years, cervical dilation > 4 cm, ruptured membranes, allergy to study drugs, a fetus showing signs of malformation, intrauterine growth restriction, or non-reassuring well-being, multiple pregnancy
Interventions	Magnesium sulphate 4 g administered by IV bolus over 15 min, followed by 2-3 g/h and titrated to uterine contractions and AEs vs nifedipine 30 mg orally with an additional 30 mg in 20 min if required, followed by an additional 30 mg after 30 min if required, followed by 30 mg twice/d for a further 5 d
Outcomes	Delay by 48 h
Notes	

Badshah 2019

Methods	2-arm active RCT
Participants	154 women were randomised from 1 centre in Pakistan between July 2016- Janurary 2017. Population: women with threatened preterm birth (20+0 to 37+0 weeks' gestation) with singleton pregnancy and intact membranes. Definition of threatened preterm birth: contractions resulting in cervical dilation > 1 cm and effacement of ≥ 50% Exclusion criteria: ruptured membranes, maternal or fetal factors for imminent birth
Interventions	Nifedipine 20 mg orally, followed by 20 mg in 1 h if required, followed by 20 mg every 6 h for 48 h. GTN 10 mg administered transdermally for 24 h, with an additional 10 mg in 1 h if the contractions did not cease. After 24 h a fresh patch was applied. Patches were not removed until 12 h after cessation of contractions
Outcomes	Delay by 48 h, pregnancy prolongation, headache
Notes	

Bina 2012

Methods	2-arm RCT, placebo-controlled
Participants	100 women were randomised from 1 centre in Bangladesh. Population: women with threatened preterm birth between 24+0 and 34+0 weeks' gestation with singleton pregnancies, intact membranes Definition of threatened preterm birth: > 2 contractions in 10 min with cervical dilatation < 3 cm Exclusion criteria: any fetal or maternal problems (further details NR)
Interventions	Nifedipine 20 mg administered sublingually every 30 min for 1 h, followed by 20-40 mg orally for 24 h. Further doses given at the judgement of physicians until at least 12 h of < 6 contractions/h vs placebo
Outcomes	Delay by 48 h, birth < 32/40, birth < 37/40, nausea or vomiting, neonatal death, GA at delivery, birthweight, birthweight < 2500 g, SAEs, respiratory morbidity, neurodevelopmental morbidity, gastrointestinal morbidity, neonatal infection
Notes	

Caliskan 2015

Methods	2-arm active RCT
Participants	48 women were randomised from 1 tertiary referral centre in Turkey (dates NR). Population: women with threatened preterm birth between 27+0 to 34+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: ≥ 2 uterine contractions in 10 min and cervical change Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (cardiac, hypotension), placenta praevia, cervical cerclage, urinary tract infection, a fetus showing signs of non-reassuring well-being, growth restriction or allergy/sensitivity to study drugs
Interventions	Magnesium sulphate 6 g administered IV over 20-30 min, followed 3 g/h for 12 h after contractions had stopped vs glyceryl trinitrate 0.4 mg/h transdermally with an additional patch after 1 h from the application of the first if ongoing uterine activity, patches were removed after 24 h
Outcomes	Pregnancy prolongation, GA at birth, mean birthweight, headache, palpitation, nausea or vomiting
Notes	The tocolytic drug was changed due to persistent contractions in 4 women from the magnesium sulphate group and in 3 women from glyceryl trinitrate group, and these women were excluded from the study.

Chawanpaiboon 2011

Methods	2-arm RCT, placebo-controlled
Participants	150 women were randomised from 1 centre in Thailand between May 2007 and December 2008. Population: women between 28+0 and 35+0 weeks' gestation with threatened preterm birth with singleton pregnancies and intact membranes

Chawanpaiboon 2011 *(Continued)*

	Definition of threatened preterm birth: regular and painful contractions Exclusion criteria: women with cervical insufficiency, cervical dilation of ≥ 3 cm, ruptured membranes
Interventions	Nifedipine 20 mg administered orally every 30 min, 3 times followed by 20 mg every 12 h until 34 weeks vs no treatment with half of the group receiving Proluton Depot 250 mg IM once/week until 34 weeks of gestation
Outcomes	GA at birth, mean birthweight
Notes	Bricanyl administered IV could be given as a rescue treatment. If any complication or contraindication of either nifedipine or Proluton Depot was found, the contraction inhibition was changed to IV bricanyl and the woman was excluded from the study.

Chawanpaiboon 2012

Methods	2-arm RCT
Participants	188 women were randomised from 1 centre in Thailand between December 2009 and December 2010. Population: women with threatened preterm birth between 26+0 and 35+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: painful and regular contractions Exclusion criteria: dilatation of ≥ 3 cm, cervical insufficiency, ruptured membranes, urinary tract infection, bacterial vaginosis
Interventions	Nifedipine 20 mg orally every 30 min for 3 times, then 20 mg every 12 h until 34 weeks' gestation vs bed rest
Outcomes	GA at birth, mean birthweight
Notes	Unsuccessful cessation of uterine contraction was defined as continuing contractions during and after inhibition for 12 h. If the inhibition failed and there was no contraindication to use bricanyl IV, then bricanyl was used.

Dhawle 2013

Methods	2-arm active RCT
Participants	84 women form 1 tertiary centre in India (dates NR) Population: women with threatened preterm labour between 26+0 to 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: 4 contractions in 20 min or 8 in 1 h with cervical dilation of > 1 cm or > 80% effacement Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (hypotension, hypertension, cardiac disease), ruptured membranes, cervical dilation > 4 cm, tocolytic use in current pregnancy, a fetus showing signs of non-reassuring well-being, growth restriction, malformation or demise

Dhawle 2013 *(Continued)*

Interventions	GTN 10 mg administered transdermally over 24 h and an additional patch if contractions persisted. At the end of 24 h patches were replaced vs nifedipine 20 mg administered orally with an additional 20 mg in 60 min if contractions continued, followed by 20 mg orally every 6 h for 48 h
Outcomes	Delay by 48 h, delay by 7 d, pregnancy prolongation, birthweight < 2500 g, respiratory morbidity, neonatal infection, palpitations, headache, tachycardia, hypotension, cessation of treatment due to AEs, birth before 34 weeks, birth before 37 weeks
Notes	Inability of the drug to prolong gestation for a minimum period of 48 h or persistence of uterine contractions even after study drugs was considered to be a treatment failure. Under such circumstances, the therapy was discontinued and subsequent management was left to the labour ward team.

Eftekhari 2012

Methods	2-arm active RCT
Participants	120 women were randomised from 1 centre in Iran. Population: women with threatened preterm birth between 28+0 and 32+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min or 8 in 1 h, cervical dilation of ≥ 1 cm, effacement of ≥ 80% Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions or complications (myasthenia gravis, pre-eclampsia), ruptured membranes, cervical dilation > 4 cm, placental malformation, a fetus showing signs of non-reassuring well-being or fetal malformation, allergy to study drugs
Interventions	Indomethacin 50 mg administered rectally with an additional 50 mg in 1-2 h if contractions continued, followed by 25 mg orally every 6 h up to 48 h vs magnesium sulphate 4 g administered IV bolus, followed by 2-3 g/h titrated to uterine contractions for 48 h
Outcomes	Mean birthweight, GA at birth, delay by 48 h, pregnancy prolongation, headache, nausea or vomiting, respiratory morbidity, neonatal death before 28 d
Notes	

Esmaeilzadeh 2017

Methods	2-arm active RCT
Participants	125 women were randomised from 1 hospital in Iran between 2014 and 2015. Population: women with threatened preterm birth between 24+0 to 34+0 weeks' gestation with a prior singleton pregnancy and currently a singleton pregnancy Definition of threatened preterm birth: ≥ 4 contractions in 20 min and cervical dilation > 5 cm and effacement Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), multiple pregnancy, maternal medical condition (pre-eclampsia, liver disease, heart disease, hypertension), placenta praevia, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, demise, malformation

Esmaeilzadeh 2017 *(Continued)*

Interventions	Magnesium sulphate 4 g administered via IV bolus followed by 2 g/h for 12 h after contractions stopped vs nifedipine 10 mg administered orally every 20 min titrated to uterine contractions with a maximum of 4 doses, followed by 20 mg every 6 h for 24 h, followed by 20 mg every 8 h for an additional 24 h (total treatment time 48 h)
Outcomes	Delay by 48 h, dyspnoea, hypotension, nausea or vomiting, headache
Notes	

Faisal 2020

Methods	2-arm active RCT
Participants	60 women were randomised from 1 centre in Pakistan between May-October 2007. Population: women with threatened preterm birth between 24+0 to 36+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: ≥ 2 contractions in 10 min with cervical dilation and effacement Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding), maternal medical conditions, low-lying placenta, a fetus showing signs of anomalies, cervical dilation > 4 cm, scarred uterus
Interventions	Magnesium sulphate 4 g administered by IV bolus followed by 1 g for a maximum of 48 h vs nifedipine 20 mg administered orally followed by 10 mg after 30 min followed by 20 mg 3 times/d for 48 h
Outcomes	Pregnancy prolongation, nausea or vomiting, headache, tachycardia
Notes	

Faraji 2013

Methods	2-arm active RCT
Participants	100 women were randomised from 1 centre in Iran (dates NR). Population: women with threatened preterm birth between 24+0 and 37+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: 4 contractions in 20 min or 8 contractions in 1 h, with at least 1 cm dilation and 50% effacement Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), ruptured membranes, pre-eclampsia, hypotension, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction
Interventions	Magnesium sulphate 4 g via IV bolus over 30 min, followed by 2 g/h until stopping or reducing uterine contractions vs nifedipine 10 mg sublingual, followed by an additional 10 mg if required every 15 min; until a maximum dose of 40 mg for 1 h, with a minimal dose of 60 mg every day for 3 d then decreased gradually to 20 mg/d up to 36 weeks of gestation
Outcomes	Delay in birth by 48 h

Faraji 2013 *(Continued)*

Notes	

Ghomian 2015

Methods	2-arm RCT, active-controlled
Participants	139 women were randomised from 1 centre in Iran between October 2013-October 2014. Population: women with threatened preterm birth between 24+0 to 34+0 weeks' gestation with singleton pregnancies and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min, cervical dilation of ≥ 1 cm and cervical effacement of ≥ 80% Exclusion criteria: maternal or fetal conditions requiring immediate birth, multiple pregnancy, premature rupture of membranes, previous tocolysis use, cervical dilation of ≥ 4 cm, a fetus showing signs of malformation or demise, allergy to study drugs
Interventions	GTN patch 10 mg administered by subcuticular patch for 24 h. An additional 10 mg was applied in 1 h if contractions continued. Patch(es) were left on for 48 h vs nifedipine 20 mg administered orally for 1 h, followed by 10 mg every 6 h for 12 h, followed by 5 mg every 6 h for 24 h, followed by 5 mg every 8 h for 24 h. If either tocolytic was ineffective the treatment was stopped and another tocolytic was prescribed.
Outcomes	Delay in birth by 48 h, GA at birth, mean birthweight, respiratory morbidity, gastrointestinal morbidity, headache, tachycardia, nausea or vomiting, cessation of treatment due to AEs, hypotension
Notes	If either tocolytic was ineffective the treatment was stopped and another tocolytic was prescribed, however these women were removed form the analyses.

Hamza 2016

Methods	2-arm RCT, active-controlled
Participants	58 women were randomised across 2 centres in Pakistan between July 2012-June 2013. Population: women between 24+0 to 36+6 weeks' gestation with threatened preterm birth Definition of threatened preterm birth: not defined Exclusion criteria: NR
Interventions	Ritodrine administered IV vs GTN patch administered transdermally. No further details are reported
Outcomes	Delay by 48 h, headache, tachycardia, dyspnoea, hypotension
Notes	

IRCT2015042621947N1

Methods	2-arm RCT, active-controlled

IRCT2015042621947N1 *(Continued)*

Participants	Population: women with singleton pregnancy, intact amniotic membrane, GA between 24-34 weeks, positive tocometry Exclusion criteria: premature rupture of membranes, vaginal bleeding, chorioamnionitis, dilatation > 2 cm and cervical effacement exceeding 80%, polyhydramnios, oligohydramnios, intrauterine fetal demise, intrauterine growth restriction, fetal distress, smoking and alcohol abuse, systemic disease, congenital anomalies, uterine anomalies, celecoxib intolerance
Interventions	Magnesium sulphate IV initial dose 4 g and then 2 g/h for 24 h with a 100 mg celecoxib capsule and if needed its continuation every 8 h for 24 h vs magnesium sulphate IV initial dose 4 g and then 2 g/h for 24 h with a placebo capsule and if needed its continuation every 8 h for 24 h
Outcomes	Change in cervical dilatation 1 h, 24 h, and 48 h after the onset of drug use
Notes	Trial completed, data unpublished, trial team contacted

Jamil 2020

Methods	2-arm active RCT
Participants	100 women were randomised from 1 centre in Pakistan between March 2017 and February 2018. Population: women with threatened preterm birth between 28+0 to 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min with cervical dilation > 2 cm and/or effacement > 70% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (cardiac, hypertension or hypotension), ruptured membranes, cervical dilation > 4 cm, tocolytic use in current pregnancy, a fetus showing signs of non-reassuring well-being, growth restriction, demise of malformation. All women were screened for urinary tract infections and GBS and treated accordingly
Interventions	GTN 5 mg administered transdermally over 12 h with an additional patch in 1 h if contractions continued, patches followed by 1-2 patches in 12 h for a total of 24 h vs nifedipine 10 mg administered orally with an additional 10 mg if contractions persisted after 60 min, followed by 10 mg every 8 h for 48 h
Outcomes	Prolongation of pregnancy, delay by 48 h, delay by 7 d, GA at birth, respiratory morbidity, headache, palpitations, tachycardia, hypotension, cessation of treatment due to AEs, birthweight < 2500 g
Notes	The inability of the drug to prolong gestation for a minimum period of 48 h or persistence of uterine contractions even after 10 mg of NTG or 20 mg of nifedipine was considered to be a treatment failure. Under such circumstances, the therapy was discontinued and subsequent management was left to the labour ward team.

Khooshideh 2017

Methods	2-arm active RCT
Participants	220 women were randomised from 1 centre in Iran between 2014 and 2016.

Khooshideh 2017 *(Continued)*

	Population: women with threatened preterm birth between 32+0 to 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 1 contractions in 10 min with cervical change, or cervical dilation of ≥ 2 cm and 80% effacement Exclusion criteria: contraindication to tocolysis (severe vaginal bleeding), maternal medical condition (pre-eclampsia, hypertension, hypotension, diabetes), medical or surgical complications (cardiac arrhythmia, myasthenia), ruptured membranes, cervical dilation > 4 cm, previous preterm birth, uterine malformation, polyhydramnios
Interventions	Magnesium sulphate 6 g via IV bolus followed by a 2 g/h infusion for 48 h vs nifedipine 10 mg administered orally every 20 min for 1 h (3 doses), followed by 10 mg every 6 h for 48 h
Outcomes	Delay by 48 h, SAEs, hypotension, dyspnoea, nausea or vomiting, headache, palpitation, respiratory morbidity
Notes	

Kim 2001

Methods	3-arm active controlled randomised trial
Participants	180 women with documented preterm labour were randomly assigned to receive magnesium sulphate (n = 60), ritodrine hydrochloride (n = 60) and nifedipine (n = 60) as initial tocolytic therapy. 30 women with documented preterm labour were allocated to administer fluid only and bed rest as control group. Patient could be switched to another tocolytic regimen if they continued to have contractions or AEs.
Interventions	Magnesium sulphate, ritodrine hydrochloride, nifedipine
Outcomes	The main outcome variables examined were d gain in utero, success rate, AEs and neonatal outcome
Notes	Unable to obtain translation

Lee 2004

Methods	2-arm active RCT
Participants	Women between 24 and 34 weeks' gestation with documented preterm labour were randomly assigned to receive transdermal GTN (n = 24) or IV ritodrine (n = 35) as initial tocolytic therapy
Interventions	Women in the GTN group were administered 0.2 mg/h released transdermal patch on the pregnant women's abdomen directly. Women in the ritodrine group were treated 0.025 mg/min as initial dose. The dose increased at 15-min intervals until uterine contractions were inhibited or AEs became intolerable. The maximum recommended dose was 0.20 mg/min.
Outcomes	Failure of tocolysis, time to uterine quiescence, time gained in utero, and frequency of AEs.
Notes	Unable to obtain translation

Lotfalizadeh 2010

Methods	2-arm active RCT
Participants	80 women were randomised across 2 centres in Iran between 2007 and 2008. Population: women with threatened preterm birth between 26+0 and 34+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min or 8 in 1 h, with cervical dilation of ≥ 1 cm and effacement of ≥ 50% Exlcusion criteria: contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (severe pre-eclampsia), maternal disease (renal or cardiac), maternal hypotension or bradycardia, ruptured membranes, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction or demise, cervical dilation > 4 cm
Interventions	Nifedipine 10 mg orally every 20 min, up to 4 times, followed by 20 mg every 6 h in the first 24 h, followed by 20 mg every 8 h in the second 24 h, and finally, 10 mg doses every 8 h in the third 24-h period vs magnesium sulphate 4 g administered via IV bolus over 15 min, followed by doses of 2-3 g/h for 12 h
Outcomes	Delay by 48 h, delay by 7 d, headache, hypotension, tachycardia, nausea or vomiting, dyspnoea
Notes	

Madkour 2013

Methods	3-arm active RCT
Participants	150 women were randomised across 2 centres in the United Arab Emirates between June 2010 and July 2011. Population: women with threatened preterm birth between 26+0 to 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 30 min and cervical dilation up to 3 cm and cervical effacement of ≥ 50% Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection), ruptured membranes, a fetus showing signs of non-reassuring well-being requiring immediate birth, allergy to the study drugs
Interventions	Atosiban 6.75 mg administered by IV bolus, followed by 300 µg/min for 3 h, followed by 100 µg/min 48-96 h vs nifedipine 20 mg orally, followed by 20 mg after 30 min, followed by 20 mg every 3-8 h for 48-72 h with a maximum dose of 160 mg/d, followed by 30-60 mg daily if required vs atosiban 6.75 mg administered by IV bolus with nifedipine 20 mg orally, followed by 20 mg after 30 min, followed by atosiban 300 µg/min for 3 h and nifedipine 20 mg every 3-8 h for 48-72 h and atosiban 100 µg/min 48-96 h with nifedipine 30-60 mg daily if required
Outcomes	Delay by 7 d, headache, palpitations
Notes	

Mesdaghinia 2012

Methods	2-arm active RCT

Mesdaghinia 2012 *(Continued)*

Participants	60 women were randomised from 1 centre in Iran over a 2-year period. Population: women with threatened preterm birth between 24+0 to 32+0 weeks' gestation with intact membranes Threatened preterm labour was defined as ≥ 2 contractions in 10 min with cervical dilation up to 3 cm and effacement up to 50% Excluson criteria: contraindications to tocolysis (severe vaginal bleeding), maternal medical condition (kidney problems, myasthenia gravis, gastrointestinal bleeding), ruptured membranes, oligohydramnios, cervical dilation ≥ 4 cm, a fetus showing signs of non-reassuring well-being, allergy to study medication
Interventions	Magnesium sulphate 4 g administered via IV bolus, followed by 2-3 g/h titrated to uterine contractions until 12 h after the cessation of contractions vs indomethacin 50 mg administered rectally every 6 h for 24 h
Outcomes	Delay by 48 h, nausea or vomiting, headache, tachycardia
Notes	

Mirteimoori 2009

Methods	2-arm RCT, active-controlled
Participants	42 women were randomised from 1 centre in Iran (dates NR). Population: women with threatened preterm birth between 27+0 to 37+0 weeks with intact membranes Definition of threatened preterm birth: ≥ 4 uterine contractions in 20 min with or without cervical dilation < 4 cm and/or effacement of < 80% Exclusion criteria: contraindication to tocolysis (suspected uterine infection or severe vaginal bleeding), placenta praevia, urinary tract infection, maternal hypertension or renal insufficiency, ruptured membranes, a fetus showing signs of growth restriction, malformation, sensitivity or allergy to study drugs, cervical dilation > 4 cm
Interventions	Magnesium sulphate 4 g/h administered by IV bolus vs glyceryl trinitrate 5 mg/24 h administered transdermally
Outcomes	Pregnancy prolongation, SAEs
Notes	

Mirzamoradi 2014

Methods	2-arm RCT, placebo-controlled
Participants	92 women were randomised from 1 centre in Iran. Population: women with threatened preterm birth at < 34+0 weeks of gestation with singleton pregnancies and premature rupture of membranes who had not previously used magnesium sulphate in order to curb labour complaint in a recent pregnancy

Mirzamoradi 2014 *(Continued)*

	Definition of threatened preterm birth: persistent uterine contractions (e.g. at least 4 every 20 min or 8 every 60 min) with premature rupture of membranes or cervical dilation of 1-3 cm or effacement > 50% or a change in cervical dilation or effacement detected by serial examinations Exclusion criteria: probable case of chorioamnionitis, progress of labour as 4 cm cervical dilatation, allergy or medical complications in combination with magnesium sulphate, fatal fetal anomalies, non reassuring fetal status, severe fetal growth restriction, severe pre-eclampsia or eclampsia, maternal haemorrhage with haemodynamic instability
Interventions	4 g of magnesium sulphate dissolved in 100 mL of normal saline solution for 20 min to reach loading dose, then 2 g of magnesium sulphate dissolved in 100 mL of normal saline by infusion every h. Infusion was continued until 24 h after complete cessation of uterine contractions vs placebo Cointerventions: antenatal corticosteroid, 1 g of oral azithromycin and ampicillin 2 g IV every 6 h for 48 h, followed by amoxicillin (500 mg orally 3 times daily) for an additional 5 d
Outcomes	Birthweight, infant death, respiratory morbidity, neurological morbidity, neonatal sepsis
Notes	

Nankali 2014

Methods	2-arm RCT, placebo-controlled
Participants	84 women were randomised from 1 centre in Iran. Population: women with threatened preterm birth between 27+0 and 35+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: ≥ 4 contractions in 20 min or Bishop score of ≥ 3 Exclusion criteria: contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), serious maternal disease (cardiac), fetal or maternal reasons for imminent delivery, placental abnormalities, preterm rupture of membranes, multiple pregnancy, cervical dilation of ≥ 5 cm, sensitivity to tocolysis or tocolytic treatment in previous 24 h, previous caesarean section, a fetus with malformations
Interventions	10 mg GTN patch 10 mg administered transdermally followed by 10 mg in 1 h for 24 h, patches were removed and replaced by 2, 10-mg patches for an additional 24 h (48 h in total) vs placebo patch administered transdermally followed by another patch 1 h later, patches were removed and replaced by 2, 10-mg patches for an additional 24 h (48 h in total)
Outcomes	Delay in birth by 48 h, palpitations, headache, nausea or vomiting, pregnancy prolongation
Notes	

Nauman 2020

Methods	2-arm active-controlled randomised trial
Participants	120 women were randomised from 1 centre in Pakistan between July 2012 and June 2013. Population: women between 24+0 and 36+6 weeks' gestation with singleton pregnancy with threatened preterm birth

Nauman 2020 *(Continued)*

	Definition of threatened preterm birth: regular contractions at frequent intervals with cervical change Exclusion criteria: contraindications for tocolysis (suspected uterine infection or severe vaginal bleeding), maternal medical disease (cardiac, hypertension, severe pre-eclampsia, diabetes, hyperthyroidism), cervical incompetence, multiple pregnancy
Interventions	Nifedipine 20 mg administered orally followed by 10 mg every 6 h for 48 h vs betasympathomimetic drug (terbutaline) administered by IV infusion(0.5 mg/1 mL ampoule) at the rate of 8-10 drops/min and titrated to contractions and AEs for up to 48 h
Outcomes	Delay in birth by 48 h, nausea or vomiting, tachycardia, hypotension
Notes	

NCT00486824

Methods	2-arm active-controlled double-dummy randomised trial
Participants	Population: women between 24-34 weeks' gestation diagnosed with preterm labour
Interventions	100 mg oral indomethacin vs 30 mg oral nifedipine. Then women receive either 25 mg of oral indomethacin every 6 h for 48 h, or 20 mg of oral nifedipine every 6 h for 48 h. Tocolysis beyond 48 h will not be used.
Outcomes	Maternal AEs and delivery outcomes will be assessed from questionnaires administered by the study team following treatment, and/or from review of the patient's medical records
Notes	

Nikbakht 2014

Methods	2-arm RCT, active-controlled
Participants	100 women were randomised across 2 centres in Iran in 2002. Population: women with threatened preterm birth between 24+0 to 37+0 weeks' gestation with intact membranes Definition of threatened preterm birth: ≥ 4 contractions with cervical change of < 4 cm and effacement of > 50% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (cardiac, liver), maternal complications (pre-eclampsia), cervical dilation > 5 cm, a fetus showing signs of non-reassuring well-being or malformations
Interventions	Nifedipine 10 mg administered orally and titrated to uterine contractions with a maximum dose of 30 mg/h in the first h, followed by 10 mg every 6 h vs magnesium sulphate 10 g administered via IV bolus followed by 5 g IM every 4 h
Outcomes	Delay by 48 h, delay by 7 d, hypotension, cessation of treatment due to AEs, headache, SAE
Notes	Women could receive another tocolytic (cox-inhibitor) if the initial randomised treatment failed - time point that treatment was considered as failure and additional tocolysis given NR

Ozhan Baykal 2015

Methods	2-arm RCT, active-controlled
Participants	60 women were randomised from 1 centre in Turkey (dates NR). Population: women with threatened preterm birth between 24+0 to 36+0 weeks' gestation with intact membranes and singleton pregnancy Definition of threatened preterm birth: ≥ 2 contractions in 10 min with cervical change of ≥ 2 cm and effacement Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), multiple pregnancy, ruptured membranes, polyhydramnios, cervical dilation > 5 cm and effacement of 80%, maternal disease (heart, lung, thyroid), maternal medical conditions (high blood pressure, diabetes, pre-eclampsia, gestational diabetes), a fetus showing signs of non-reassuring well-being, intrauterine growth restriction or malformations, allergy or sensitivity to study drugs
Interventions	Nifedipine 10 mg orally every 20 min for 1 h followed by 10 mg every 6 h for 24 h (maximum 60 mg) vs ritodrine administered IV 0.05 mg/min (12 mL/h) and titrated to uterine contractions to a maximum of 0.08 mg/min (20 mL/h) and continued for 12 h after contractions had stopped
Outcomes	Dyspnoea, gastrointestinal morbidity, headache, mean birthweight, nausea or vomiting, neonatal infection, neurodevelopmental morbidity, perinatal death, pregnancy prolongation, pulmonary oedema, tachycardia
Notes	

PriyadarshiniBai 2013

Methods	2-arm-active RCT
Participants	60 women were randomised from centres in India (number NR) between October 2006-August 2008. Population: women with threatened preterm birth between 28+0 to 36+0 weeks' gestation Definition of threatened preterm birth: ≥ 1 contraction in 10 min with cervical effacement and dilation < 3 cm Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), prior tocolysis use in the past 7 d, maternal medical disease (diabetes, cardiac, hyperthyroidism), maternal medical disorders (pre-eclampsia, severe anaemia), cervical dilation > 4 cm, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, malformation, demise
Interventions	Ritodrine 50 µg/min administered by IV infusion and increased by 50 µg/min every 30 min and titrated to uterine contractions or maternal AEs up to a maximum of 350 µg/min for at least 2 d and gradually reduced, followed by 10 mg orally before the end of the IV infusion followed by 10 mg orally every 2 h for 24 h with a maximum daily dose not exceeding 120 mg, followed by 10-20 mg every 4-6 h until 34 weeks vs nifedipine 20 mg orally followed by another 20 mg orally after 30 min if contractions persisted, followed by 20 mg orally every 3-8 h for 72 h and maximum dose did not exceed 160 mg/d. After 72 h tocolytic therapy was omitted. No maintenance therapy was given.
Outcomes	Delay by 48 h, delay by 7 d, palpitation, nausea or vomiting, hypotension, mean birthweight, stillbirth

PriyadarshiniBai 2013 *(Continued)*

Notes	In case of recurrence, treatment was given as per randomisation - same regime

Saadati 2014

Methods	2-arm active RCT
Participants	600 women were randomised between centres in Iran (number NR) between March and August 2013. Population: women with threatened preterm birth between 24+0 and 33+6 weeks' gestation Definition of threatened preterm birth: ≥ 4 uterine contractions in 20 min or 8 in 1 h and cervical dilation of ≥ 2 cm or effacement of ≥ 80% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal or fetal condition requiring immediate birth, premature rupture of membranes, maternal medical conditions (pre-eclampsia, renal or hepatic dysfunction, peptic ulcer), a fetus showing signs of non-reassuring well-being, intrauterine growth restriction or demise, sensitivity to study drugs, previous tocolytic use
Interventions	Magnesium sulphate 4 g administered by IV bolus followed by 1 g/h for maximum 48 h vs celecoxib 100 mg orally every 12 h for maximum duration of 48 h
Outcomes	GA at birth, delay by 48 h
Notes	In all women, the drug was stopped immediately if the uterine preterm contractions did not stop

Sachan 2012

Methods	2-arm- active RCT
Participants	100 women were randomised from 1 centre in India (1 year but dates NR). Population: women with threatened preterm birth between 24+0 and 37+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: 4 contractions in 20 min or 8 in 60 min, cervical dilatation of > 1 cm, cervical effacement of > 80% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), ruptured membrane, maternal medical conditions (severe hypertension, eclampsia), a fetus showing signs of non-reassuring well-being, growth restrictions, malformation or demise, sensitivity to study drugs. 2 women in the isoxsuprine group had a urine infection and 1 in the GTN group
Interventions	Isoxsuprine administered by IM injection every 8 h till 24 h of contractions ceased followed by 10 mg orally every 8 h for 1 week vs GTN 10 mg administered transdermally for 24 h, if contractions continued after 1 h of placement of first GTN patch, 1 additional GTN patch of same dose was applied, both patches continued for 24 h, followed by replacement patches for a further 24 h
Outcomes	Birth before 28 weeks, birth before 32 weeks, birth before 34 weeks, birth before 37 weeks, delay by 48 h, delay by 7 d, respiratory morbidity, tachycardia, palpitation, neonatal death before 28 d, hypotension, pulmonary oedema, SAE

Sachan 2012 *(Continued)*

Notes	If contractions unchanged or increased at the end of 4 h after GTN administration, all the patches were removed. Such women were grouped under failed tocolysis. These women were then given conventional tocolytic agent

Shafaie 2014

Methods	2-arm active RCT
Participants	80 women were randomised from 2 centres in Iran (dates NR) Population: women with threatened preterm birth between 26+0 and 34+0 weeks' gestation Definition of threatened preterm birth: 1 contraction in 10 min with cervical dilation up to 3 cm, or cervical effacement of ≤ 50% or less or pressure in the pelvis or back or vaginal discharge Exclusion criteria: > 3 cm dilated
Interventions	Magnesium sulphate 4 g via IV bolus followed by 2 g/h vs nifedipine 20 mg orally with an additional 20 mg if the contractions continued after 30 min, followed by 20 mg every 3-8 h up to 48 h
Outcomes	The study did not report any outcomes of interest
Notes	

Shirazi 2015

Methods	2-arm active RCT
Participants	182 women were randomised from 1 centre in Pakistan between December 2014-June 2015. Population: women with threatened preterm birth between 28+0 and 36+0 weeks' gestation with intact membranes and singleton pregnancy. Definition of threatened preterm birth: 3 contractions in 10 min and cervical dilation < 4 cm Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical disease (liver, cardiac), maternal medical disorder (pre-eclampsia, hypotension), maternal age < 16 years or > 35 years, cervical dilation > 4 cm, ruptured membranes, allergy to study drugs, a fetus showing signs of malformation, intrauterine growth restriction, or non-reassuring well-being, multiple pregnancy
Interventions	Magnesium sulphate 4 g administered by IV bolus over 15 min, followed by 2-3 g/h and titrated to uterine contractions and AEs vs nifedipine 30 mg orally with an additional 30 mg in 20 min if required, followed by an additional 30 mg after 30 min if required, followed by 30 mg twice/d for further 5 d
Outcomes	Delay by 48 h
Notes	

Song 2002a

Methods	2-arm active RCT
Participants	60 women randomised Population: women between 24 and 34 weeks' gestation with documented preterm labour
Interventions	Nicardipine group 40 mg loading dose and then 20 mg every 2 h as needed to stop contractions (total 80 mg) vs magnesium sulphate 4 g loading dose for 20 min and then maintenance dose of 2-3 g/h until uterine contractions were inhibited or AEs became intolerable. Women could be switched to another tocolytic regimen if they continued to have contractions after 6 h of therapy.
Outcomes	Failure of tocolysis, time to uterine contractions ≤ 5 times/h, time to uterine quiescence, time gained in utero, and frequency of adverse medication effects
Notes	Unable to obtain translation

Song 2002b

Methods	2-arm active-controlled randomised trial
Participants	63 women randomised Population: women between 24 and 34 weeks' gestation with documented preterm labour
Interventions	Nicardipine 40 mg loading dose and then 20 mg every 2 h as needed to stop contractions (total 80 mg) vs ritodrine 0.05 mg/min as initial dose. The dose was increased at 15-min intervals until uterine contractions were inhibited or AEs became intolerable. The maximum recommended dose was 0.35 mg/min. Women could be switched to another tocolytic regimen if they continued to have contractions after 6 h of therapy.
Outcomes	Failure of tocolysis, time to uterine contractions ≤ 5 times/h, time to uterine quiescence, time gained in utero, and frequency of adverse medication effects
Notes	Unable to obtain translation

Songthamwat 2018

Methods	2-arm RCT, placebo-controlled
Participants	206 women were randomised from 1 centre in Thailand between December and July 31 2017. Population: women with threatened preterm birth between 24+0 to 36+0 weeks with intact membranes Definition of threatened preterm birth: ≥ 1 uterine contraction in 10 min Exclusion criteria: contradictions for tocolysis, study medication allergy, cervical dilation of ≥ 2 cm, ruptured membranes, cervical incompetence
Interventions	Nifedipine 20 mg administered orally, followed by 20 mg every 30 min with a maximum total of 3 doses and titrated to uterine contractions, followed by 20 mg every 8 h vs placebo orally with the same schedule

Songthamwat 2018 *(Continued)*

Outcomes	Delay by 48 h, GA at birth, pregnancy prolongation, birth before 37 weeks, headache, hypotension, maternal infection, mean birthweight, tachycardia, serious adverse affects, respiratory morbidity, neonatal death before 28 d, neonatal infection
Notes	

Tabassum 2016

Methods	2-arm RCT, active-controlled
Participants	250 women were randomised from 1 centre in Pakistan between May 2015 and November 2015. Population: women with threatened preterm birth between 28+0 and 36+6 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: not defined Exclusion criteria: maternal complications (pre-eclampsia), multiple pregnancy, ruptured membranes
Interventions	Magnesium sulphate vs nifedipine administered orally (no other details reported)
Outcomes	Delay by 48 h
Notes	

Toghroli 2020

Methods	2-arm active RCT
Participants	211 women were randomised from 1 centre in Iran (dates NR). Population: women with threatened preterm birth between 25+0 and 32+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: regular contractions over 20 min or cervical change of 1 cm dilation/h or effacement of ≥ 80% Exclusion criteria: contraindication of tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (pre-eclampsia, diabetes), placental abruption, ruptured membranes, cervical dilation > 4 cm, a fetus showing signs of non-reassuring well-being, malformations
Interventions	Indomethacin 50 mg administered via injection (no further detail reported) for 8 h, followed by 4 further doses vs magnesium sulphate 4 g followed by 2 g IV at least 12 h after contractions stopped
Outcomes	Delay by 7 d, pregnancy prolongation, GA at birth, respiratory morbidity, gastrointestinal morbidity
Notes	

Xu 2016

Methods	2-arm active RCT
Participants	70 women were randomised from 1 centre in China between June 2011 and June 2015. Population: women with threatened preterm birth between 26+0 to 33+6 weeks' gestation who had undergone assisted reproductive technology Definition of threatened preterm birth: ≥ 4 contractions in 30 min and cervical effacement Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical conditions (hypertension, severe pre-eclampsia), maternal medical disease (cardiac, diabetes, hyperthyroidism, pheochromocytoma, asthma attacks), urinary tract infection, placental or amniotic fluid abnormalities, a fetus showing signs of malformation, intrauterine growth restriction, contraindications to study drugs
Interventions	Atosiban 6.75 mg administered by IV bolus in under 1 min, followed by 300 µg/min for 3 h, followed by 100 µg/min up to 45 h, the maximum was 330 µg vs ritodrine 100 mg administered via IV infusion and titrated to uterine contractions at a rate of 0.05 mg/min every 10 min with the maximum of 0.35 mg/min for at least 12-18 h after contractions stopped
Outcomes	Delay by 48 h, delay by 7 d, GA at birth, perinatal death, tachycardia, nausea or vomiting, headache, hypotension, dyspnoea, respiratory morbidity, neurodevelopmental morbidity, neonatal infection
Notes	

Yasmin 2016

Methods	2-arm RCT, active-controlled
Participants	50 women were randomised from 1 centre in Pakistan between September 2015- September 2015. Population: women with threatened preterm birth between 28+0 to 34+5 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 30 min with cervical dilation of < 4 cm and effacement of at least 50% Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection), hypotension, cervical dilation > 4 cm, multiple pregnancy, ruptured membranes, a fetus showing signs of non-reassuring well-being, malformations
Interventions	Nifedipine 10 mg orally every 15 min for 1 h followed by 10 mg every 8 h for 48 h vs GTN 5 mg administered transdermally followed by 5 mg 12 h later
Outcomes	Delay by 48 h, delay by 7 d, palpitations, headache, hypotension, nausea or vomiting, neonatal death before 7 d
Notes	

Zangooei 2011

Methods	2-arm RCT
Participants	64 women were randomised form 1 centre in Iran (dates NR).

Zangooei 2011 *(Continued)*

	Population: women with threatened preterm birth between 28+0 and 32+0 weeks' gestation with ruptured membranes and singleton pregnancy Threatened preterm birth was not defined Exclusion criteria: contraindications for tocolysis (suspected intrauterine infection or severe vaginal bleeding), maternal medical condition (diabetes, pre-eclampsia), maternal or fetal condition requiring immediate birth, previous antibiotic use within 1 week, multiple pregnancy, a fetus showing signs of non-reassuring well-being
Interventions	Magnesium sulphate 2 g administered IV for 48 h vs no tocolysis
Outcomes	Neonatal death within 7 d
Notes	

AE: adverse effect; **GA:** gestational age; **GBS:** group B streptococcus; **IM:** intramuscular(ly); **IV:** intravenous(ly); **NR:** NR; SAE: serious adverse effect

Characteristics of ongoing studies *[ordered by study ID]*

CTRI/2017/11/010518

Study name	Atosiban (6.75 mg) injection to delay preterm birth
Methods	2-arm RCT, placebo-controlled
Participants	75 women from centres in India Population: women with threatened preterm birth between 24+0 and 33+0 weeks' gestation with intact membranes Definition of preterm birth: uterine contractions with or without cervical changes Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection, severe vaginal bleeding), preterm rupture of membranes, eclampsia and severe pre-eclampsia requiring delivery, a fetus showing signs of intrauterine growth restriction, non-reassuring well-being, demise, malformation, placental insufficiency, praevia or abruption
Interventions	Atosiban 6.75 mg administered via IV bolus injection once given over 1 min vs placebo 0.9 mL IV bolus injection once given over 1 min
Outcomes	Evaluation of time gained in utero after initiation of treatment for 48 h (until birth). Evaluation of safety and tolerability (until birth)
Starting date	
Contact information	
Notes	Registered: 15 November 2017

EUCTR2007-004506-27-FR

Study name	Interest of tocolysis in the management of premature rupture of membranes between 24 and 34 weeks of amenorrhea- TOCOPREMA

EUCTR2007-004506-27-FR *(Continued)*

Methods	2-arm RCT
Participants	Women from centres in France (number of women or centres NR). Population: women with threatened preterm birth between 24+0 and 34+0 weeks' gestation with ruptured membranes Definition of threatened preterm birth: ruptured membranes Exclusion criteria: women with ruptured membranes > 48 h, contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), a fetus showing signs of malformation or non-reassuring well-being, sensitivities or allergy to the study medications
Interventions	Adalate 10 mg administered orally vs no treatment (no other details reported)
Outcomes	Delay in birth by 48 h
Starting date	20 December 2007
Contact information	Not provided
Notes	Registered: 14 November 2007

EUCTR2017-002579-25-FI

Study name	OBE022 added-on to atosiban in threatened spontaneous preterm labour, proof of concept study
Methods	2-arm RCT
Participants	130 women from centres in Spain and Finland (number of centres NR) Population: women with threatened preterm birth between 24+0 and 34+0 weeks Definition of threatened preterm birth: ≥ 4 contractions in 30 min and cervical dilation 1-4 cm Exclusion criteria: women with ruptured membranes > 48 h, contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), a fetus showing signs of malformation or non-reassuring well-being, sensitivities or allergy to the study medications
Interventions	Atosiban with oral OBE022 vs atosiban with oral placebo (no other details reported)
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 37 weeks, pregnancy prolongation
Starting date	31 October 2017
Contact information	ObsEva SA
Notes	Registered 11 August 2017

EUCTR2018-004482-14-FR

Study name	Tocolysis in the management of preterm premature rupture of membranes before 34 weeks of gestation: a double-blinded randomized controlled trial - TOCOPROM

EUCTR2018-004482-14-FR *(Continued)*

Methods	2-arm RCT, placebo-controlled
Participants	850 women from centres in France Population: women with threatened preterm birth between 22+0 and 33+6 weeks' gestation with ruptured membranes and singleton pregnancy Definition of threatened preterm birth: ruptured membranes Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), previous tocolysis, a fetus showing signs of non-reassuring well-being, intrauterine growth restriction, or demise, > 24 h before ruptured membranes diagnosis, maternal medical conditions (angina, hepatic insufficiency, cardiovascular shock, hypotension), participation in other trial, allergy to study drugs, cervical dilation > 5 cm
Interventions	Nifedipine orally (no other details reported) vs placebo
Outcomes	Fetal death (in utero fetal death occurring from randomisation to birth), neonatal death up to discharge from hospital (death from birth to discharge, in delivery room or in NICU), and/or neonatal severe morbidity
Starting date	14 August 2019
Contact information	DRCI Hôpital Saint Louis
Notes	Registered: 3 July 2019

IRCT20190819044568N1

Study name	Preterm labour inhibition
Methods	2-arm active RCT
Participants	200 women from centres in Iran Population: women with threatened preterm birth between 24+0 and 32+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 2 contractions in 10 min plus cervical dilatation < 4 cm and effacement < 50%-60% Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), multiple pregnancy, maternal medical conditions (kidney failure, peptic ulcer), allergy to study medication, cervical dilation > 4 cm
Interventions	Magnesium sulphate 4-6 g administered IV followed by 2 g/ h for a maximum of 48 h or up to 12 h after discontinuation of uterine contractions followed by indomethacin administered rectally 100 mg twice a day for 2 d vs magnesium sulphate 4-6 g administered IV followed by 2 g/h for a maximum of 48 h or up to 12 h after discontinuation of uterine contractions followed by placebo suppositories twice/d for 2 d
Outcomes	Cessation of contractions
Starting date	20 March 2020
Contact information	Qazvin University of Medical Sciences

IRCT20190819044568N1 *(Continued)*

Notes	Registered: 23 November 2020

IRCT20201017049052N1

Study name	Effect of magnesium sulphate and nifedipine in preterm labour
Methods	2-arm active-controlled RCT
Participants	100 women from centres in Iran Population: women with threatened preterm birth between 28+0 and 34+0 weeks' gestation Definition of threatened preterm birth: not defined Exclusion criteria: any contraindication for tocolysis (including allergy to study medications or continuing the pregnancy)
Interventions	Nifedipine 20 mg orally and then every 6 h for 24 h vs magnesium sulphate 4 g IV and then 2 g/h for 24 h
Outcomes	Delay in birth by 48 h, adverse effects
Starting date	1 June 2019
Contact information	Ahvaz University of Medical Sciences
Notes	Registered: 23 November 2020

NCT00466128

Study name	Indomethacin vs placebo in women with preterm premature rupture of membranes
Methods	2-arm RCT, placebo-controlled
Participants	116 women from centres in the USA Population: women with threatened preterm birth between 24+0 and 32+0 weeks' gestation with ruptured membranes Definition of threatened preterm birth: ruptured membranes Exclusion criteria: contraindications to tocolysis (suspected intrauterine infection or severe vaginal bleeding), multiple pregnancy, active preterm labour, a fetus showing signs of non-reassuring well-being, demise, malformation, maternal medical condition (active herpes, increased viral load), cervical cerclage, rupture of membranes > 72 h
Interventions	Indomethacin 50 mg administered orally followed by 25 mg every 6 h vs placebo
Outcomes	Delay in birth by 48 h, delay by 7 d, birthweight, Apgar scores, sepsis, respiratory distress syndrome, intraventricular haemorrhage, necrotizing enterocolitis, NICU hospitalisation days, patent ductus arteriosis, chorioamnionitis, endometritis, labour induction, placental abruption, cesarean section
Starting date	April 2007

NCT00466128 *(Continued)*

Contact information	Thomas Jefferson University
Notes	Registered: 27 April 2007

NCT01869361

Study name	Indomethacin for tocolysis
Methods	2-arm RCT, placebo-controlled
Participants	84 women from centres in the USA Population: women with threatened preterm birth between 23+0 and 31+6 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: 1 contraction in 10 min or 6 in 1 h with cervical dilation > 1 cm and effacement Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), multiple pregnancy, rupture membranes, cervical dilation > 6 cm, a fetus showing signs of non-reassuring well-being or malformation, demise
Interventions	Indomethacin 50 mg orally followed by 25 mg every 6 h for a total of 8 doses over 48 h vs placebo
Outcomes	Delay in birth by 48 h, delay in birth by 7 d, birth before 37 weeks, maternal or fetal complications
Starting date	1 October 2020
Contact information	MetroHealth Medical Center
Notes	Registered: 5 June 2013

NCT02725736

Study name	Tocolytic therapy for preterm labor in multiple gestation
Methods	2-arm RCT, active-controlled
Participants	140 women from centres in Israel Population: women with threatened preterm birth between 24+0 and 32+6 weeks' gestation with multiple pregnancy Definition of threatened preterm birth: not defined Exclusion criteria: any contraindication for tocolysis (including allergy to study medications or continuing the pregnancy) Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), ruptured membranes, a fetus showing signs of non-reassuring well-being or malformation, demise, previous tocolytic therapy or betamethasone
Interventions	Atosiban was given as a single loading IV dose, 6.75 mg in 0.9% sodium chloride solution, followed by an IV infusion of 300 µg/min in 0.9% sodium chloride solution for the first 3 h and then 100 µg/min for another 45 h vs nifedipine given as a loading dose of 20 mg orally followed by another 2

NCT02725736 *(Continued)*

	doses of 20 mg, 20-30 min apart as needed. Maintenance was started after 6 h with 20-40 mg 4 times/d for a total of 48 h
Outcomes	Delay in birth by 48 h, neonatal death before 28 d, respiratory morbidity
Starting date	1 April 2016
Contact information	Tel-Aviv Sourasky Medical Center
Notes	Not yet recruiting

NCT03129945

Study name	Comparison of nifedipine vs indomethacin for acute preterm labor
Methods	2-arm RCT, active-controlled
Participants	450 women from centres in the USA Population: women with threatened preterm birth between 24+0 and 31+5 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 6 contractions in 60 min and cervical dilation ≥ 1 cm or effacement > 25% Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), a fetus showing signs of non-reassuring well-being, demise, malformation, maternal medical conditions (cardiac lesions or maternal hypotension, hypertension requiring treatment, kidney disorder, platelet dysfunction or bleeding disorders, hepatic dysfunction, gastrointestinal ulcerative disease, renal dysfunction and asthma, severe pre-eclampsia or eclampsia, maternal bleeding with haemodynamic instability), rupture of membranes, participation in another interventional study that influences neonatal morbidity or mortality, participation in this trial earlier in the pregnancy, maternal allergy to either indomethacin or nifedipine, aspirin and other NSAIDs
Interventions	Nifedipine 10 mg orally and repeated every 20 min for a maximum dose of 30 mg in the first h followed by 20 mg every 6 h for the first 48 h vs indomethacin 100 mg orally as a loading dose followed by 50 mg every 6 h for the first 48 h of treatment
Outcomes	Delay in birth by 48 h, birth before 32 weeks' gestation
Starting date	17 January 2017
Contact information	University of California, Irvine
Notes	Registered: 26 April 2017

NCT03298191

Study name	Tocolysis in prevention of preterm labor
Methods	3-arm RCT, active-controlled
Participants	300 women from centres in Egypt

NCT03298191 *(Continued)*

	Population: women with threatened preterm birth between 24+0 and 37+0 weeks' gestation with intact membranes Definition of threatened preterm birth: 4 contractions in 30 min, cervical dilation < 3 cm Exclusion criteria: contraindications to tocolysis (severe vaginal bleeding or suspected intrauterine infection), ruptured membranes, a fetus showing signs of non-reassuring well-being or malformation, demise
Interventions	Magnesium sulphate vs ritodrine vs calcium channel blocker - no other details reported
Outcomes	Pregnancy prolongation
Starting date	2 October 2017
Contact information	Assiut University
Notes	

NCT03542552

Study name	Nifedipine vs magnesium sulfate for prevention of preterm labor in symptomatic placenta previa
Methods	2-arm RCT, active-controlled
Participants	176 women from centres in Egypt Population: women with threatened preterm birth between 28+0 and 37+0 weeks' gestation with placenta praevia Definition of threatened preterm birth: contractions with placenta praevia Exclusion criteria: contraindication to tocolysis (severe vaginal bleeding), a fetus showing signs of demise, non-reassuring well-being, severe maternal medical conditions or bleeding disorders
Interventions	Nifedipine 10 mg orally every 20 min for 3 doses, followed by 10 mg every 6 h vs magnesium sulphate 6 g IV followed by a 2 g/h infusion
Outcomes	Pregnancy prolongation
Starting date	1 June 2018
Contact information	Assiut University
Notes	Registered 31 May 2018

NCT04404686

Study name	Vaginal indomethacin for preterm labor
Methods	2-arm RCT, active-controlled
Participants	300 women from centres in Israel Population: women with threatened preterm birth between 24+0 and 31+6 weeks' gestation

NCT04404686 *(Continued)*

	Definition of threatened preterm birth: ≥ 1 contraction in 10 min with ≥ 1 cm cervical dilation or 80% effacement Exclusion criteria: ruptured membranes, severe vaginal bleeding, cervical dilation > 5 cm, a fetus showing signs of malformation, demise, non-reassuring well-being, maternal medical conditions (hypotension, mitral valve stenosis), cervical cerclage, tocolysis in this pregnancy
Interventions	Indomethacin 100 mg administered vaginally followed by a second 100 mg the following day vs nifedipine 20 mg orally every 20 min for 1 h followed by 20 mg every 8 h for 48 h
Outcomes	Pregnancy prolongation, GA at birth, birth before 28 weeks, birth before 34 weeks, birth before 37 weeks, mean birthweight, ICU admission
Starting date	NR
Contact information	Hadassah Medical Organization
Notes	Registered: 27 May 2020

NCT04846621

Study name	Comparative study between nicorandil and nifedipine for the treatment of preterm labour
Methods	2-arm RCT, active-controlled
Participants	230 women from centres in Egypt Population: women with threatened preterm birth between 28+0 and 34+0 weeks' gestation with singleton pregnancy and intact membranes Definition of threatened preterm birth: ≥ 4 contractions in 20 min or 8 in 60 min and cervical dilation ≥ 3 cm Cervical length < 20 mm on transvaginal ultrasound, cervical length between 20 mm to < 30 mm on transvaginal ultrasound and positive fFN test. (This criterion will not be relied upon in this study because it is costly and widely not available in most laboratories). Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection or severe vaginal bleeding), a fetus showing signs of non-reassuring well-being, demise, malformation, ruptured membranes, multiple pregnancy, poly- or oligohydramnios, maternal medical conditions, cervical dilation > 4 cm
Interventions	Nicorandil 20 mg orally initially followed by 10 mg every 8 h for 48 h vs nifedipine orally loading dose 20 mg followed by 10 mg every 8 h for 48 h
Outcomes	Delay in birth by 48 h, Apgar score
Starting date	1 June 2020
Contact information	Ain Shams University
Notes	Registered 15 April 2021

NTR6646

Study name	Assessing the safety and effectiveness of tocolysis for preterm labour
Methods	2-arm RCT, placebo-controlled
Participants	1514 women from centres in the Netherlands, Belgium, UK and Ireland Population: women with threatened preterm birth between 30+0 and 33+6 weeks' gestation Definition of threatened preterm birth: regular uterine contractions and either ruptured membranes, cervical length of 15-30 mm and a positive fFN test Exclusion criteria: triplet pregnancy or more, contraindication for tocolysis (suspected intrauterine infection), previous treatment for threatened preterm birth with corticosteroids in current pregnancy, a fetus showing signs of non-reassuring well-being or malformation
Interventions	Atosiban vs placebo
Outcomes	Bronchopulmonary dysplasia at 36 weeks postmenstrual age (PMA), periventricular leukomalacia > grade 1, intraventricular haemorrhage > grade 2, necrotising enterocolitis = stage 2, retinopathy of prematurity > grade 2 or need for laser therapy, culture-proven sepsis and perinatal death, birth within 48 h, time to delivery, GA at delivery, birthweight, number of d on invasive mechanical ventilation, length of admission in NICU, asphyxia, meningitis, pneumothorax and mortality until 3 months corrected age, maternal infection, maternal adverse effects and costs
Starting date	2 October 2017
Contact information	Academic Medical Center
Notes	Registered: 24 August 2017

PACTR202004681537890

Study name	Prevention of premature birth by nifedipine alone or with indomethacin
Methods	2-arm RCT, active-controlled
Participants	346 women from centres in Sudan Population: women with threatened preterm birth between 25+0 and 34+0 weeks Definition of preterm birth: uterine contractions, at least 3 contractions/30 min, and cervical length of ≤ 10 mm or 11-30 mm or ruptured membranes Exclusion criteria: contraindication to tocolysis (suspected intrauterine infection, severe vaginal bleeding), maternal medical conditions (angina, myocardial infarction, hypotension), a fetus showing signs of non-reassuring well-being, malformation, > 5 cm cervical dilatation, cerclage, tocolytic treatment for > 6 h prior to arrival in a participating hospital
Interventions	Nifedipine 20 mg orally combined with a rectal placebo. If contraction inhibition occurs for 2 h, the woman will continue receiving 20 mg of oral nifedipine every 4 h for 48 h, the maximum dose should not exceed 180 mg/d. Rectal placebo will be repeated after 90 min of the first dosage and then it will be prescribed every 4 h vs nifedipine 20 mg, may be followed by 20 mg every 4 h indomethacin 100 mg rectal suppositories, may be followed by oral 25 mg every 4 h
Outcomes	Delay in birth by 48 h, GA at birth, neonatal mortality, lung diseases, severe intraventricular haemorrhage, periventricular leukomalacia, sepsis, necrotising enterocolitis

PACTR202004681537890 *(Continued)*

Starting date	20 June 2020
Contact information	Wad Medani Hospital
Notes	Registered: 8 August 2020

TCTR20200617001

Study name	Effect of non-tocolytic drugs to delivery of pregnant women with threatened preterm labour and cervical length > 25 millimetre: a randomised controlled trial
Methods	2-arm RCT
Participants	Women from centres in Thailand Population: women with threatened preterm birth between 20+0 to 36+6 weeks Definition of threatened preterm birth: ≥ 1 contractions in 10 min or 4 times in 20 min or 8 times in 60 min and cervical length ≤ 25 mm Exclusion criteria: need emergency treatment with tocolytic drugs, active bleeding, previously received tocolytic drugs, placenta praevia, placental abruption, previous cervical cerclage and urinary tract infection
Interventions	Bed rest and tocolysis vs no treatment
Outcomes	Birth after 37 weeks, GA at birth, maternal and neonatal complications, hospital costs
Starting date	10 September 2020
Contact information	Siriraj Hospital
Notes	Registered: 17 June 2020

fFN: fetal fibronectin; **GA:** gestational age; **ICU:** intensive care unit; **IV:** intravenous(ly); **NICU:** neonatal intensive care unit; **NR:** not reported; **NSAID:** non-steroidal anti-inflammatory drug; **RCT:** randomised controlled trial

DATA AND ANALYSES

Comparison 1. Betamimetics vs placebo or no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Delay in birth by 48 hours	10	1399	Risk Ratio (IV, Random, 95% CI)	1.27 [1.11, 1.45]
1.2 Delay in birth by 7 days	8	1102	Risk Ratio (IV, Random, 95% CI)	1.46 [1.09, 1.97]
1.3 Neonatal death before 28 days	14	1763	Risk Ratio (IV, Random, 95% CI)	0.94 [0.56, 1.59]

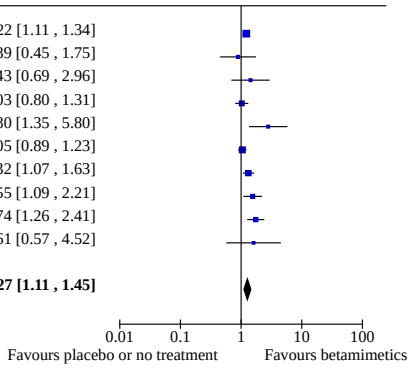
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4 Pregnancy prolongation (time from trial entry to birth in days)	7	1176	Mean Difference (IV, Random, 95% CI)	1.86 [-2.24, 5.95]
1.5 Serious adverse effects of drugs	5	344	Risk Ratio (IV, Random, 95% CI)	0.50 [0.05, 4.94]
1.6 Maternal infection	4	222	Risk Ratio (IV, Random, 95% CI)	1.44 [0.82, 2.51]
1.7 Cessation of treatment due to adverse effects	5	1081	Risk Ratio (IV, Random, 95% CI)	9.62 [4.33, 21.36]
1.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.9 Birth before 32 weeks' gestation	3	561	Risk Ratio (IV, Random, 95% CI)	0.86 [0.73, 1.01]
1.10 Birth before 34 weeks' gestation	2	209	Risk Ratio (IV, Random, 95% CI)	0.32 [0.04, 2.85]
1.11 Birth before 37 weeks' gestation	4	1024	Risk Ratio (IV, Random, 95% CI)	0.99 [0.58, 1.72]
1.12 Maternal death	3	825	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.13 Pulmonary oedema	5	1012	Risk Ratio (IV, Random, 95% CI)	3.03 [0.12, 74.23]
1.14 Dyspnoea	2	814	Risk Ratio (IV, Random, 95% CI)	12.09 [4.66, 31.39]
1.15 Palpitations	7	1320	Risk Ratio (IV, Random, 95% CI)	8.55 [5.71, 12.79]
1.16 Headaches	4	974	Risk Ratio (IV, Random, 95% CI)	2.94 [1.17, 7.35]
1.17 Nausea or vomiting	5	1167	Risk Ratio (IV, Random, 95% CI)	1.77 [1.29, 2.41]
1.18 Tachycardia	5	493	Risk Ratio (IV, Random, 95% CI)	1.72 [0.57, 5.17]
1.19 Maternal cardiac arrhythmias	4	860	Risk Ratio (IV, Random, 95% CI)	3.43 [0.84, 13.89]
1.20 Maternal hypotension	2	136	Risk Ratio (IV, Random, 95% CI)	1.55 [0.12, 19.43]
1.21 Perinatal death	14	1702	Risk Ratio (IV, Random, 95% CI)	1.08 [0.75, 1.55]
1.22 Stillbirth	9	1298	Risk Ratio (IV, Random, 95% CI)	1.24 [0.66, 2.33]
1.23 Neonatal death before 7 days	10	1446	Risk Ratio (IV, Random, 95% CI)	1.02 [0.50, 2.05]
1.24 Neurodevelopmental morbidity	4	978	Risk Ratio (IV, Random, 95% CI)	0.71 [0.45, 1.14]
1.25 Gastrointestinal morbidity	2	149	Risk Ratio (IV, Random, 95% CI)	0.50 [0.12, 2.16]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.26 Respiratory morbidity	10	1530	Risk Ratio (IV, Random, 95% CI)	0.98 [0.72, 1.33]
1.27 Mean birthweight	9	1298	Mean Difference (IV, Random, 95% CI)	68.28 [-10.92, 147.49]
1.28 Birthweight < 2000 g	1	53	Risk Ratio (IV, Random, 95% CI)	1.74 [1.04, 2.91]
1.29 Birthweight < 2500 g	8	1400	Risk Ratio (IV, Random, 95% CI)	0.92 [0.79, 1.06]
1.30 Gestational age at birth	7	1241	Mean Difference (IV, Random, 95% CI)	0.09 [-0.56, 0.75]
1.31 Neonatal infection	5	999	Risk Ratio (IV, Random, 95% CI)	1.47 [0.71, 3.06]

Analysis 1.1. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	277	352	230	356	22.8%	1.22 [1.11 , 1.34]
Christensen 1980	7	14	9	16	3.3%	0.89 [0.45 , 1.75]
Cotton 1984	10	19	7	19	2.9%	1.43 [0.69 , 2.96]
Garite 1987	30	39	30	40	13.4%	1.03 [0.80 , 1.31]
Ingemarsson 1976	14	15	5	15	2.9%	2.80 [1.35 , 5.80]
Larsen 1980	125	150	39	49	18.8%	1.05 [0.89 , 1.23]
Larsen 1986	44	49	34	50	15.4%	1.32 [1.07 , 1.63]
Leveno 1986	37	54	23	52	9.0%	1.55 [1.09 , 2.21]
Matsuda 1993	34	39	21	42	10.0%	1.74 [1.26 , 2.41]
Spellacy 1979	6	14	4	15	1.5%	1.61 [0.57 , 4.52]
Total (95% CI)		**745**		**654**	**100.0%**	**1.27 [1.11 , 1.45]**
Total events:	584		402			

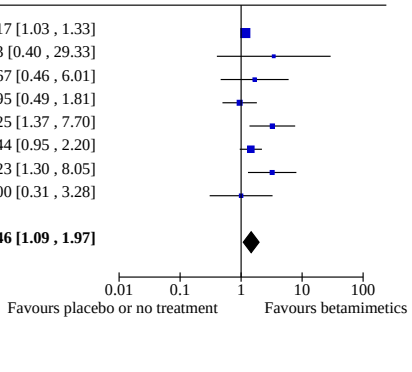
Heterogeneity: Tau² = 0.02; Chi² = 18.62, df = 9 (P = 0.03); I² = 52%
Test for overall effect: Z = 3.55 (P = 0.0004)
Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	218	352	188	356	35.4%	1.17 [1.03 , 1.33]
Christensen 1980	3	14	1	16	1.8%	3.43 [0.40 , 29.33]
Cotton 1984	5	19	3	19	4.7%	1.67 [0.46 , 6.01]
Garite 1987	12	39	13	40	13.6%	0.95 [0.49 , 1.81]
Ingemarsson 1976	13	15	4	15	9.1%	3.25 [1.37 , 7.70]
Leveno 1986	30	54	20	52	21.7%	1.44 [0.95 , 2.20]
Matsuda 1993	15	39	5	42	8.3%	3.23 [1.30 , 8.05]
Spellacy 1979	4	15	4	15	5.4%	1.00 [0.31 , 3.28]
Total (95% CI)		**547**		**555**	**100.0%**	**1.46 [1.09 , 1.97]**
Total events:	300		238			

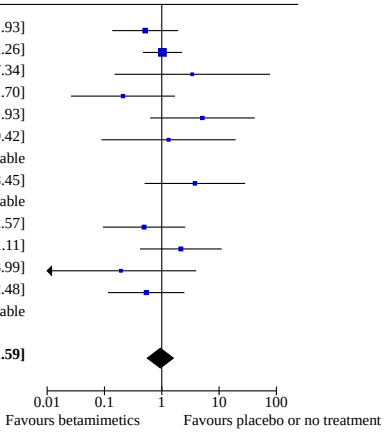
Heterogeneity: Tau² = 0.06; Chi² = 12.10, df = 7 (P = 0.10); I² = 42%
Test for overall effect: Z = 2.50 (P = 0.01)
Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Adam 1966	3	28	5	24	13.5%	0.51 [0.14 , 1.93]
Canadian Preterm Labor Investigators 1992	12	380	12	391	30.5%	1.03 [0.47 , 2.26]
Christensen 1980	1	14	0	16	2.7%	3.40 [0.15 , 77.34]
Cotton 1984	1	19	4	16	5.9%	0.21 [0.03 , 1.70]
Garite 1987	5	39	1	40	5.8%	5.13 [0.63 , 41.93]
Howard 1982	1	16	1	21	3.6%	1.31 [0.09 , 19.42]
Ingemarsson 1976	0	15	0	15		Not estimable
Larsen 1980	11	131	1	45	6.3%	3.78 [0.50 , 28.45]
Larsen 1986	0	49	0	50		Not estimable
Leveno 1986	2	56	4	55	9.1%	0.49 [0.09 , 2.57]
Matsuda 1993	4	39	2	42	9.2%	2.15 [0.42 , 11.11]
Sakamoto 1985	0	99	2	96	2.9%	0.19 [0.01 , 3.99]
Spellacy 1979	2	14	4	15	10.4%	0.54 [0.12 , 2.48]
Walters 1977	0	21	0	17		Not estimable
Total (95% CI)		**920**		**843**	**100.0%**	**0.94 [0.56 , 1.59]**
Total events:	42		36			

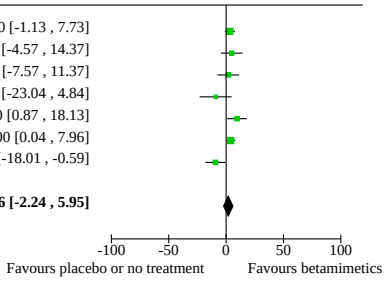
Heterogeneity: Tau² = 0.07; Chi² = 10.99, df = 10 (P = 0.36); I² = 9%
Test for overall effect: Z = 0.21 (P = 0.83)
Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Betamimetics Mean	Betamimetics SD	Betamimetics Total	Placebo or no treatment Mean	Placebo or no treatment SD	Placebo or no treatment Total	Weight	Mean Difference IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	27.8	30	352	24.5	30.2	356	21.9%	3.30 [-1.13 , 7.73]
Cotton 1984	12	14.9	19	7.1	14.9	19	11.4%	4.90 [-4.57 , 14.37]
Guinn 1997	59.6	25.9	61	57.7	38.2	118	11.4%	1.90 [-7.57 , 11.37]
Howard 1982	30.8	22.5	15	39.9	17.4	18	6.7%	-9.10 [-23.04 , 4.84]
Larsen 1986	33.9	21.9	49	24.4	21.9	50	12.8%	9.50 [0.87 , 18.13]
Matsuda 1993	8.9	8.8	39	4.9	9.4	42	23.1%	4.00 [0.04 , 7.96]
Walters 1977	53.5	13.9	21	62.8	13.4	17	12.6%	-9.30 [-18.01 , -0.59]
Total (95% CI)			**556**			**620**	**100.0%**	**1.86 [-2.24 , 5.95]**

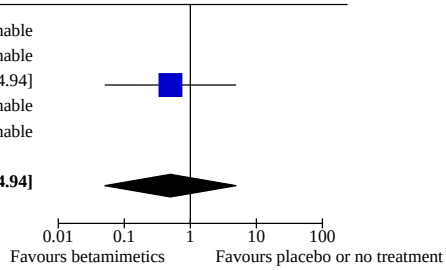
Heterogeneity: Tau² = 14.83; Chi² = 13.14, df = 6 (P = 0.04); I² = 54%
Test for overall effect: Z = 0.89 (P = 0.37)
Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Christensen 1980	0	14	0	16		Not estimable
Garite 1987	0	39	0	40		Not estimable
Ingemarsson 1976	1	15	2	15	100.0%	0.50 [0.05 , 4.94]
Larsen 1986	0	49	0	50		Not estimable
Leveno 1986	0	54	0	52		Not estimable
Total (95% CI)		**171**		**173**	**100.0%**	**0.50 [0.05 , 4.94]**
Total events:	1		2			

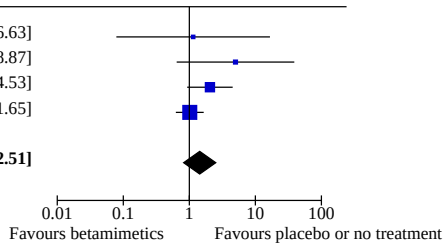
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.55)
Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 6: Maternal infection

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Christensen 1980	1	14	1	16	4.2%	1.14 [0.08 , 16.63]
Cotton 1984	5	19	1	19	6.9%	5.00 [0.64 , 38.87]
Garite 1987	14	39	7	40	32.9%	2.05 [0.93 , 4.53]
Matsuda 1993	16	34	19	41	56.0%	1.02 [0.62 , 1.65]
Total (95% CI)		**106**		**116**	**100.0%**	**1.44 [0.82 , 2.51]**
Total events:	36		28			

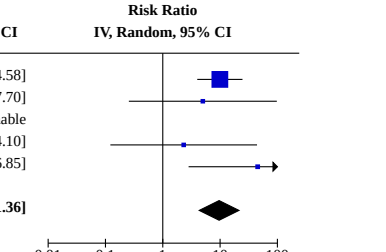
Heterogeneity: Tau² = 0.08; Chi² = 3.93, df = 3 (P = 0.27); I² = 24%
Test for overall effect: Z = 1.27 (P = 0.21)
Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	49	352	5	356	77.2%	9.91 [4.00 , 24.58]
Cotton 1984	2	19	0	19	7.2%	5.00 [0.26 , 97.70]
Ingemarsson 1976	0	15	0	15		Not estimable
Larsen 1980	3	150	0	49	7.3%	2.32 [0.12 , 44.10]
Leveno 1986	23	54	0	52	8.3%	45.29 [2.82 , 726.85]
Total (95% CI)		**590**		**491**	**100.0%**	**9.62 [4.33 , 21.36]**
Total events:	77		5			

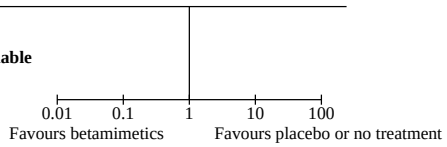
Heterogeneity: Tau² = 0.00; Chi² = 2.28, df = 3 (P = 0.52); I² = 0%
Test for overall effect: Z = 5.56 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.8. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

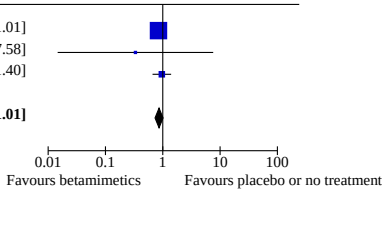
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 1.9. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	104	213	123	212	81.1%	0.84 [0.70 , 1.01]
Ingemarsson 1976	0	15	1	15	0.3%	0.33 [0.01 , 7.58]
Leveno 1986	27	54	27	52	18.6%	0.96 [0.66 , 1.40]
Total (95% CI)		**282**		**279**	**100.0%**	**0.86 [0.73 , 1.01]**
Total events:	131		151			

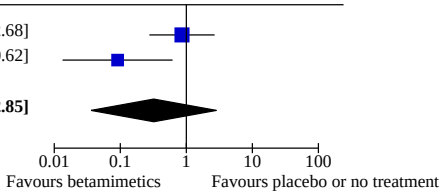
Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 2 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.82 (P = 0.07)
Test for subgroup differences: Not applicable



Analysis 1.10. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Guinn 1997	4	61	9	118	56.2%	0.86 [0.28 , 2.68]
Ingemarsson 1976	1	15	11	15	43.8%	0.09 [0.01 , 0.62]
Total (95% CI)		**76**		**133**	**100.0%**	**0.32 [0.04 , 2.85]**
Total events:	5		20			

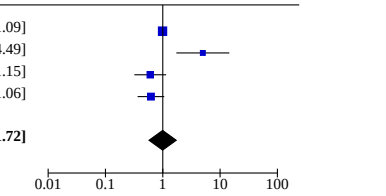
Heterogeneity: Tau² = 1.88; Chi² = 3.90, df = 1 (P = 0.05); I² = 74%
Test for overall effect: Z = 1.02 (P = 0.31)
Test for subgroup differences: Not applicable



Analysis 1.11. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	240	352	245	356	34.8%	0.99 [0.90 , 1.09]
Cotton 1984	15	19	3	19	15.1%	5.00 [1.73 , 14.49]
Guinn 1997	10	61	32	118	23.8%	0.60 [0.32 , 1.15]
Larsen 1986	14	49	23	50	26.3%	0.62 [0.36 , 1.06]
Total (95% CI)		**481**		**543**	**100.0%**	**0.99 [0.58 , 1.72]**
Total events:	279		303			

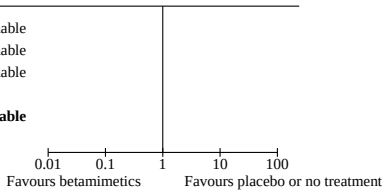
Heterogeneity: Tau² = 0.22; Chi² = 14.04, df = 3 (P = 0.003); I² = 79%
Test for overall effect: Z = 0.02 (P = 0.98)
Test for subgroup differences: Not applicable



Analysis 1.12. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 12: Maternal death

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	0	352	0	356		Not estimable
Cotton 1984	0	19	0	19		Not estimable
Garite 1987	0	39	0	40		Not estimable
Total (95% CI)		**410**		**415**		**Not estimable**
Total events:	0		0			

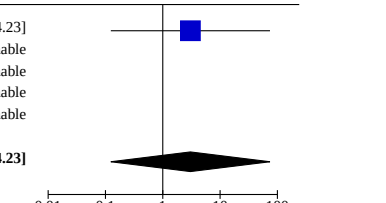
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 1.13. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 13: Pulmonary oedema

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	1	352	0	356	100.0%	3.03 [0.12 , 74.23]
Cotton 1984	0	19	0	19		Not estimable
Garite 1987	0	39	0	40		Not estimable
Leveno 1986	0	54	0	52		Not estimable
Matsuda 1993	0	39	0	42		Not estimable
Total (95% CI)		**503**		**509**	**100.0%**	**3.03 [0.12 , 74.23]**
Total events:	1		0			

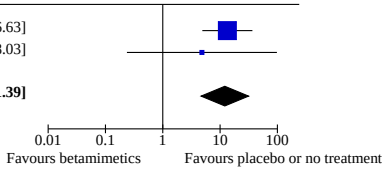
Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)
Test for subgroup differences: Not applicable



Analysis 1.14. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 14: Dyspnoea

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	53	352	4	356	90.0%	13.40 [4.90 , 36.63]
Leveno 1986	2	54	0	52	10.0%	4.82 [0.24 , 98.03]
Total (95% CI)		**406**		**408**	**100.0%**	**12.09 [4.66 , 31.39]**
Total events:	55		4			

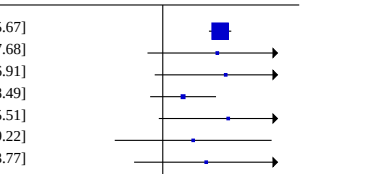
Heterogeneity: Tau² = 0.00; Chi² = 0.40, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 5.12 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.15. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 15: Palpitations

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	188	352	19	356	81.0%	10.01 [6.39 , 15.67]
Larsen 1980	13	150	0	49	2.1%	8.94 [0.54 , 147.68]
Leveno 1986	6	54	0	52	2.0%	12.53 [0.72 , 216.91]
Sakamoto 1985	7	98	3	95	9.3%	2.26 [0.60 , 8.49]
Spellacy 1979	6	14	0	15	2.1%	13.87 [0.85 , 225.51]
Tohoku 1984	1	22	0	25	1.6%	3.39 [0.15 , 79.22]
Walters 1977	3	21	0	17	1.9%	5.73 [0.32 , 103.77]
Total (95% CI)		**711**		**609**	**100.0%**	**8.55 [5.71 , 12.79]**
Total events:	224		22			

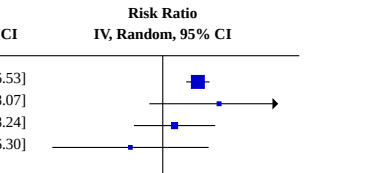
Heterogeneity: Tau² = 0.00; Chi² = 4.95, df = 6 (P = 0.55); I² = 0%
Test for overall effect: Z = 10.43 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.16. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 16: Headaches

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	81	352	20	356	61.1%	4.10 [2.57 , 6.53]
Larsen 1980	14	150	0	49	9.3%	9.60 [0.58 , 158.07]
Spellacy 1979	3	14	2	15	21.9%	1.61 [0.31 , 8.24]
Walters 1977	0	21	1	17	7.6%	0.27 [0.01 , 6.30]
Total (95% CI)		**537**		**437**	**100.0%**	**2.94 [1.17 , 7.35]**
Total events:	98		23			

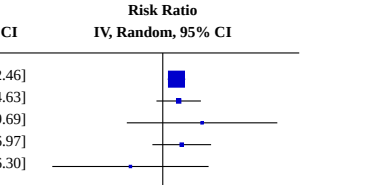
Heterogeneity: Tau² = 0.30; Chi² = 4.28, df = 3 (P = 0.23); I² = 30%
Test for overall effect: Z = 2.30 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 1.17. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 17: Nausea or vomiting

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	72	352	42	356	78.8%	1.73 [1.22 , 2.46]
Larsen 1980	29	150	5	49	12.2%	1.89 [0.78 , 4.63]
Sakamoto 1985	2	98	0	95	1.1%	4.85 [0.24 , 99.69]
Spellacy 1979	6	14	3	15	7.0%	2.14 [0.66 , 6.97]
Walters 1977	0	21	1	17	1.0%	0.27 [0.01 , 6.30]
Total (95% CI)		**635**		**532**	**100.0%**	**1.77 [1.29 , 2.41]**
Total events:	109		51			

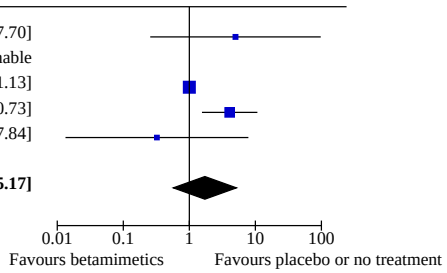
Heterogeneity: Tau² = 0.00; Chi² = 1.93, df = 4 (P = 0.75); I² = 0%
Test for overall effect: Z = 3.58 (P = 0.0003)
Test for subgroup differences: Not applicable



Analysis 1.18. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 18: Tachycardia

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	19	0	19	10.6%	5.00 [0.26 , 97.70]
Howard 1982	0	15	0	18		Not estimable
Ingemarsson 1976	15	15	15	15	45.9%	1.00 [0.88 , 1.13]
Larsen 1980	50	150	4	49	34.1%	4.08 [1.55 , 10.73]
Sakamoto 1985	0	98	1	95	9.5%	0.32 [0.01 , 7.84]
Total (95% CI)		**297**		**196**	**100.0%**	**1.72 [0.57 , 5.17]**
Total events:	67		20			

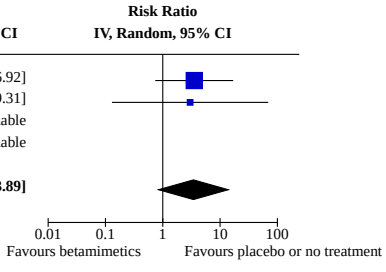
Heterogeneity: Tau² = 0.68; Chi² = 9.61, df = 3 (P = 0.02); I² = 69%
Test for overall effect: Z = 0.97 (P = 0.33)
Test for subgroup differences: Not applicable



Analysis 1.19. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	7	352	2	356	80.1%	3.54 [0.74 , 16.92]
Cotton 1984	1	19	0	19	19.9%	3.00 [0.13 , 69.31]
Howard 1982	0	15	0	18		Not estimable
Matsuda 1993	0	39	0	42		Not estimable
Total (95% CI)		**425**		**435**	**100.0%**	**3.43 [0.84 , 13.89]**
Total events:	8		2			

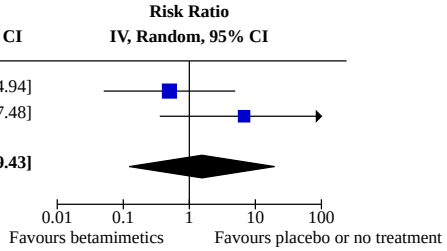
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.72 (P = 0.08)
Test for subgroup differences: Not applicable



Analysis 1.20. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 20: Maternal hypotension

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ingemarsson 1976	1	15	2	15	56.5%	0.50 [0.05 , 4.94]
Leveno 1986	3	54	0	52	43.5%	6.75 [0.36 , 127.48]
Total (95% CI)		**69**		**67**	**100.0%**	**1.55 [0.12 , 19.43]**
Total events:	4		2			

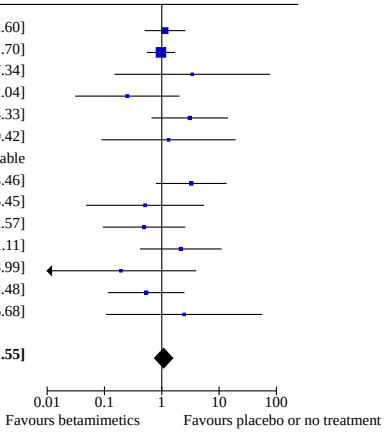
Heterogeneity: Tau² = 1.58; Chi² = 1.87, df = 1 (P = 0.17); I² = 47%
Test for overall effect: Z = 0.34 (P = 0.73)
Test for subgroup differences: Not applicable



Analysis 1.21. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 21: Perinatal death

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Adam 1966	9	27	7	24	19.7%	1.14 [0.50 , 2.60]
Canadian Preterm Labor Investigators 1992	22	352	23	356	41.4%	0.97 [0.55 , 1.70]
Christensen 1980	1	14	0	16	1.4%	3.40 [0.15 , 77.34]
Cotton 1984	1	19	4	19	3.0%	0.25 [0.03 , 2.04]
Garite 1987	6	39	2	40	5.6%	3.08 [0.66 , 14.33]
Howard 1982	1	16	1	21	1.8%	1.31 [0.09 , 19.42]
Ingemarsson 1976	0	15	0	15		Not estimable
Larsen 1980	19	131	2	45	6.6%	3.26 [0.79 , 13.46]
Larsen 1986	1	49	2	50	2.4%	0.51 [0.05 , 5.45]
Leveno 1986	2	56	4	55	4.8%	0.49 [0.09 , 2.57]
Matsuda 1993	4	39	2	42	4.9%	2.15 [0.42 , 11.11]
Sakamoto 1985	0	99	2	96	1.4%	0.19 [0.01 , 3.99]
Spellacy 1979	2	14	4	15	5.6%	0.54 [0.12 , 2.48]
Walters 1977	1	21	0	17	1.3%	2.45 [0.11 , 56.68]
Total (95% CI)		**891**		**811**	**100.0%**	**1.08 [0.75 , 1.55]**
Total events:	69		53			

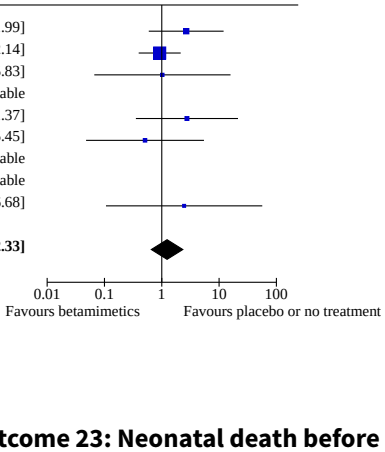
Heterogeneity: Tau² = 0.00; Chi² = 10.93, df = 12 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.40 (P = 0.69)
Test for subgroup differences: Not applicable



Analysis 1.22. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 22: Stillbirth

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Adam 1966	6	27	2	24	17.7%	2.67 [0.59 , 11.99]
Canadian Preterm Labor Investigators 1992	10	352	11	356	56.2%	0.92 [0.40 , 2.14]
Garite 1987	1	39	1	40	5.3%	1.03 [0.07 , 15.83]
Howard 1982	0	16	0	21		Not estimable
Larsen 1980	8	131	1	45	9.5%	2.75 [0.35 , 21.37]
Larsen 1986	1	49	2	50	7.1%	0.51 [0.05 , 5.45]
Matsuda 1993	0	39	0	42		Not estimable
Spellacy 1979	0	14	0	15		Not estimable
Walters 1977	1	21	0	17	4.1%	2.45 [0.11 , 56.68]
Total (95% CI)		**688**		**610**	**100.0%**	**1.24 [0.66 , 2.33]**
Total events:	27		17			

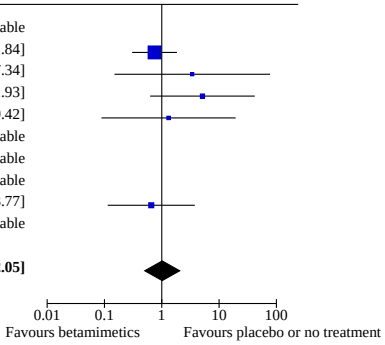
Heterogeneity: Tau² = 0.00; Chi² = 2.80, df = 5 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.66 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 1.23. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Adam 1966	0	28	0	24		Not estimable
Canadian Preterm Labor Investigators 1992	8	380	11	391	60.9%	0.75 [0.30 , 1.84]
Christensen 1980	1	14	0	16	5.0%	3.40 [0.15 , 77.34]
Garite 1987	5	39	1	40	11.2%	5.13 [0.63 , 41.93]
Howard 1982	1	16	1	21	6.8%	1.31 [0.09 , 19.42]
Ingemarsson 1976	0	15	0	15		Not estimable
Larsen 1980	0	150	0	49		Not estimable
Larsen 1986	0	49	0	50		Not estimable
Leveno 1986	2	56	3	55	16.1%	0.65 [0.11 , 3.77]
Walters 1977	0	21	0	17		Not estimable
Total (95% CI)		**768**		**678**	**100.0%**	**1.02 [0.50 , 2.05]**
Total events:	17		16			

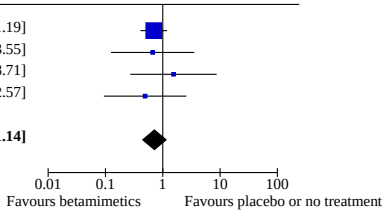
Heterogeneity: Tau² = 0.00; Chi² = 3.57, df = 4 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.05 (P = 0.96)
Test for subgroup differences: Not applicable



Analysis 1.24. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	21	370	31	380	76.8%	0.70 [0.41 , 1.19]
Cotton 1984	2	19	3	19	7.9%	0.67 [0.13 , 3.55]
Garite 1987	3	39	2	40	7.3%	1.54 [0.27 , 8.71]
Leveno 1986	2	56	4	55	8.0%	0.49 [0.09 , 2.57]
Total (95% CI)		**484**		**494**	**100.0%**	**0.71 [0.45 , 1.14]**
Total events:	28		40			

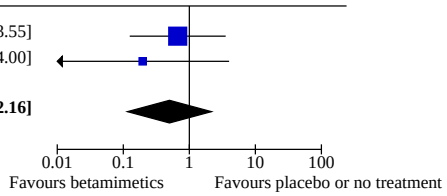
Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 3 (P = 0.81); I² = 0%
Test for overall effect: Z = 1.40 (P = 0.16)
Test for subgroup differences: Not applicable



Analysis 1.25. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	19	3	19	76.5%	0.67 [0.13 , 3.55]
Leveno 1986	0	56	2	55	23.5%	0.20 [0.01 , 4.00]
Total (95% CI)		**75**		**74**	**100.0%**	**0.50 [0.12 , 2.16]**
Total events:	2		5			

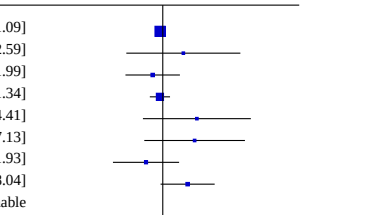
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 0.93 (P = 0.35)
Test for subgroup differences: Not applicable



Analysis 1.26. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 26: Respiratory morbidity

Study or Subgroup	Betamimetics Events	Betamimetics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	123	370	141	380	45.4%	0.90 [0.74 , 1.09]
Christensen 1980	2	14	1	16	1.8%	2.29 [0.23 , 22.59]
Cotton 1984	4	19	6	19	7.0%	0.67 [0.22 , 1.99]
Garite 1987	20	39	23	40	28.4%	0.89 [0.59 , 1.34]
Howard 1982	3	16	1	21	2.0%	3.94 [0.45 , 34.41]
Larsen 1980	11	150	1	49	2.3%	3.59 [0.48 , 27.13]
Larsen 1986	3	49	6	50	5.0%	0.51 [0.14 , 1.93]
Matsuda 1993	9	34	4	41	7.1%	2.71 [0.92 , 8.04]
Sakamoto 1985	0	99	0	95		Not estimable
Spellacy 1979	0	14	3	15	1.1%	0.15 [0.01 , 2.71]
Total (95% CI)		**804**		**726**	**100.0%**	**0.98 [0.72 , 1.33]**
Total events:	175		186			

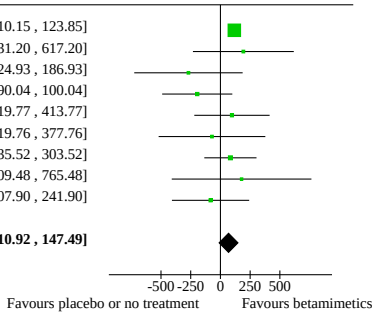
Heterogeneity: Tau² = 0.05; Chi² = 10.57, df = 8 (P = 0.23); I² = 24%
Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable



Analysis 1.27. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 27: Mean birthweight

Study or Subgroup	Betamimetics Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	2317	48	380	2200	49	391	60.8%	117.00 [110.15 , 123.85]
Cotton 1984	1841	678	19	1648	656	19	3.3%	193.00 [-231.20 , 617.20]
Howard 1982	2487	656	16	2756	756	21	2.9%	-269.00 [-724.93 , 186.93]
Larsen 1980	2550	889	131	2745	865	45	6.4%	-195.00 [-490.04 , 100.04]
Larsen 1986	2845	804	49	2748	804	50	5.7%	97.00 [-219.77 , 413.77]
Leake 1983	1963	594	17	2034	755	18	3.0%	-71.00 [-519.76 , 377.76]
Matsuda 1993	1881	515	34	1797	441	41	10.7%	84.00 [-135.52 , 303.52]
Spellacy 1979	1984	700	14	1806	907	15	1.8%	178.00 [-409.48 , 765.48]
Walters 1977	3132	585	21	3215	436	17	5.4%	-83.00 [-407.90 , 241.90]
Total (95% CI)			**681**			**617**	**100.0%**	**68.28 [-10.92 , 147.49]**

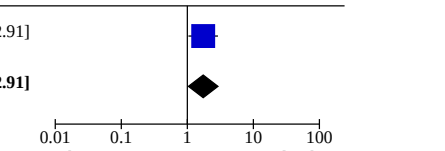
Heterogeneity: Tau² = 2672.85; Chi² = 9.43, df = 8 (P = 0.31); I² = 15%
Test for overall effect: Z = 1.69 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 1.28. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	16	23	12	30	100.0%	1.74 [1.04 , 2.91]
Total (95% CI)		**23**		**30**	**100.0%**	**1.74 [1.04 , 2.91]**
Total events:	16		12			

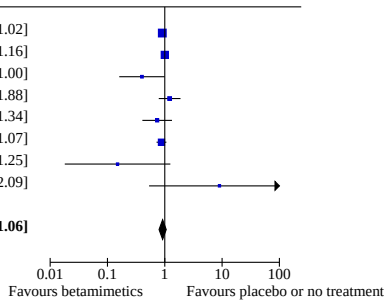
Heterogeneity: Not applicable
Test for overall effect: Z = 2.11 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 1.29. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	212	380	241	391	31.9%	0.91 [0.80 , 1.02]
Cotton 1984	18	19	18	19	28.2%	1.00 [0.86 , 1.16]
Ingemarsson 1976	4	15	10	15	2.4%	0.40 [0.16 , 1.00]
Larsen 1980	57	129	16	44	8.6%	1.22 [0.79 , 1.88]
Larsen 1986	13	49	18	50	5.1%	0.74 [0.41 , 1.34]
Leveno 1986	41	56	46	55	23.1%	0.88 [0.72 , 1.07]
Sakamoto 1985	1	80	5	60	0.5%	0.15 [0.02 , 1.25]
Walters 1977	5	21	0	17	0.3%	9.00 [0.53 , 152.09]
Total (95% CI)		**749**		**651**	**100.0%**	**0.92 [0.79 , 1.06]**
Total events:	351		354			

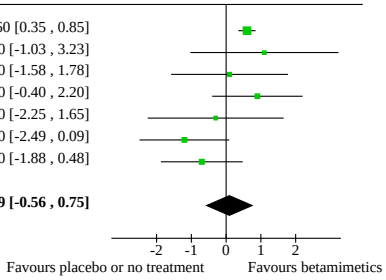
Heterogeneity: Tau² = 0.01; Chi² = 12.09, df = 7 (P = 0.10); I² = 42%
Test for overall effect: Z = 1.17 (P = 0.24)
Test for subgroup differences: Not applicable



Analysis 1.30. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 30: Gestational age at birth

Study or Subgroup	Betamimetics Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	34	1.7	380	33.4	1.8	391	30.3%	0.60 [0.35 , 0.85]
Cotton 1984	33.1	3.3	19	32	3.4	19	7.3%	1.10 [-1.03 , 3.23]
Guinn 1997	38.2	2.4	61	38.1	8.7	118	10.3%	0.10 [-1.58 , 1.78]
Larsen 1986	37.2	3.3	49	36.3	3.3	50	14.1%	0.90 [-0.40 , 2.20]
Leake 1983	33.5	2.9	17	33.8	3	18	8.3%	-0.30 [-2.25 , 1.65]
Matsuda 1993	30	3.4	39	31.2	2.4	42	14.2%	-1.20 [-2.49 , 0.09]
Walters 1977	38.5	2.1	21	39.2	1.6	17	15.6%	-0.70 [-1.88 , 0.48]
Total (95% CI)			**586**			**655**	**100.0%**	**0.09 [-0.56 , 0.75]**

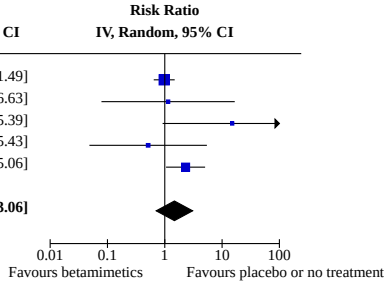
Heterogeneity: Tau² = 0.35; Chi² = 12.81, df = 6 (P = 0.05); I² = 53%
Test for overall effect: Z = 0.28 (P = 0.78)
Test for subgroup differences: Not applicable



Analysis 1.31. Comparison 1: Betamimetics vs placebo or no treatment, Outcome 31: Neonatal infection

Study or Subgroup	Betamimetics Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Canadian Preterm Labor Investigators 1992	38	380	40	391	45.8%	0.98 [0.64 , 1.49]
Christensen 1980	1	14	1	16	6.6%	1.14 [0.08 , 16.63]
Cotton 1984	7	19	0	19	6.1%	15.00 [0.92 , 245.39]
Garite 1987	1	39	2	40	8.2%	0.51 [0.05 , 5.43]
Matsuda 1993	15	39	7	42	33.3%	2.31 [1.05 , 5.06]
Total (95% CI)		**491**		**508**	**100.0%**	**1.47 [0.71 , 3.06]**
Total events:	62		50			

Heterogeneity: Tau² = 0.26; Chi² = 7.22, df = 4 (P = 0.12); I² = 45%
Test for overall effect: Z = 1.04 (P = 0.30)
Test for subgroup differences: Not applicable



Comparison 2. COX inhibitors vs placebo or no treatment

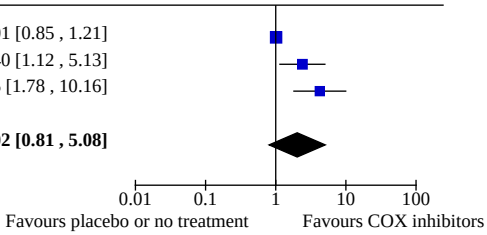
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Delay in birth by 48 hours	3	113	Risk Ratio (IV, Random, 95% CI)	2.02 [0.81, 5.08]
2.2 Delay in birth by 7 days	2	83	Risk Ratio (IV, Random, 95% CI)	2.05 [0.41, 10.33]
2.3 Neonatal death before 28 days	3	114	Risk Ratio (IV, Random, 95% CI)	0.77 [0.22, 2.72]
2.4 Pregnancy prolongation (time from trial entry to birth in days)	1	47	Mean Difference (IV, Random, 95% CI)	-0.30 [-6.32, 5.72]
2.5 Serious adverse effects of drugs	2	67	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.6 Maternal infection	2	77	Risk Ratio (IV, Random, 95% CI)	1.46 [0.64, 3.34]
2.7 Cessation of treatment due to adverse effects	1	36	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.11 Birth before 37 weeks' gestation	1	36	Risk Ratio (IV, Random, 95% CI)	0.21 [0.07, 0.62]
2.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.17 Nausea or vomiting	1	36	Risk Ratio (IV, Random, 95% CI)	5.00 [0.26, 97.37]
2.18 Tachycardia	1	36	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.20 Maternal hypotension	1	36	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.21 Perinatal death	3	114	Risk Ratio (IV, Random, 95% CI)	0.63 [0.19, 2.09]
2.22 Stillbirth	3	114	Risk Ratio (IV, Random, 95% CI)	0.31 [0.01, 7.15]
2.23 Neonatal death before 7 days	1	31	Risk Ratio (IV, Random, 95% CI)	0.94 [0.15, 5.84]
2.24 Neurodevelopmental morbidity	1	47	Risk Ratio (IV, Random, 95% CI)	Not estimable
2.25 Gastrointestinal morbidity	2	78	Risk Ratio (IV, Random, 95% CI)	0.91 [0.25, 3.37]
2.26 Respiratory morbidity	2	78	Risk Ratio (IV, Random, 95% CI)	0.80 [0.47, 1.36]
2.27 Mean birthweight	2	67	Mean Difference (IV, Random, 95% CI)	713.61 [402.54, 1024.67]
2.28 Birthweight < 2000 g	1	36	Risk Ratio (IV, Random, 95% CI)	0.50 [0.05, 5.04]
2.29 Birthweight < 2500 g	1	36	Risk Ratio (IV, Random, 95% CI)	0.21 [0.07, 0.62]
2.30 Gestational age at birth	3	114	Mean Difference (IV, Random, 95% CI)	2.61 [-0.62, 5.84]
2.31 Neonatal infection	2	78	Risk Ratio (IV, Random, 95% CI)	0.51 [0.23, 1.14]

Analysis 2.1. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	23	25	20	22	39.3%	1.01 [0.85 , 1.21]
Niebyl 1980	12	15	5	15	31.4%	2.40 [1.12 , 5.13]
Zuckerman 1984	17	18	4	18	29.4%	4.25 [1.78 , 10.16]
Total (95% CI)		**58**		**55**	**100.0%**	**2.02 [0.81 , 5.08]**
Total events:	52		29			

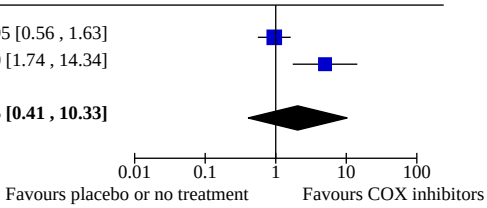
Heterogeneity: Tau² = 0.55; Chi² = 14.14, df = 2 (P = 0.0008); I² = 86%
Test for overall effect: Z = 1.50 (P = 0.13)
Test for subgroup differences: Not applicable



Analysis 2.2. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 2: Delay in birth by 7 days

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	13	25	12	22	53.9%	0.95 [0.56 , 1.63]
Zuckerman 1984	15	18	3	18	46.1%	5.00 [1.74 , 14.34]
Total (95% CI)		**43**		**40**	**100.0%**	**2.05 [0.41 , 10.33]**
Total events:	28		15			

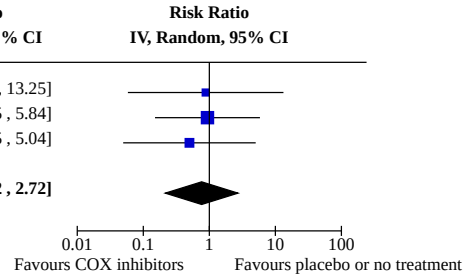
Heterogeneity: Tau² = 1.19; Chi² = 7.55, df = 1 (P = 0.006); I² = 87%
Test for overall effect: Z = 0.87 (P = 0.39)
Test for subgroup differences: Not applicable



Analysis 2.3. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 3: Neonatal death before 28 days

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	1	25	1	22	21.8%	0.88 [0.06 , 13.25]
Niebyl 1980	2	16	2	15	48.0%	0.94 [0.15 , 5.84]
Zuckerman 1984	1	18	2	18	30.1%	0.50 [0.05 , 5.04]
Total (95% CI)		**59**		**55**	**100.0%**	**0.77 [0.22 , 2.72]**
Total events:	4		5			

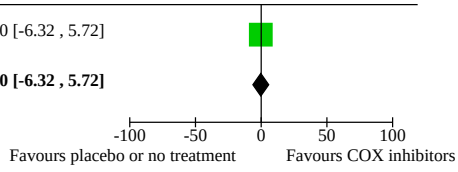
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 0.41 (P = 0.68)
Test for subgroup differences: Not applicable



Analysis 2.4. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	COX inhibitors Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ehsanipoor 2011	8	8.8	25	8.3	11.8	22	100.0%	-0.30 [-6.32 , 5.72]
Total (95% CI)			**25**			**22**	**100.0%**	**-0.30 [-6.32 , 5.72]**

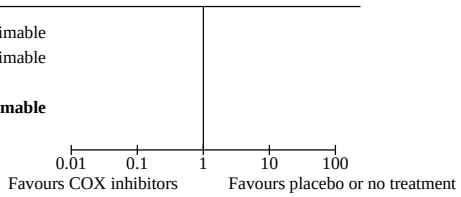
Heterogeneity: Not applicable
Test for overall effect: Z = 0.10 (P = 0.92)
Test for subgroup differences: Not applicable



Analysis 2.5. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Niebyl 1980	0	16	0	15		Not estimable
Zuckerman 1984	0	18	0	18		Not estimable
Total (95% CI)		**34**		**33**		**Not estimable**
Total events:	0		0			

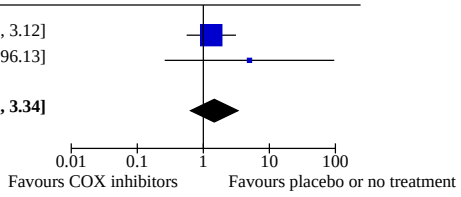
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.6. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	9	25	6	22	92.2%	1.32 [0.56 , 3.12]
Niebyl 1980	2	15	0	15	7.8%	5.00 [0.26 , 96.13]
Total (95% CI)		**40**		**37**	**100.0%**	**1.46 [0.64 , 3.34]**
Total events:	11		6			

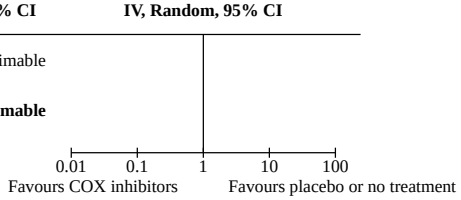
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.72$, df = 1 (P = 0.40); $I^2 = 0\%$
Test for overall effect: Z = 0.91 (P = 0.37)
Test for subgroup differences: Not applicable



Analysis 2.7. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Zuckerman 1984	0	18	0	18		Not estimable
Total (95% CI)		**18**		**18**		**Not estimable**
Total events:	0		0			

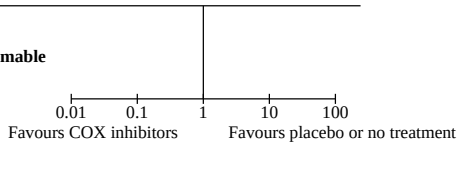
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.8. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

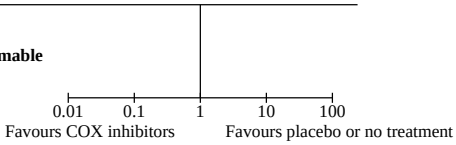
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.9. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

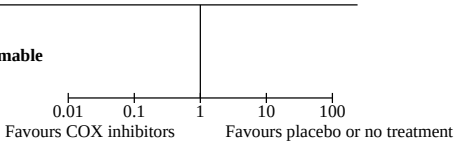
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.10. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

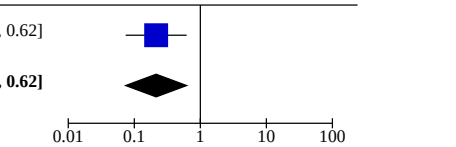
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.11. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Zuckerman 1984	3	18	14	18	100.0%	0.21 [0.07 , 0.62]
Total (95% CI)		**18**		**18**	**100.0%**	**0.21 [0.07 , 0.62]**
Total events:	3		14			

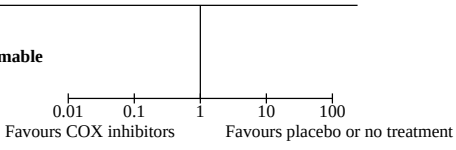
Heterogeneity: Not applicable
Test for overall effect: Z = 2.84 (P = 0.004)
Test for subgroup differences: Not applicable



Analysis 2.12. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

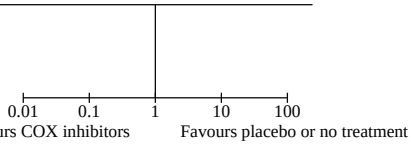
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.13. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 13: Pulmonary oedema

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

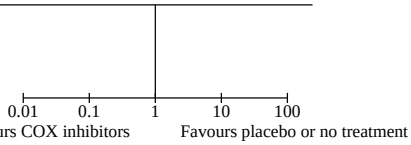
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.14. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

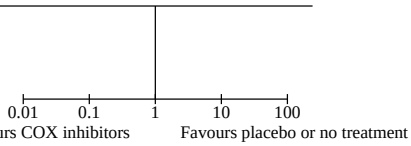
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.15. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

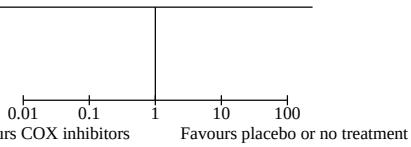
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.16. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 16: Headaches

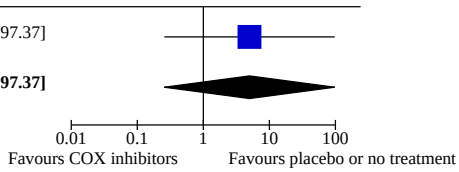
Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



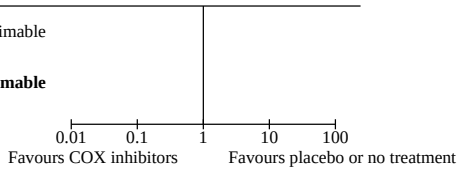
Analysis 2.17. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 17: Nausea or vomiting

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Zuckerman 1984	2	18	0	18	100.0%	5.00 [0.26 , 97.37]
Total (95% CI)		**18**		**18**	**100.0%**	**5.00 [0.26 , 97.37]**
Total events:	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
Test for subgroup differences: Not applicable						



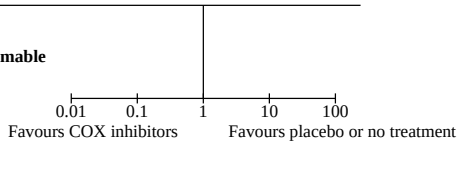
Analysis 2.18. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 18: Tachycardia

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Zuckerman 1984	0	18	0	18		Not estimable
Total (95% CI)		**18**		**18**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



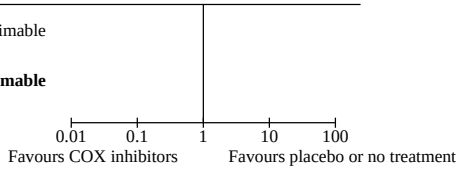
Analysis 2.19. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 2.20. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 20: Maternal hypotension

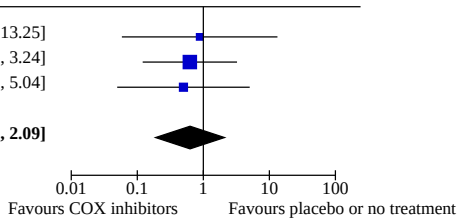
Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Zuckerman 1984	0	18	0	18		Not estimable
Total (95% CI)		**18**		**18**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 2.21. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 21: Perinatal death

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	1	25	1	22	19.6%	0.88 [0.06 , 13.25]
Niebyl 1980	2	16	3	15	53.3%	0.63 [0.12 , 3.24]
Zuckerman 1984	1	18	2	18	27.0%	0.50 [0.05 , 5.04]
Total (95% CI)		**59**		**55**	**100.0%**	**0.63 [0.19 , 2.09]**
Total events:	4		6			

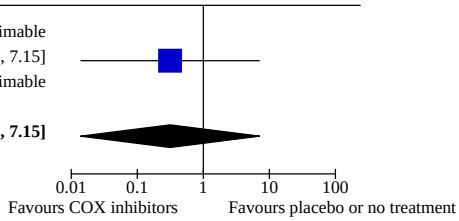
Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 2 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.76 (P = 0.45)
Test for subgroup differences: Not applicable



Analysis 2.22. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 22: Stillbirth

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	0	25	0	22		Not estimable
Niebyl 1980	0	16	1	15	100.0%	0.31 [0.01 , 7.15]
Zuckerman 1984	0	18	0	18		Not estimable
Total (95% CI)		**59**		**55**	**100.0%**	**0.31 [0.01 , 7.15]**
Total events:	0		1			

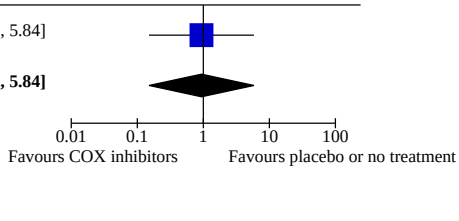
Heterogeneity: Not applicable
Test for overall effect: Z = 0.73 (P = 0.47)
Test for subgroup differences: Not applicable



Analysis 2.23. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 23: Neonatal death before 7 days

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Niebyl 1980	2	16	2	15	100.0%	0.94 [0.15 , 5.84]
Total (95% CI)		**16**		**15**	**100.0%**	**0.94 [0.15 , 5.84]**
Total events:	2		2			

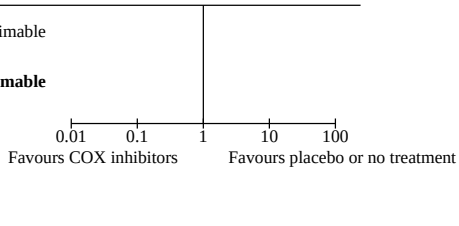
Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.94)
Test for subgroup differences: Not applicable



Analysis 2.24. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	0	25	0	22		Not estimable
Total (95% CI)		**25**		**22**		**Not estimable**
Total events:	0		0			

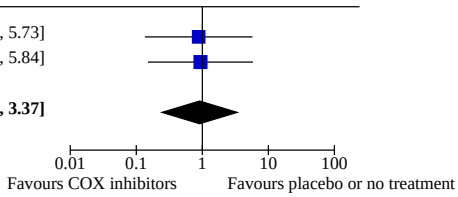
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.25. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	2	25	2	22	48.8%	0.88 [0.14 , 5.73]
Niebyl 1980	2	16	2	15	51.2%	0.94 [0.15 , 5.84]
Total (95% CI)		**41**		**37**	**100.0%**	**0.91 [0.25 , 3.37]**
Total events:	4		4			

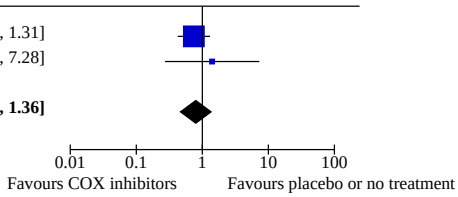
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.14 (P = 0.89)
Test for subgroup differences: Not applicable



Analysis 2.26. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 26: Respiratory morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	11	25	13	22	89.5%	0.74 [0.42 , 1.31]
Niebyl 1980	3	16	2	15	10.5%	1.41 [0.27 , 7.28]
Total (95% CI)		**41**		**37**	**100.0%**	**0.80 [0.47 , 1.36]**
Total events:	14		15			

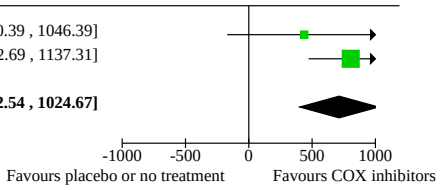
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 1 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.84 (P = 0.40)
Test for subgroup differences: Not applicable



Analysis 2.27. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 27: Mean birthweight

Study or Subgroup	COX inhibitors Mean	COX inhibitors SD	COX inhibitors Total	Placebo or no treatment Mean	Placebo or no treatment SD	Placebo or no treatment Total	Weight	Mean Difference IV, Random, 95% CI
Niebyl 1980	2358	876	16	1920	852	15	24.9%	438.00 [-170.39 , 1046.39]
Zuckerman 1984	2833	496	18	2028	521	18	75.1%	805.00 [472.69 , 1137.31]
Total (95% CI)			**34**			**33**	**100.0%**	**713.61 [402.54 , 1024.67]**

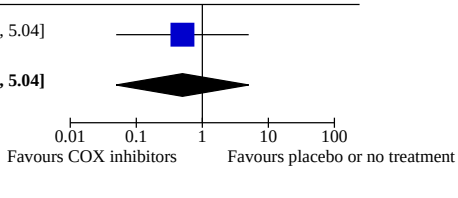
Heterogeneity: Tau² = 4793.39; Chi² = 1.08, df = 1 (P = 0.30); I² = 7%
Test for overall effect: Z = 4.50 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 2.28. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 28: Birthweight < 2000 g

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Zuckerman 1984	1	18	2	18	100.0%	0.50 [0.05 , 5.04]
Total (95% CI)		**18**		**18**	**100.0%**	**0.50 [0.05 , 5.04]**
Total events:	1		2			

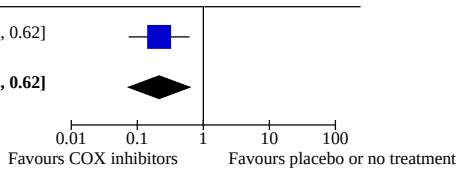
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)
Test for subgroup differences: Not applicable



Analysis 2.29. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 29: Birthweight < 2500 g

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Zuckerman 1984	3	18	14	18	100.0%	0.21 [0.07 , 0.62]
Total (95% CI)		**18**		**18**	**100.0%**	**0.21 [0.07 , 0.62]**
Total events:	3		14			

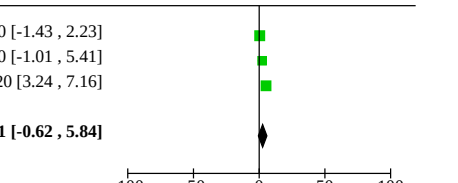
Heterogeneity: Not applicable
Test for overall effect: Z = 2.84 (P = 0.004)
Test for subgroup differences: Not applicable



Analysis 2.30. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 30: Gestational age at birth

Study or Subgroup	COX inhibitors Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ehsanipoor 2011	31	2.8	25	30.6	3.5	22	35.8%	0.40 [-1.43 , 2.23]
Niebyl 1980	35.2	4.4	16	33	4.7	15	28.9%	2.20 [-1.01 , 5.41]
Zuckerman 1984	36.4	3	18	31.2	3	18	35.2%	5.20 [3.24 , 7.16]
Total (95% CI)			**59**			**55**	**100.0%**	**2.61 [-0.62 , 5.84]**

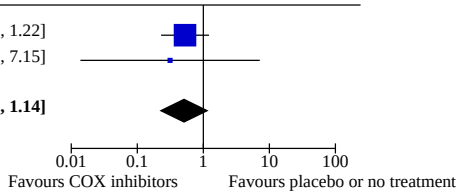
Heterogeneity: Tau² = 6.71; Chi² = 12.38, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 1.58 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 2.31. Comparison 2: COX inhibitors vs placebo or no treatment, Outcome 31: Neonatal infection

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ehsanipoor 2011	6	25	10	22	93.4%	0.53 [0.23 , 1.22]
Niebyl 1980	0	16	1	15	6.6%	0.31 [0.01 , 7.15]
Total (95% CI)		**41**		**37**	**100.0%**	**0.51 [0.23 , 1.14]**
Total events:	6		11			

Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 1 (P = 0.75); I² = 0%
Test for overall effect: Z = 1.64 (P = 0.10)
Test for subgroup differences: Not applicable



Comparison 3. Calcium channel blockers vs placebo or no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Delay in birth by 48 hours	4	311	Risk Ratio (IV, Random, 95% CI)	1.87 [1.06, 3.28]
3.2 Delay in birth by 7 days	5	384	Risk Ratio (IV, Random, 95% CI)	1.25 [0.86, 1.82]
3.3 Neonatal death before 28 days	2	143	Risk Ratio (IV, Random, 95% CI)	5.18 [0.26, 103.15]
3.4 Pregnancy prolongation (time from trial entry to birth in days)	2	138	Mean Difference (IV, Random, 95% CI)	4.71 [0.32, 9.10]
3.5 Serious adverse effects of drugs	1	50	Risk Ratio (IV, Random, 95% CI)	Not estimable

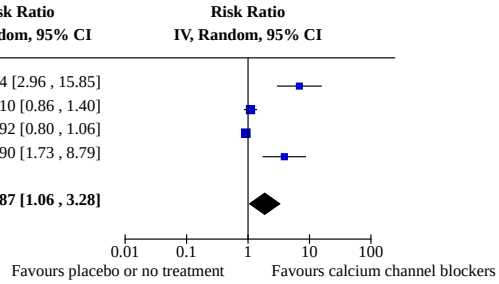
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.7 Cessation of treatment due to adverse effects	3	211	Risk Ratio (IV, Random, 95% CI)	1.13 [0.67, 1.88]
3.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.10 Birth before 34 weeks' gestation	1	73	Risk Ratio (IV, Random, 95% CI)	5.84 [0.74, 46.11]
3.11 Birth before 37 weeks' gestation	4	334	Risk Ratio (IV, Random, 95% CI)	0.98 [0.71, 1.35]
3.12 Maternal death	1	50	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.16 Headaches	2	162	Risk Ratio (IV, Random, 95% CI)	2.92 [0.29, 28.90]
3.17 Nausea or vomiting	1	73	Risk Ratio (IV, Random, 95% CI)	0.78 [0.23, 2.67]
3.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.21 Perinatal death	3	216	Risk Ratio (IV, Random, 95% CI)	5.02 [0.60, 41.80]
3.22 Stillbirth	1	88	Risk Ratio (IV, Random, 95% CI)	Not estimable
3.23 Neonatal death before 7 days	2	143	Risk Ratio (IV, Random, 95% CI)	5.18 [0.26, 103.15]
3.24 Neurodevelopmental morbidity	2	128	Risk Ratio (IV, Random, 95% CI)	3.11 [0.13, 73.11]
3.25 Gastrointestinal morbidity	2	128	Risk Ratio (IV, Random, 95% CI)	5.98 [0.74, 48.42]
3.26 Respiratory morbidity	2	128	Risk Ratio (IV, Random, 95% CI)	0.66 [0.01, 31.39]
3.27 Mean birthweight	3	216	Mean Difference (IV, Random, 95% CI)	19.52 [-258.79, 297.82]
3.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.29 Birthweight < 2500 g	1	88	Risk Ratio (IV, Random, 95% CI)	0.96 [0.60, 1.54]
3.30 Gestational age at birth	3	211	Mean Difference (IV, Random, 95% CI)	-0.01 [-1.64, 1.62]
3.31 Neonatal infection	2	128	Risk Ratio (IV, Random, 95% CI)	0.98 [0.39, 2.45]

Analysis 3.1. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ara 2008	35	45	5	44	18.8%	6.84 [2.96 , 15.85]
Hawkins 2019	36	46	30	42	30.4%	1.10 [0.86 , 1.40]
Nijman 2016	23	25	25	25	31.6%	0.92 [0.80 , 1.06]
Zhang 2002	39	56	5	28	19.3%	3.90 [1.73 , 8.79]
Total (95% CI)		**172**		**139**	**100.0%**	**1.87 [1.06 , 3.28]**
Total events:	133		65			

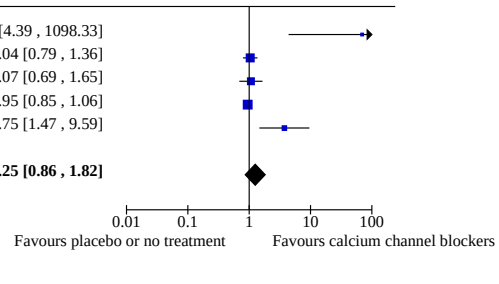
Heterogeneity: Tau² = 0.26; Chi² = 32.63, df = 3 (P < 0.00001); I² = 91%
Test for overall effect: Z = 2.18 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 3.2. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ara 2008	35	45	0	44	1.8%	69.46 [4.39 , 1098.33]
Hawkins 2019	33	46	29	42	29.6%	1.04 [0.79 , 1.36]
Nijman 2016	16	25	15	25	23.8%	1.07 [0.69 , 1.65]
Vis 2014	34	37	35	36	34.0%	0.95 [0.85 , 1.06]
Zhang 2002	30	56	4	28	10.9%	3.75 [1.47 , 9.59]
Total (95% CI)		**209**		**175**	**100.0%**	**1.25 [0.86 , 1.82]**
Total events:	148		83			

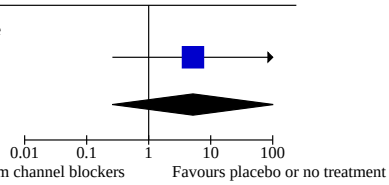
Heterogeneity: Tau² = 0.10; Chi² = 17.72, df = 4 (P = 0.001); I² = 77%
Test for overall effect: Z = 1.18 (P = 0.24)
Test for subgroup differences: Not applicable



Analysis 3.3. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hawkins 2019	0	46	0	42		Not estimable
Nijman 2016	2	27	0	28	100.0%	5.18 [0.26 , 103.15]
Total (95% CI)		**73**		**70**	**100.0%**	**5.18 [0.26 , 103.15]**
Total events:	2		0			

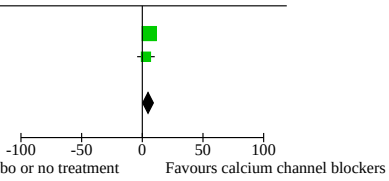
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 3.4. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Hawkins 2019	36.7	13.4	46	31	13	42	63.3%	5.70 [0.18 , 11.22]
Nijman 2016	11	11.1	25	8	14.8	25	36.7%	3.00 [-4.25 , 10.25]
Total (95% CI)			**71**			**67**	**100.0%**	**4.71 [0.32 , 9.10]**

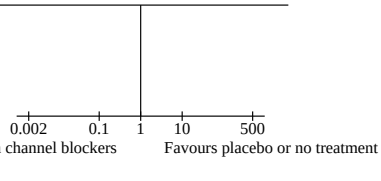
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.10 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 3.5. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Nijman 2016	0	25	0	25		Not estimable
Total (95% CI)		**25**		**25**		**Not estimable**
Total events:	0		0			

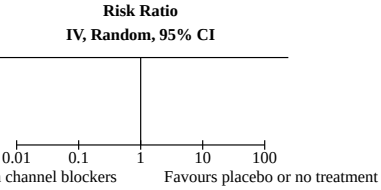
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.6. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 6: Maternal infection

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

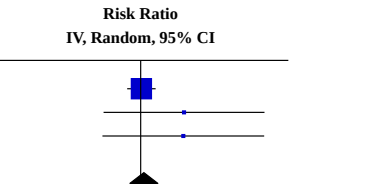
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.7. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hawkins 2019	18	46	16	42	94.2%	1.03 [0.61 , 1.74]
Nijman 2016	2	25	0	25	2.9%	5.00 [0.25 , 99.16]
Vis 2014	2	37	0	36	2.9%	4.87 [0.24 , 98.02]
Total (95% CI)		**108**		**103**	**100.0%**	**1.13 [0.67 , 1.88]**
Total events:	22		16			

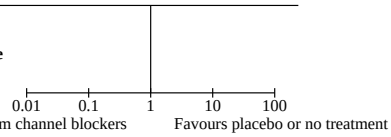
Heterogeneity: Tau² = 0.00; Chi² = 1.99, df = 2 (P = 0.37); I² = 0%
Test for overall effect: Z = 0.45 (P = 0.65)
Test for subgroup differences: Not applicable



Analysis 3.8. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

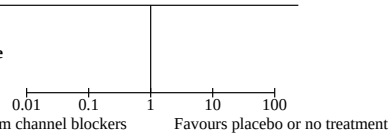
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.9. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

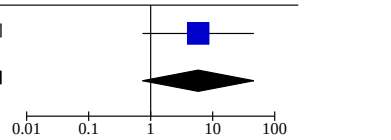
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.10. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Vis 2014	6	37	1	36	100.0%	5.84 [0.74 , 46.11]
Total (95% CI)		**37**		**36**	**100.0%**	**5.84 [0.74 , 46.11]**
Total events:	6		1			

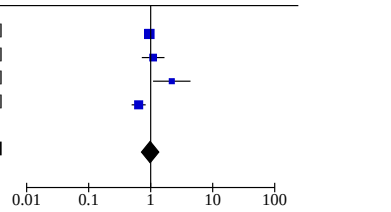
Heterogeneity: Not applicable
Test for overall effect: Z = 1.67 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 3.11. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ara 2008	43	45	44	44	35.3%	0.96 [0.89 , 1.03]
Hawkins 2019	24	46	20	42	22.2%	1.10 [0.72 , 1.67]
Vis 2014	18	37	8	36	13.4%	2.19 [1.09 , 4.39]
Zhang 2002	32	56	25	28	29.1%	0.64 [0.49 , 0.83]
Total (95% CI)		**184**		**150**	**100.0%**	**0.98 [0.71 , 1.35]**
Total events:	117		97			

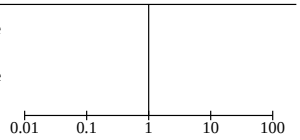
Heterogeneity: Tau² = 0.07; Chi² = 14.75, df = 3 (P = 0.002); I² = 80%
Test for overall effect: Z = 0.12 (P = 0.90)
Test for subgroup differences: Not applicable



Analysis 3.12. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 12: Maternal death

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Nijman 2016	0	25	0	25		Not estimable	
Total (95% CI)		**25**		**25**		**Not estimable**	
Total events:	0		0				

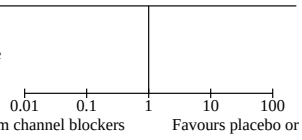
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.13. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 13: Pulmonary oedema

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

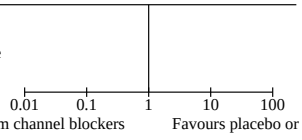
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.14. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 14: Dyspnoea

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

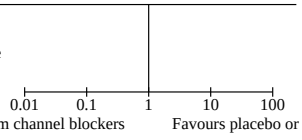
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.15. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 15: Palpitations

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

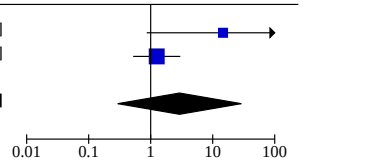
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.16. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 16: Headaches

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ara 2008	7	45	0	44	34.4%	14.67 [0.86 , 249.42]
Vis 2014	9	37	7	36	65.6%	1.25 [0.52 , 3.00]
Total (95% CI)		**82**		**80**	**100.0%**	**2.92 [0.29 , 28.90]**
Total events:	16		7			

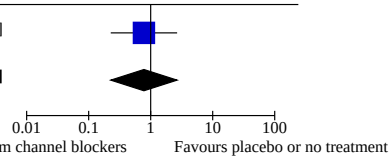
Heterogeneity: Tau² = 1.89; Chi² = 2.65, df = 1 (P = 0.10); I² = 62%
Test for overall effect: Z = 0.92 (P = 0.36)
Test for subgroup differences: Not applicable



Analysis 3.17. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 17: Nausea or vomiting

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Vis 2014	4	37	5	36	100.0%	0.78 [0.23 , 2.67]
Total (95% CI)		**37**		**36**	**100.0%**	**0.78 [0.23 , 2.67]**
Total events:	4		5			

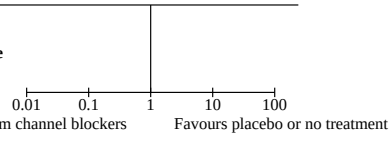
Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)
Test for subgroup differences: Not applicable



Analysis 3.18. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 18: Tachycardia

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

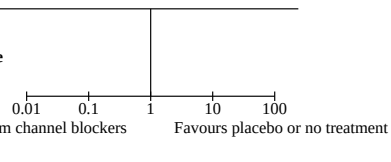
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.19. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

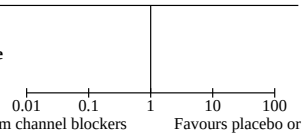
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.20. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 20: Maternal hypotension

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

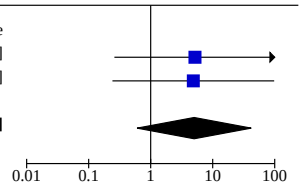
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.21. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 21: Perinatal death

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hawkins 2019	0	46	0	42		Not estimable
Nijman 2016	2	27	0	28	50.2%	5.18 [0.26 , 103.15]
Vis 2014	2	37	0	36	49.8%	4.87 [0.24 , 98.02]
Total (95% CI)		**110**		**106**	**100.0%**	**5.02 [0.60 , 41.80]**
Total events:	4		0			

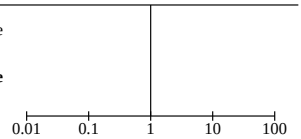
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1 (P = 0.98); $I^2 = 0\%$
Test for overall effect: Z = 1.49 (P = 0.14)
Test for subgroup differences: Not applicable



Analysis 3.22. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 22: Stillbirth

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hawkins 2019	0	46	0	42		Not estimable
Total (95% CI)		**46**		**42**		**Not estimable**
Total events:	0		0			

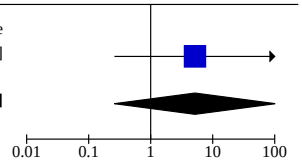
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.23. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hawkins 2019	0	46	0	42		Not estimable
Nijman 2016	2	27	0	28	100.0%	5.18 [0.26 , 103.15]
Total (95% CI)		**73**		**70**	**100.0%**	**5.18 [0.26 , 103.15]**
Total events:	2		0			

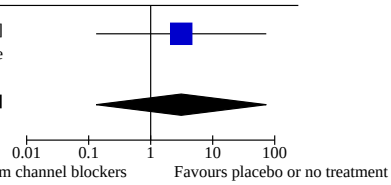
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 3.24. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Nijman 2016	1	27	0	28	100.0%	3.11 [0.13 , 73.11]
Vis 2014	0	37	0	36		Not estimable
Total (95% CI)		**64**		**64**	**100.0%**	**3.11 [0.13 , 73.11]**
Total events:	1		0			

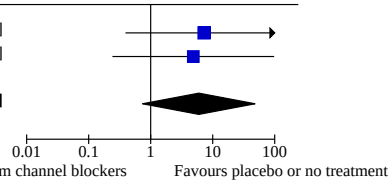
Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.48)
Test for subgroup differences: Not applicable



Analysis 3.25. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Nijman 2016	3	27	0	28	51.4%	7.25 [0.39 , 134.07]
Vis 2014	2	37	0	36	48.6%	4.87 [0.24 , 98.02]
Total (95% CI)		**64**		**64**	**100.0%**	**5.98 [0.74 , 48.42]**
Total events:	5		0			

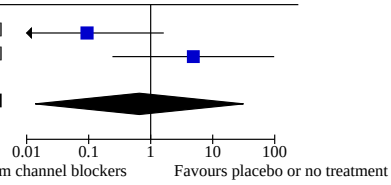
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.85); I² = 0%
Test for overall effect: Z = 1.67 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 3.26. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 26: Respiratory morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Nijman 2016	0	27	5	28	50.8%	0.09 [0.01 , 1.62]
Vis 2014	2	37	0	36	49.2%	4.87 [0.24 , 98.02]
Total (95% CI)		**64**		**64**	**100.0%**	**0.66 [0.01 , 31.39]**
Total events:	2		5			

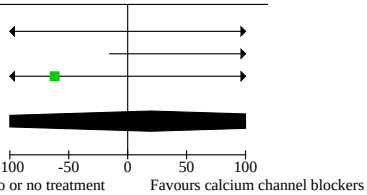
Heterogeneity: Tau² = 5.55; Chi² = 3.49, df = 1 (P = 0.06); I² = 71%
Test for overall effect: Z = 0.21 (P = 0.83)
Test for subgroup differences: Not applicable



Analysis 3.27. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 27: Mean birthweight

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Hawkins 2019	2585	612	46	2759	849	42	33.1%	-174.00 [-485.78 , 137.78]
Nijman 2016	1745	497	27	1424	755	28	31.0%	321.00 [-15.67 , 657.67]
Vis 2014	2750	626	37	2812	597	36	35.9%	-62.00 [-342.57 , 218.57]
Total (95% CI)			**110**			**106**	**100.0%**	**19.52 [-258.79 , 297.82]**

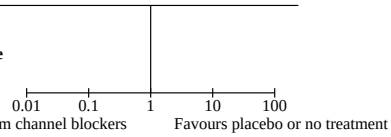
Heterogeneity: Tau² = 35611.98; Chi² = 4.87, df = 2 (P = 0.09); I² = 59%
Test for overall effect: Z = 0.14 (P = 0.89)
Test for subgroup differences: Not applicable



Analysis 3.28. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

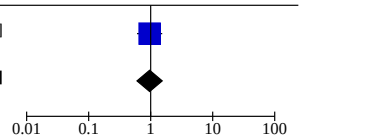
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 3.29. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hawkins 2019	20	46	19	42	100.0%	0.96 [0.60 , 1.54]
Total (95% CI)		**46**		**42**	**100.0%**	**0.96 [0.60 , 1.54]**
Total events:	20		19			

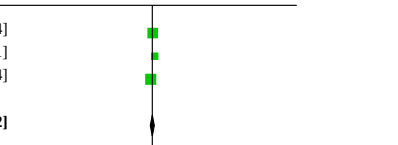
Heterogeneity: Not applicable
Test for overall effect: Z = 0.17 (P = 0.87)
Test for subgroup differences: Not applicable



Analysis 3.30. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 30: Gestational age at birth

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Hawkins 2019	36	3	46	35.7	3.4	42	38.4%	0.30 [-1.04 , 1.64]
Nijman 2016	32	4.2	25	30	5.8	25	20.5%	2.00 [-0.81 , 4.81]
Vis 2014	37	2.9	37	38.3	2.1	36	41.1%	-1.30 [-2.46 , -0.14]
Total (95% CI)			**108**			**103**	**100.0%**	**-0.01 [-1.64 , 1.62]**

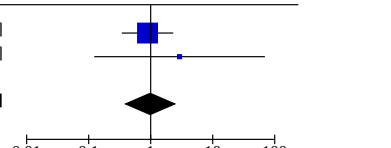
Heterogeneity: Tau² = 1.34; Chi² = 6.16, df = 2 (P = 0.05); I² = 68%
Test for overall effect: Z = 0.01 (P = 0.99)
Test for subgroup differences: Not applicable



Analysis 3.31. Comparison 3: Calcium channel blockers vs placebo or no treatment, Outcome 31: Neonatal infection

Study or Subgroup	Calcium channel blockers Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Nijman 2016	6	27	7	28	91.7%	0.89 [0.34 , 2.31]
Vis 2014	1	37	0	36	8.3%	2.92 [0.12 , 69.43]
Total (95% CI)		**64**		**64**	**100.0%**	**0.98 [0.39 , 2.45]**
Total events:	7		7			

Heterogeneity: Tau² = 0.00; Chi² = 0.50, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.04 (P = 0.97)
Test for subgroup differences: Not applicable

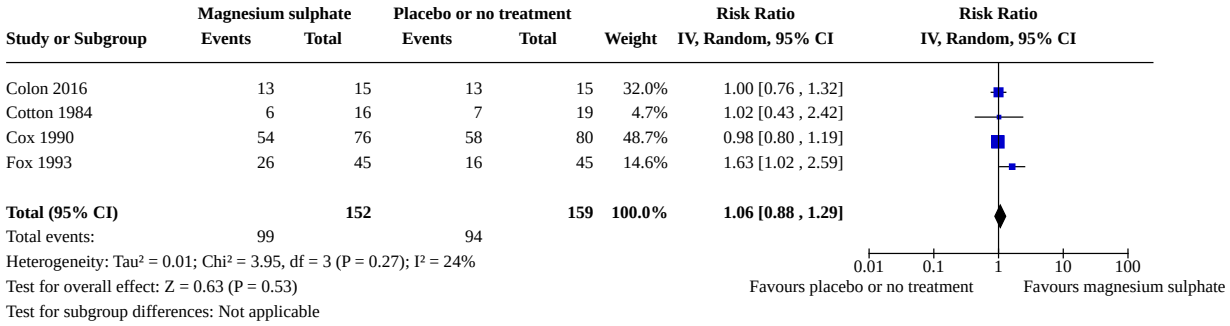


Comparison 4. Magnesium sulphate vs placebo or no treatment

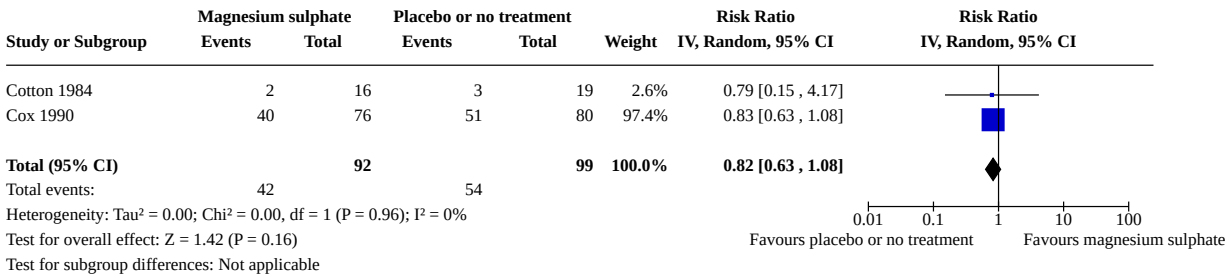
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Delay in birth by 48 hours	4	311	Risk Ratio (IV, Random, 95% CI)	1.06 [0.88, 1.29]
4.2 Delay in birth by 7 days	2	191	Risk Ratio (IV, Random, 95% CI)	0.82 [0.63, 1.08]
4.3 Neonatal death before 28 days	5	473	Risk Ratio (IV, Random, 95% CI)	0.89 [0.15, 5.09]
4.4 Pregnancy prolongation (time from trial entry to birth in days)	4	310	Mean Difference (IV, Random, 95% CI)	0.33 [-3.39, 4.04]
4.5 Serious adverse effects of drugs	2	120	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.6 Maternal infection	1	35	Risk Ratio (IV, Random, 95% CI)	2.38 [0.24, 23.84]
4.7 Cessation of treatment due to adverse effects	3	281	Risk Ratio (IV, Random, 95% CI)	9.82 [1.25, 77.31]
4.8 Birth before 28 weeks' gestation	1	145	Risk Ratio (IV, Random, 95% CI)	1.10 [0.60, 2.05]
4.9 Birth before 32 weeks' gestation	2	301	Risk Ratio (IV, Random, 95% CI)	1.14 [0.92, 1.43]
4.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.11 Birth before 37 weeks' gestation	1	35	Risk Ratio (IV, Random, 95% CI)	0.79 [0.15, 4.17]
4.12 Maternal death	1	35	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.13 Pulmonary oedema	2	65	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.16 Headaches	1	30	Risk Ratio (IV, Random, 95% CI)	3.00 [0.13, 68.26]
4.17 Nausea or vomiting	1	30	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.18 Tachycardia	1	35	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.20 Maternal hypotension	1	156	Risk Ratio (IV, Random, 95% CI)	3.16 [0.13, 76.30]
4.21 Perinatal death	5	476	Risk Ratio (IV, Random, 95% CI)	1.07 [0.16, 7.15]
4.22 Stillbirth	3	410	Risk Ratio (IV, Random, 95% CI)	5.70 [0.28, 116.87]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.23 Neonatal death before 7 days	3	351	Risk Ratio (IV, Random, 95% CI)	2.37 [0.43, 13.01]
4.24 Neurodevelopmental morbidity	4	445	Risk Ratio (IV, Random, 95% CI)	0.63 [0.20, 1.96]
4.25 Gastrointestinal morbidity	4	445	Risk Ratio (IV, Random, 95% CI)	0.90 [0.39, 2.12]
4.26 Respiratory morbidity	5	475	Risk Ratio (IV, Random, 95% CI)	1.10 [0.68, 1.78]
4.27 Mean birthweight	5	475	Mean Difference (IV, Random, 95% CI)	12.65 [-99.04, 124.35]
4.28 Birthweight < 2000 g	2	191	Risk Ratio (IV, Random, 95% CI)	1.08 [0.82, 1.41]
4.29 Birthweight < 2500 g	2	202	Risk Ratio (IV, Random, 95% CI)	0.95 [0.83, 1.09]
4.30 Gestational age at birth	5	456	Mean Difference (IV, Random, 95% CI)	-0.61 [-1.35, 0.12]
4.31 Neonatal infection	3	219	Risk Ratio (IV, Random, 95% CI)	0.74 [0.26, 2.15]

Analysis 4.1. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 1: Delay in birth by 48 hours



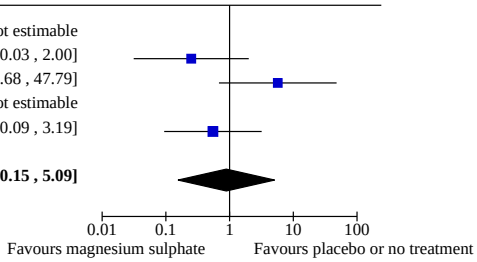
Analysis 4.2. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 2: Delay in birth by 7 days



Analysis 4.3. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	0	17	0	14		Not estimable
Cotton 1984	1	16	4	16	32.0%	0.25 [0.03 , 2.00]
Cox 1990	5	78	1	89	31.3%	5.71 [0.68 , 47.79]
Fox 1993	0	45	0	45		Not estimable
How 1998	2	84	3	69	36.7%	0.55 [0.09 , 3.19]
Total (95% CI)		**240**		**233**	**100.0%**	**0.89 [0.15 , 5.09]**
Total events:	8		8			

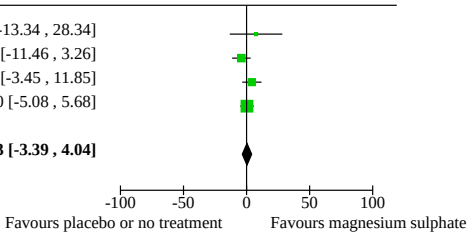
Heterogeneity: Tau² = 1.36; Chi² = 4.65, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 0.13 (P = 0.89)
Test for subgroup differences: Not applicable



Analysis 4.4. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Magnesium sulphate Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Colon 2016	53	28.2	15	45.5	30.02	15	3.2%	7.50 [-13.34 , 28.34]
Cotton 1984	3	6	15	7.1	14.9	19	25.5%	-4.10 [-11.46 , 3.26]
Cox 1990	26.6	26.1	76	22.4	22.4	80	23.6%	4.20 [-3.45 , 11.85]
Fox 1993	15.7	12.5	45	15.4	13.5	45	47.7%	0.30 [-5.08 , 5.68]
Total (95% CI)			**151**			**159**	**100.0%**	**0.33 [-3.39 , 4.04]**

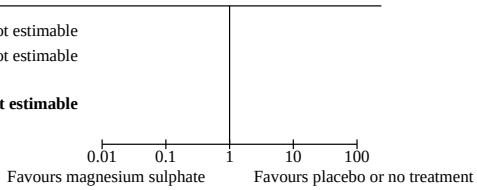
Heterogeneity: Tau² = 0.00; Chi² = 2.83, df = 3 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.86)
Test for subgroup differences: Not applicable



Analysis 4.5. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	0	15	0	15		Not estimable
Fox 1993	0	45	0	45		Not estimable
Total (95% CI)		**60**		**60**		**Not estimable**
Total events:	0		0			

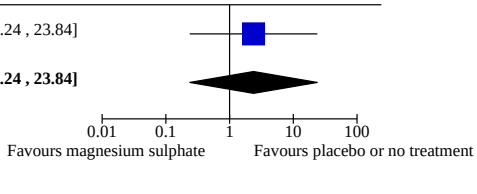
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.6. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 6: Maternal infection

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	16	1	19	100.0%	2.38 [0.24 , 23.84]
Total (95% CI)		**16**		**19**	**100.0%**	**2.38 [0.24 , 23.84]**
Total events:	2		1			

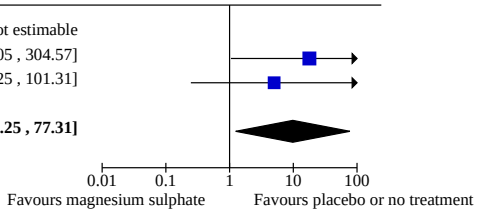
Heterogeneity: Not applicable
Test for overall effect: Z = 0.74 (P = 0.46)
Test for subgroup differences: Not applicable



Analysis 4.7. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	0	16	0	19		Not estimable
Cox 1990	8	76	0	80	53.0%	17.88 [1.05 , 304.57]
Fox 1993	2	45	0	45	47.0%	5.00 [0.25 , 101.31]
Total (95% CI)		**137**		**144**	**100.0%**	**9.82 [1.25 , 77.31]**
Total events:	10		0			

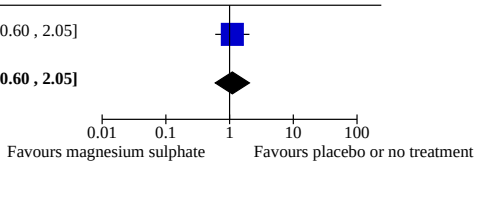
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 2.17 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 4.8. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
How 1998	18	78	14	67	100.0%	1.10 [0.60 , 2.05]
Total (95% CI)		**78**		**67**	**100.0%**	**1.10 [0.60 , 2.05]**
Total events:	18		14			

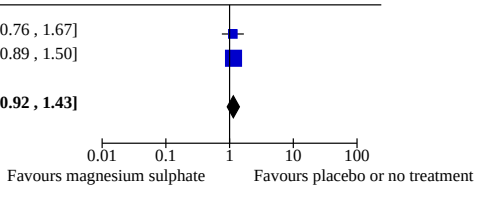
Heterogeneity: Not applicable
Test for overall effect: Z = 0.32 (P = 0.75)
Test for subgroup differences: Not applicable



Analysis 4.9. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cox 1990	31	76	29	80	30.7%	1.13 [0.76 , 1.67]
How 1998	51	78	38	67	69.3%	1.15 [0.89 , 1.50]
Total (95% CI)		**154**		**147**	**100.0%**	**1.14 [0.92 , 1.43]**
Total events:	82		67			

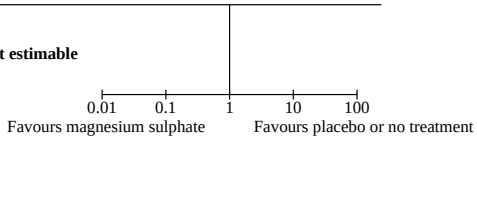
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.92); I² = 0%
Test for overall effect: Z = 1.20 (P = 0.23)
Test for subgroup differences: Not applicable



Analysis 4.10. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

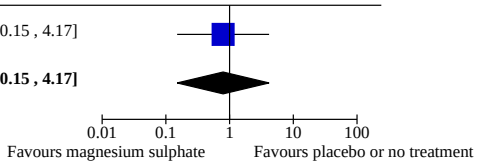
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.11. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	16	3	19	100.0%	0.79 [0.15 , 4.17]
Total (95% CI)		**16**		**19**	**100.0%**	**0.79 [0.15 , 4.17]**
Total events:	2		3			

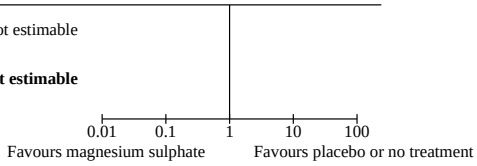
Heterogeneity: Not applicable
Test for overall effect: Z = 0.28 (P = 0.78)
Test for subgroup differences: Not applicable



Analysis 4.12. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 12: Maternal death

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	0	16	0	19		Not estimable
Total (95% CI)		**16**		**19**		**Not estimable**
Total events:	0		0			

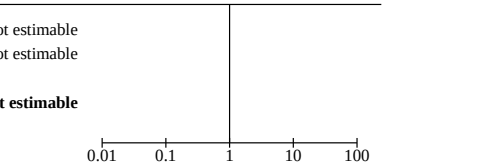
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.13. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 13: Pulmonary oedema

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	0	15	0	15		Not estimable
Cotton 1984	0	16	0	19		Not estimable
Total (95% CI)		**31**		**34**		**Not estimable**
Total events:	0		0			

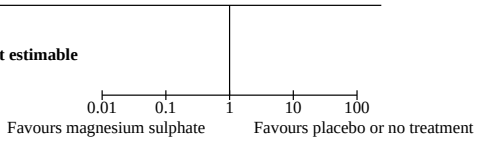
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.14. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 14: Dyspnoea

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

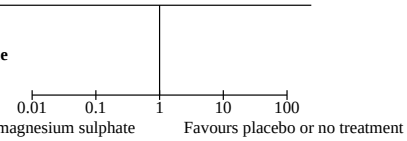
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.15. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 15: Palpitations

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

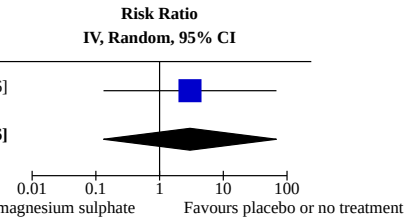
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.16. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 16: Headaches

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	1	15	0	15	100.0%	3.00 [0.13 , 68.26]
Total (95% CI)		**15**		**15**	**100.0%**	**3.00 [0.13 , 68.26]**
Total events:	1		0			

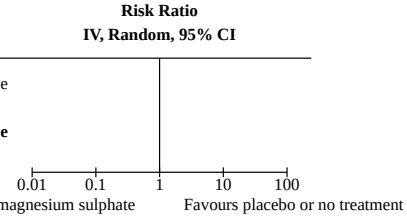
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 4.17. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 17: Nausea or vomiting

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	0	15	0	15		Not estimable
Total (95% CI)		**15**		**15**		**Not estimable**
Total events:	0		0			

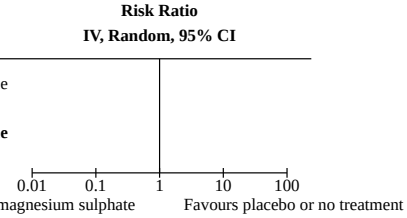
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.18. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 18: Tachycardia

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	0	16	0	19		Not estimable
Total (95% CI)		**16**		**19**		**Not estimable**
Total events:	0		0			

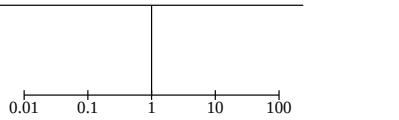
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.19. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

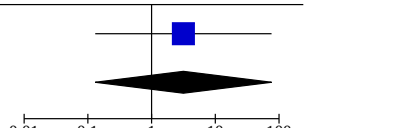
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 4.20. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 20: Maternal hypotension

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cox 1990	1	76	0	80	100.0%	3.16 [0.13 , 76.30]
Total (95% CI)		**76**		**80**	**100.0%**	**3.16 [0.13 , 76.30]**
Total events:	1		0			

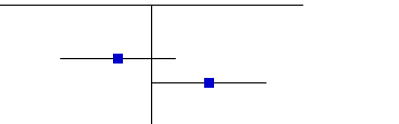
Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)
Test for subgroup differences: Not applicable



Analysis 4.21. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 21: Perinatal death

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	0	17	0	14		Not estimable
Cotton 1984	1	16	4	19	31.9%	0.30 [0.04 , 2.40]
Cox 1990	7	78	1	89	32.1%	7.99 [1.00 , 63.49]
Fox 1993	0	45	0	45		Not estimable
How 1998	2	84	3	69	35.9%	0.55 [0.09 , 3.19]
Total (95% CI)		**240**		**236**	**100.0%**	**1.07 [0.16 , 7.15]**
Total events:	10		8			

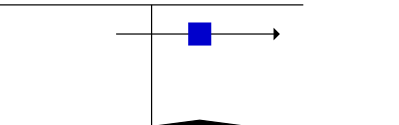
Heterogeneity: Tau² = 1.82; Chi² = 5.61, df = 2 (P = 0.06); I² = 64%
Test for overall effect: Z = 0.06 (P = 0.95)
Test for subgroup differences: Not applicable



Analysis 4.22. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 22: Stillbirth

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cox 1990	2	78	0	89	100.0%	5.70 [0.28 , 116.87]
Fox 1993	0	45	0	45		Not estimable
How 1998	0	84	0	69		Not estimable
Total (95% CI)		**207**		**203**	**100.0%**	**5.70 [0.28 , 116.87]**
Total events:	2		0			

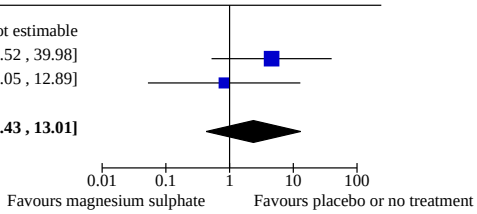
Heterogeneity: Not applicable
Test for overall effect: Z = 1.13 (P = 0.26)
Test for subgroup differences: Not applicable



Analysis 4.23. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	0	17	0	14		Not estimable
Cox 1990	4	78	1	89	61.7%	4.56 [0.52 , 39.98]
How 1998	1	84	1	69	38.3%	0.82 [0.05 , 12.89]
Total (95% CI)		**179**		**172**	**100.0%**	**2.37 [0.43 , 13.01]**
Total events:	5		2			

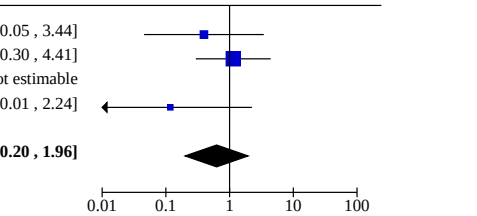
Heterogeneity: Tau² = 0.00; Chi² = 0.92, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 0.99 (P = 0.32)
Test for subgroup differences: Not applicable



Analysis 4.24. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	1	16	3	19	25.8%	0.40 [0.05 , 3.44]
Cox 1990	4	78	4	89	59.8%	1.14 [0.30 , 4.41]
Fox 1993	0	45	0	45		Not estimable
How 1998	0	84	3	69	14.4%	0.12 [0.01 , 2.24]
Total (95% CI)		**223**		**222**	**100.0%**	**0.63 [0.20 , 1.96]**
Total events:	5		10			

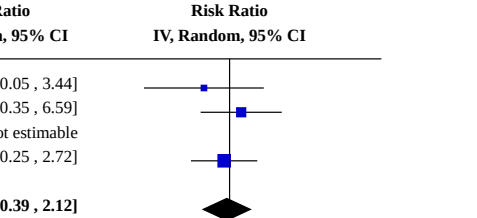
Heterogeneity: Tau² = 0.09; Chi² = 2.16, df = 2 (P = 0.34); I² = 7%
Test for overall effect: Z = 0.81 (P = 0.42)
Test for subgroup differences: Not applicable



Analysis 4.25. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	1	16	3	19	15.5%	0.40 [0.05 , 3.44]
Cox 1990	4	78	3	89	33.8%	1.52 [0.35 , 6.59]
Fox 1993	0	45	0	45		Not estimable
How 1998	5	84	5	69	50.6%	0.82 [0.25 , 2.72]
Total (95% CI)		**223**		**222**	**100.0%**	**0.90 [0.39 , 2.12]**
Total events:	10		11			

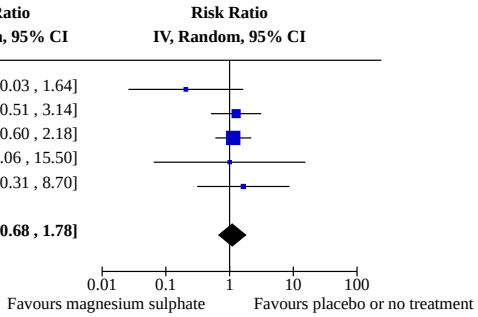
Heterogeneity: Tau² = 0.00; Chi² = 1.07, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 0.23 (P = 0.82)
Test for subgroup differences: Not applicable



Analysis 4.26. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 26: Respiratory morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	1	17	4	14	5.4%	0.21 [0.03 , 1.64]
Cotton 1984	6	15	6	19	28.1%	1.27 [0.51 , 3.14]
Cox 1990	15	78	15	89	55.1%	1.14 [0.60 , 2.18]
Fox 1993	1	45	1	45	3.1%	1.00 [0.06 , 15.50]
How 1998	4	84	2	69	8.3%	1.64 [0.31 , 8.70]
Total (95% CI)		**239**		**236**	**100.0%**	**1.10 [0.68 , 1.78]**
Total events:	27		28			

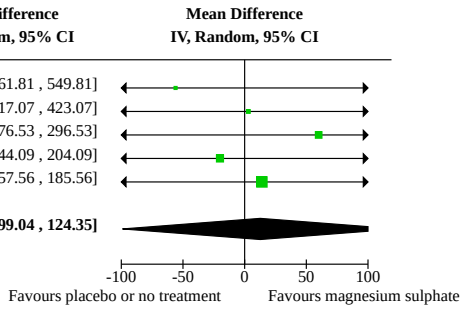
Heterogeneity: Tau² = 0.00; Chi² = 2.84, df = 4 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.70)
Test for subgroup differences: Not applicable



Analysis 4.27. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 27: Mean birthweight

Study or Subgroup	Magnesium sulphate Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Colon 2016	2533	902	17	2589	817	14	3.4%	-56.00 [-661.81 , 549.81]
Cotton 1984	1651	591	15	1648	656	19	7.1%	3.00 [-417.07 , 423.07]
Cox 1990	2264	821	78	2204	726	89	22.3%	60.00 [-176.53 , 296.53]
Fox 1993	2741	496	45	2761	585	45	24.8%	-20.00 [-244.09 , 204.09]
How 1998	1658	526	84	1644	549	69	42.4%	14.00 [-157.56 , 185.56]
Total (95% CI)			**239**			**236**	**100.0%**	**12.65 [-99.04 , 124.35]**

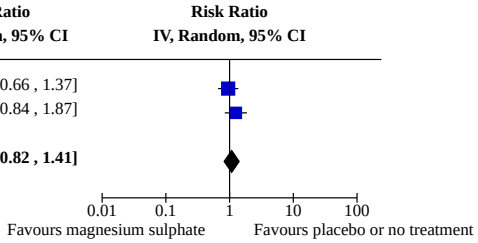
Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 4 (P = 0.99); I² = 0%
Test for overall effect: Z = 0.22 (P = 0.82)
Test for subgroup differences: Not applicable



Analysis 4.28. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	12	16	15	19	54.4%	0.95 [0.66 , 1.37]
Cox 1990	33	77	27	79	45.6%	1.25 [0.84 , 1.87]
Total (95% CI)		**93**		**98**	**100.0%**	**1.08 [0.82 , 1.41]**
Total events:	45		42			

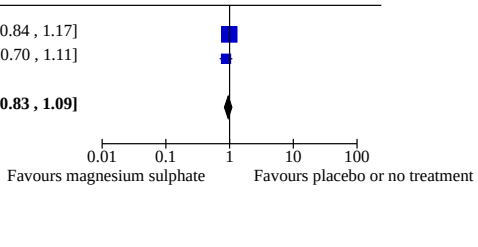
Heterogeneity: Tau² = 0.00; Chi² = 1.01, df = 1 (P = 0.32); I² = 1%
Test for overall effect: Z = 0.54 (P = 0.59)
Test for subgroup differences: Not applicable



Analysis 4.29. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	15	16	18	19	65.8%	0.99 [0.84 , 1.17]
Cox 1990	47	78	61	89	34.2%	0.88 [0.70 , 1.11]
Total (95% CI)		**94**		**108**	**100.0%**	**0.95 [0.83 , 1.09]**
Total events:	62		79			

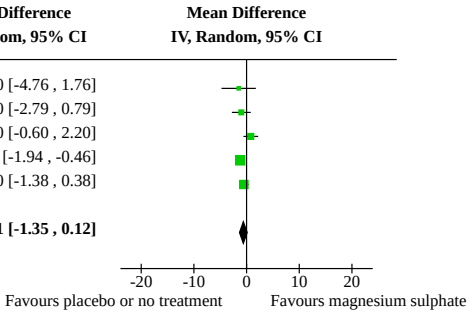
Heterogeneity: Tau² = 0.00; Chi² = 0.68, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.75 (P = 0.46)
Test for subgroup differences: Not applicable



Analysis 4.30. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 30: Gestational age at birth

Study or Subgroup	Magnesium sulphate Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Colon 2016	36	4.5	15	37.5	4.6	15	4.6%	-1.50 [-4.76 , 1.76]
Cotton 1984	31	1.9	16	32	3.4	19	12.7%	-1.00 [-2.79 , 0.79]
Cox 1990	33.8	4.4	76	33	4.5	80	18.1%	0.80 [-0.60 , 2.20]
Fox 1993	36.5	1.7	45	37.7	1.9	45	34.4%	-1.20 [-1.94 , -0.46]
How 1998	31.1	3	78	31.6	2.4	67	30.2%	-0.50 [-1.38 , 0.38]
Total (95% CI)			**230**			**226**	**100.0%**	**-0.61 [-1.35 , 0.12]**

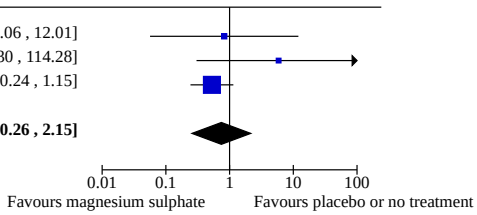
Heterogeneity: Tau² = 0.26; Chi² = 6.70, df = 4 (P = 0.15); I² = 40%
Test for overall effect: Z = 1.65 (P = 0.10)
Test for subgroup differences: Not applicable



Analysis 4.31. Comparison 4: Magnesium sulphate vs placebo or no treatment, Outcome 31: Neonatal infection

Study or Subgroup	Magnesium sulphate Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Colon 2016	1	17	1	14	13.9%	0.82 [0.06 , 12.01]
Cotton 1984	2	16	0	19	11.6%	5.88 [0.30 , 114.28]
How 1998	9	84	14	69	74.5%	0.53 [0.24 , 1.15]
Total (95% CI)		**117**		**102**	**100.0%**	**0.74 [0.26 , 2.15]**
Total events:	12		15			

Heterogeneity: Tau² = 0.24; Chi² = 2.42, df = 2 (P = 0.30); I² = 17%
Test for overall effect: Z = 0.55 (P = 0.58)
Test for subgroup differences: Not applicable



Comparison 5. Oxytocin receptor antagonists vs placebo or no treatment

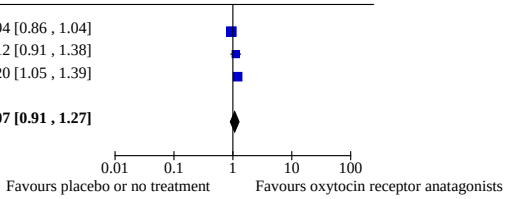
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Delay in birth by 48 hours	3	653	Risk Ratio (IV, Random, 95% CI)	1.07 [0.91, 1.27]
5.2 Delay in birth by 7 days	3	604	Risk Ratio (IV, Random, 95% CI)	1.23 [1.11, 1.37]
5.3 Neonatal death before 28 days	3	769	Risk Ratio (IV, Random, 95% CI)	4.10 [0.88, 19.13]
5.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
5.5 Serious adverse effects of drugs	4	799	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.7 Cessation of treatment due to adverse effects	4	727	Risk Ratio (IV, Random, 95% CI)	4.02 [2.05, 7.85]
5.8 Birth before 28 weeks' gestation	1	501	Risk Ratio (IV, Random, 95% CI)	3.11 [1.02, 9.51]
5.9 Birth before 32 weeks' gestation	1	287	Risk Ratio (IV, Random, 95% CI)	1.33 [0.83, 2.14]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.11 Birth before 37 weeks' gestation	3	690	Risk Ratio (IV, Random, 95% CI)	1.13 [0.98, 1.31]
5.12 Maternal death	2	524	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.16 Headaches	2	176	Risk Ratio (IV, Random, 95% CI)	1.62 [0.13, 19.74]
5.17 Nausea or vomiting	2	176	Risk Ratio (IV, Random, 95% CI)	1.60 [0.27, 9.57]
5.18 Tachycardia	1	501	Risk Ratio (IV, Random, 95% CI)	1.00 [0.14, 7.07]
5.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.21 Perinatal death	2	729	Risk Ratio (IV, Random, 95% CI)	2.25 [0.79, 6.38]
5.22 Stillbirth	3	769	Risk Ratio (IV, Random, 95% CI)	0.41 [0.04, 4.08]
5.23 Neonatal death before 7 days	2	746	Risk Ratio (IV, Random, 95% CI)	6.15 [0.74, 50.73]
5.24 Neurodevelopmental morbidity	1	489	Risk Ratio (IV, Random, 95% CI)	0.85 [0.45, 1.62]
5.25 Gastrointestinal morbidity	1	575	Risk Ratio (IV, Random, 95% CI)	0.21 [0.02, 1.76]
5.26 Respiratory morbidity	5	939	Risk Ratio (IV, Random, 95% CI)	1.22 [0.90, 1.66]
5.27 Mean birthweight	4	779	Mean Difference (IV, Random, 95% CI)	-68.13 [-228.13, 91.88]
5.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
5.30 Gestational age at birth	2	135	Mean Difference (IV, Random, 95% CI)	-0.39 [-1.41, 0.62]
5.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 5.1. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Goodwin 1994	51	56	54	56	39.1%	0.94 [0.86 , 1.04]
Richter 2005	19	20	17	20	26.6%	1.12 [0.91 , 1.38]
Romero 2000	165	246	142	255	34.3%	1.20 [1.05 , 1.39]
Total (95% CI)		**322**		**331**	**100.0%**	**1.07 [0.91 , 1.27]**
Total events:	235		213			

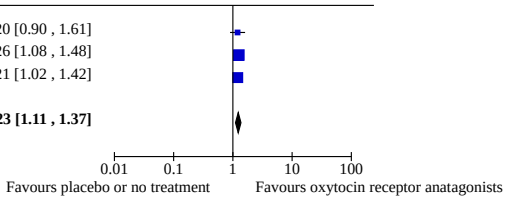
Heterogeneity: Tau² = 0.02; Chi² = 8.48, df = 2 (P = 0.01); I² = 76%
Test for overall effect: Z = 0.82 (P = 0.41)
Test for subgroup differences: Not applicable



Analysis 5.2. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Richter 2005	18	20	15	20	13.2%	1.20 [0.90 , 1.61]
Romero 2000	153	246	125	254	45.0%	1.26 [1.08 , 1.48]
Thornton 2015	30	30	28	34	41.7%	1.21 [1.02 , 1.42]
Total (95% CI)		**296**		**308**	**100.0%**	**1.23 [1.11 , 1.37]**
Total events:	201		168			

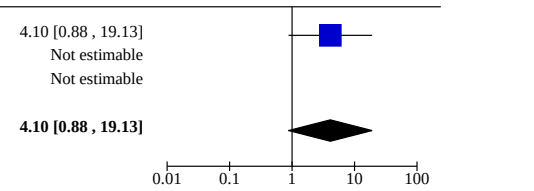
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 3.84 (P = 0.0001)
Test for subgroup differences: Not applicable



Analysis 5.3. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Oxytocin receptor antag Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	8	288	2	295	100.0%	4.10 [0.88 , 19.13]
Saade 2021	0	10	0	13		Not estimable
Thornton 2009	0	131	0	32		Not estimable
Total (95% CI)		**429**		**340**	**100.0%**	**4.10 [0.88 , 19.13]**
Total events:	8		2			

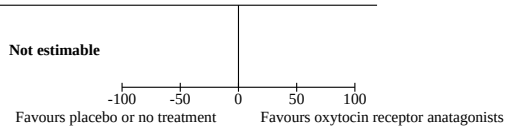
Heterogeneity: Not applicable
Test for overall effect: Z = 1.79 (P = 0.07)
Test for subgroup differences: Not applicable



Analysis 5.4. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Oxytocin receptor antagon Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**

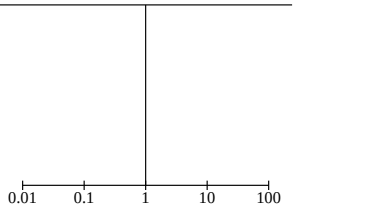
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.5. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Goodwin 1994	0	56	0	56		Not estimable
Romero 2000	0	250	0	251		Not estimable
Saade 2021	0	10	0	13		Not estimable
Thornton 2009	0	131	0	32		Not estimable
Total (95% CI)		**447**		**352**		**Not estimable**
Total events:	0		0			

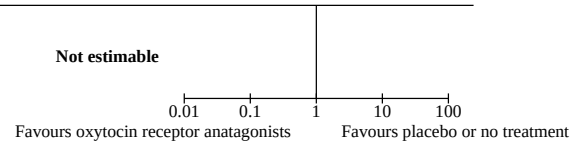
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.6. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

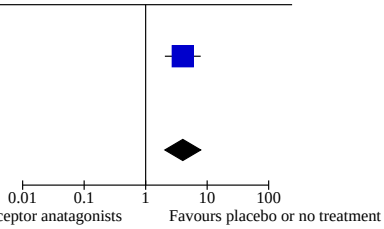
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.7. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Richter 2005	0	20	0	20		Not estimable
Romero 2000	40	250	10	251	100.0%	4.02 [2.05 , 7.85]
Saade 2021	0	10	0	13		Not estimable
Thornton 2009	0	131	0	32		Not estimable
Total (95% CI)		**411**		**316**	**100.0%**	**4.02 [2.05 , 7.85]**
Total events:	40		10			

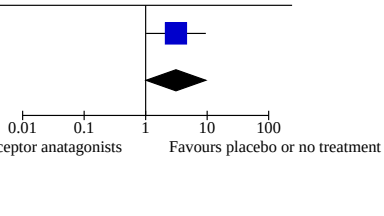
Heterogeneity: Not applicable
Test for overall effect: Z = 4.06 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 5.8. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	12	246	4	255	100.0%	3.11 [1.02 , 9.51]
Total (95% CI)		**246**		**255**	**100.0%**	**3.11 [1.02 , 9.51]**
Total events:	12		4			

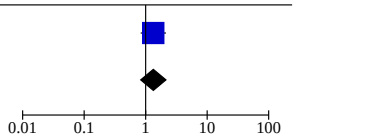
Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)
Test for subgroup differences: Not applicable



Analysis 5.9. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	35	153	23	134	100.0%	1.33 [0.83 , 2.14]
Total (95% CI)		**153**		**134**	**100.0%**	**1.33 [0.83 , 2.14]**
Total events:	35		23			

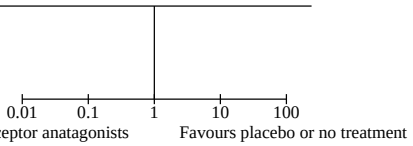
Heterogeneity: Not applicable
Test for overall effect: Z = 1.19 (P = 0.23)
Test for subgroup differences: Not applicable



Analysis 5.10. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

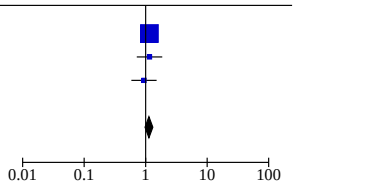
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.11. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	144	249	128	255	81.1%	1.15 [0.98 , 1.35]
Saade 2021	8	10	9	13	9.3%	1.16 [0.72 , 1.86]
Thornton 2009	50	131	13	32	9.5%	0.94 [0.59 , 1.51]
Total (95% CI)		**390**		**300**	**100.0%**	**1.13 [0.98 , 1.31]**
Total events:	202		150			

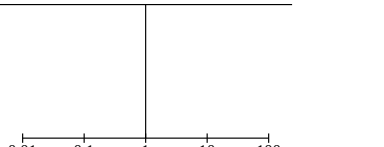
Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 2 (P = 0.72); I² = 0%
Test for overall effect: Z = 1.65 (P = 0.10)
Test for subgroup differences: Not applicable



Analysis 5.12. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 12: Maternal death

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	0	246	0	255		Not estimable
Saade 2021	0	10	0	13		Not estimable
Total (95% CI)		**256**		**268**		**Not estimable**
Total events:	0		0			

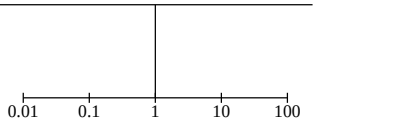
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.13. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 13: Pulmonary oedema

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

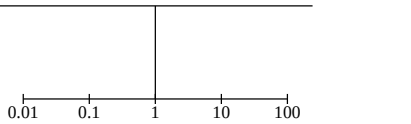
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.14. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

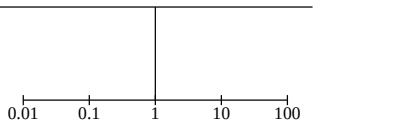
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.15. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

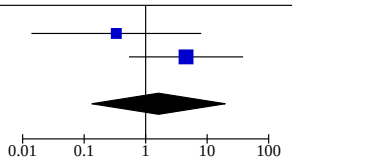
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.16. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 16: Headaches

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Goodwin 1994	0	56	1	56	39.4%	0.33 [0.01 , 8.01]
Thornton 2015	4	30	1	34	60.6%	4.53 [0.54 , 38.36]
Total (95% CI)		**86**		**90**	**100.0%**	**1.62 [0.13 , 19.74]**
Total events:	4		2			

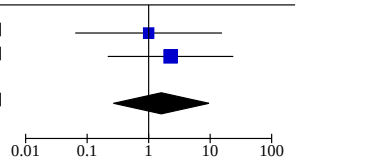
Heterogeneity: $Tau^2 = 1.50$; $Chi^2 = 1.78$, df = 1 (P = 0.18); $I^2 = 44\%$
Test for overall effect: Z = 0.38 (P = 0.70)
Test for subgroup differences: Not applicable



Analysis 5.17. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 17: Nausea or vomiting

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Goodwin 1994	1	56	1	56	42.3%	1.00 [0.06 , 15.59]
Thornton 2015	2	30	1	34	57.7%	2.27 [0.22 , 23.76]
Total (95% CI)		**86**		**90**	**100.0%**	**1.60 [0.27 , 9.57]**
Total events:	3		2			

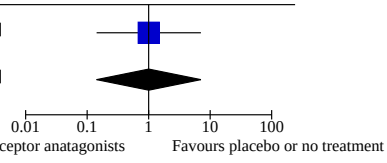
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 0.52 (P = 0.60)
Test for subgroup differences: Not applicable



Analysis 5.18. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 18: Tachycardia

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	2	250	2	251	100.0%	1.00 [0.14 , 7.07]
Total (95% CI)		**250**		**251**	**100.0%**	**1.00 [0.14 , 7.07]**
Total events:	2		2			

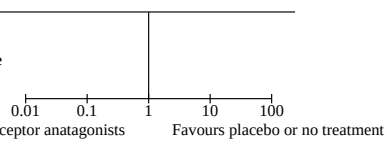
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



Analysis 5.19. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

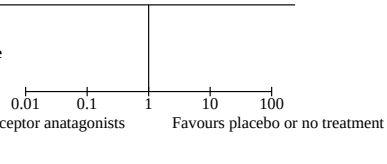
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.20. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 20: Maternal hypotension

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

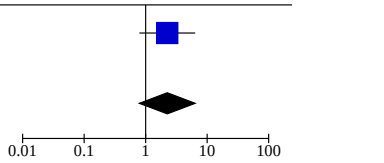
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 5.21. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 21: Perinatal death

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	11	280	5	286	100.0%	2.25 [0.79 , 6.38]
Thornton 2009	0	131	0	32		Not estimable
Total (95% CI)		**411**		**318**	**100.0%**	**2.25 [0.79 , 6.38]**
Total events:	11		5			

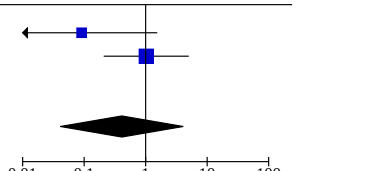
Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)
Test for subgroup differences: Not applicable



Analysis 5.22. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 22: Stillbirth

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Richter 2005	0	20	5	20	37.8%	0.09 [0.01 , 1.54]
Romero 2000	3	280	3	286	62.2%	1.02 [0.21 , 5.02]
Thornton 2009	0	131	0	32		Not estimable
Total (95% CI)		**431**		**338**	**100.0%**	**0.41 [0.04 , 4.08]**
Total events:	3		8			

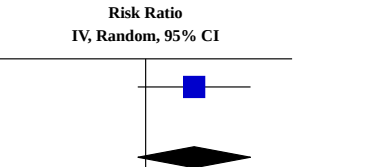
Heterogeneity: Tau² = 1.55; Chi² = 2.13, df = 1 (P = 0.14); I² = 53%
Test for overall effect: Z = 0.76 (P = 0.45)
Test for subgroup differences: Not applicable



Analysis 5.23. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	6	288	1	295	100.0%	6.15 [0.74 , 50.73]
Thornton 2009	0	131	0	32		Not estimable
Total (95% CI)		**419**		**327**	**100.0%**	**6.15 [0.74 , 50.73]**
Total events:	6		1			

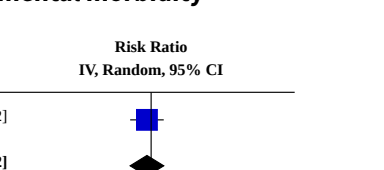
Heterogeneity: Not applicable
Test for overall effect: Z = 1.69 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 5.24. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	16	243	19	246	100.0%	0.85 [0.45 , 1.62]
Total (95% CI)		**243**		**246**	**100.0%**	**0.85 [0.45 , 1.62]**
Total events:	16		19			

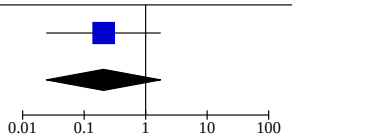
Heterogeneity: Not applicable
Test for overall effect: Z = 0.49 (P = 0.63)
Test for subgroup differences: Not applicable



Analysis 5.25. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Romero 2000	1	283	5	292	100.0%	0.21 [0.02 , 1.76]
Total (95% CI)		**283**		**292**	**100.0%**	**0.21 [0.02 , 1.76]**
Total events:	1		5			

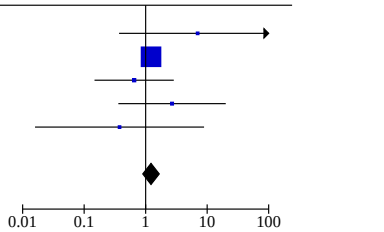
Heterogeneity: Not applicable
Test for overall effect: Z = 1.44 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 5.26. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 26: Respiratory morbidity

Study or Subgroup	Oxytocin receptor antagon Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Goodwin 1994	3	57	0	57	1.1%	7.00 [0.37 , 132.51]
Romero 2000	64	283	54	292	91.3%	1.22 [0.89 , 1.69]
Saade 2021	2	10	4	13	4.3%	0.65 [0.15 , 2.87]
Thornton 2009	11	131	1	32	2.4%	2.69 [0.36 , 20.06]
Thornton 2015	0	30	1	34	1.0%	0.38 [0.02 , 8.91]
Total (95% CI)		**511**		**428**	**100.0%**	**1.22 [0.90 , 1.66]**
Total events:	80		60			

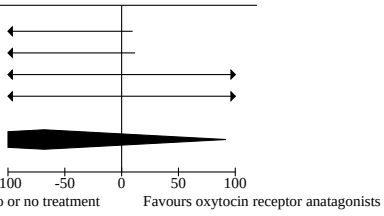
Heterogeneity: Tau² = 0.00; Chi² = 3.17, df = 4 (P = 0.53); I² = 0%
Test for overall effect: Z = 1.27 (P = 0.20)
Test for subgroup differences: Not applicable



Analysis 5.27. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 27: Mean birthweight

Study or Subgroup	Oxytocin receptor antagon Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Goodwin 1994	2996	750	57	3224	525	57	26.2%	-228.00 [-465.66 , 9.66]
Romero 2000	2337	787	286	2450	742	292	45.0%	-113.00 [-237.75 , 11.75]
Saade 2021	2121	681	10	2015	805	13	6.2%	106.00 [-501.98 , 713.98]
Thornton 2015	3099	512	30	2940	585	34	22.6%	159.00 [-109.76 , 427.76]
Total (95% CI)			**383**			**396**	**100.0%**	**-68.13 [-228.13 , 91.88]**

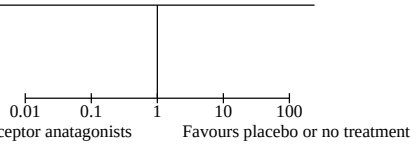
Heterogeneity: Tau² = 10748.79; Chi² = 5.12, df = 3 (P = 0.16); I² = 41%
Test for overall effect: Z = 0.83 (P = 0.40)
Test for subgroup differences: Not applicable



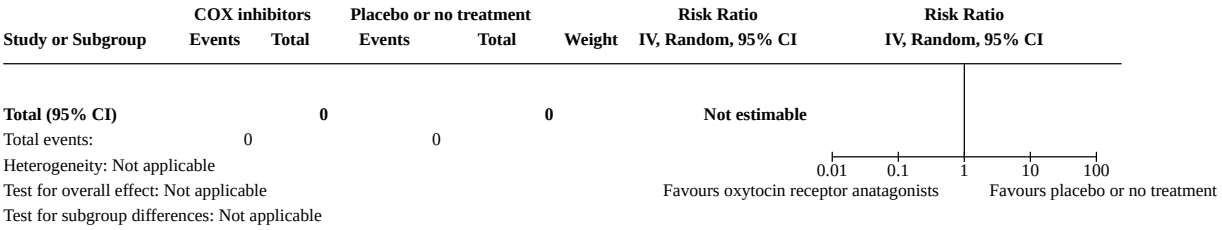
Analysis 5.28. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 28: Birthweight < 2000 g

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

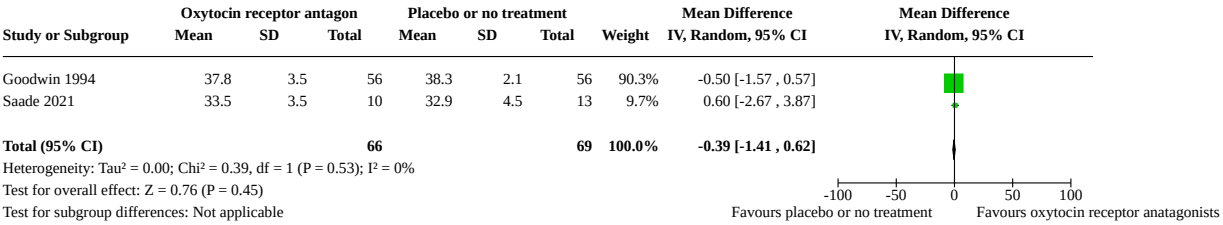
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



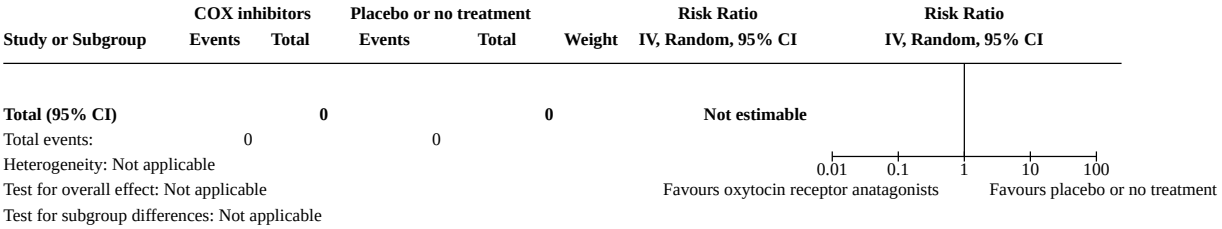
Analysis 5.29. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 29: Birthweight < 2500 g



Analysis 5.30. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 30: Gestational age at birth



Analysis 5.31. Comparison 5: Oxytocin receptor antagonists vs placebo or no treatment, Outcome 31: Neonatal infection



Comparison 6. Nitric oxide donors vs placebo or no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Delay in birth by 48 hours	2	186	Risk Ratio (IV, Random, 95% CI)	1.18 [0.76, 1.84]
6.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.3 Neonatal death before 28 days	2	186	Risk Ratio (IV, Random, 95% CI)	0.49 [0.07, 3.64]
6.4 Pregnancy prolongation (Time from trial entry to birth in days)	2	186	Mean Difference (IV, Random, 95% CI)	11.91 [3.53, 20.28]
6.5 Serious adverse effects of drugs	2	186	Risk Ratio (IV, Random, 95% CI)	Not estimable

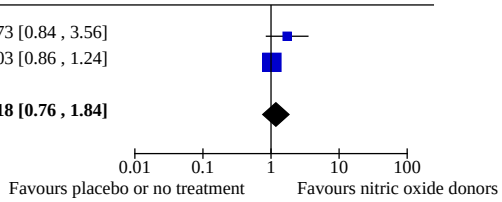
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.7 Cessation of treatment due to adverse effects	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.8 Birth before 28 weeks' gestation	1	153	Risk Ratio (IV, Random, 95% CI)	0.50 [0.23, 1.09]
6.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.10 Birth before 34 weeks' gestation	1	153	Risk Ratio (IV, Random, 95% CI)	0.93 [0.61, 1.41]
6.11 Birth before 37 weeks' gestation	2	303	Risk Ratio (IV, Random, 95% CI)	0.57 [0.17, 1.90]
6.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.13 Pulmonary oedema	1	33	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.16 Headaches	2	309	Risk Ratio (IV, Random, 95% CI)	2.00 [1.35, 2.97]
6.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.18 Tachycardia	1	156	Risk Ratio (IV, Random, 95% CI)	4.63 [0.23, 94.99]
6.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.20 Maternal hypotension	2	309	Risk Ratio (IV, Random, 95% CI)	2.51 [0.31, 20.64]
6.21 Perinatal death	2	186	Risk Ratio (IV, Random, 95% CI)	0.41 [0.06, 3.00]
6.22 Stillbirth	2	186	Risk Ratio (IV, Random, 95% CI)	0.36 [0.01, 8.59]
6.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.24 Neurodevelopmental morbidity	2	186	Risk Ratio (IV, Random, 95% CI)	1.06 [0.16, 7.04]
6.25 Gastrointestinal morbidity	2	186	Risk Ratio (IV, Random, 95% CI)	0.75 [0.06, 9.46]
6.26 Respiratory morbidity	2	186	Risk Ratio (IV, Random, 95% CI)	0.35 [0.12, 1.00]
6.27 Mean birthweight	1	33	Mean Difference (IV, Random, 95% CI)	327.00 [-272.13, 926.13]
6.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.30 Gestational age at birth	2	186	Mean Difference (IV, Random, 95% CI)	1.13 [-0.46, 2.71]
6.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 6.1. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	11	17	6	16	26.0%	1.73 [0.84 , 3.56]
Smith 2007	56	74	58	79	74.0%	1.03 [0.86 , 1.24]
Total (95% CI)		**91**		**95**	**100.0%**	**1.18 [0.76 , 1.84]**
Total events:	67		64			

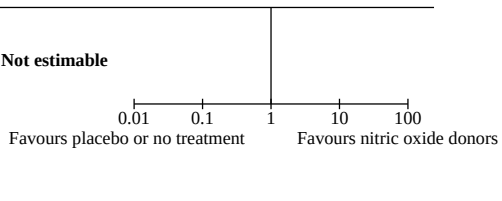
Heterogeneity: Tau² = 0.06; Chi² = 1.83, df = 1 (P = 0.18); I² = 45%
Test for overall effect: Z = 0.73 (P = 0.47)
Test for subgroup differences: Not applicable



Analysis 6.2. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 2: Delay in birth by 7 days

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

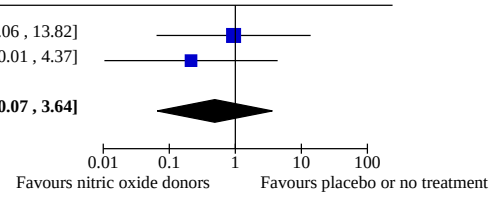
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.3. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	1	17	1	16	55.8%	0.94 [0.06 , 13.82]
Smith 2007	0	74	2	79	44.2%	0.21 [0.01 , 4.37]
Total (95% CI)		**91**		**95**	**100.0%**	**0.49 [0.07 , 3.64]**
Total events:	1		3			

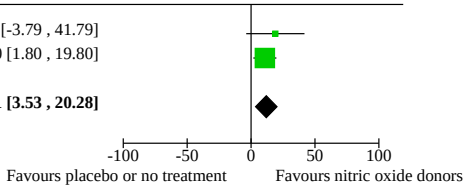
Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 1 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.70 (P = 0.48)
Test for subgroup differences: Not applicable



Analysis 6.4. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 4: Pregnancy prolongation (Time from trial entry to birth in days)

Study or Subgroup	Nitric oxide Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Smith 1999	22	31.8	17	3	34.8	16	13.5%	19.00 [-3.79 , 41.79]
Smith 2007	20.9	28.4	74	10.1	28.4	79	86.5%	10.80 [1.80 , 19.80]
Total (95% CI)			**91**			**95**	**100.0%**	**11.91 [3.53 , 20.28]**

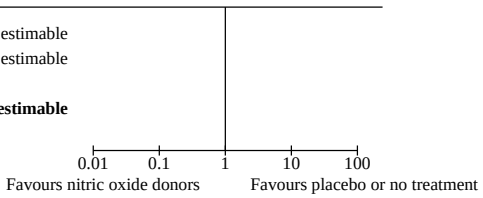
Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 1 (P = 0.51); I² = 0%
Test for overall effect: Z = 2.79 (P = 0.005)
Test for subgroup differences: Not applicable



Analysis 6.5. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Nitric oxide Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	0	17	0	16		Not estimable
Smith 2007	0	74	0	79		Not estimable
Total (95% CI)		**91**		**95**		**Not estimable**
Total events:	0		0			

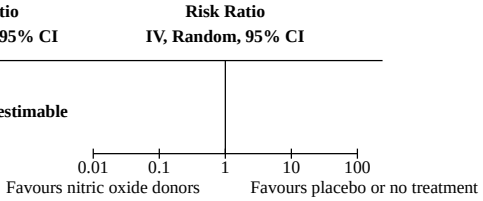
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.6. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

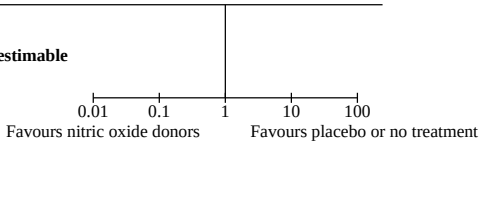
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.7. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

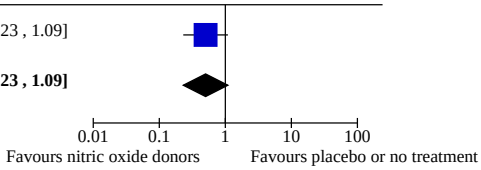
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.8. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Nitric oxide Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 2007	8	74	17	79	100.0%	0.50 [0.23 , 1.09]
Total (95% CI)		**74**		**79**	**100.0%**	**0.50 [0.23 , 1.09]**
Total events:	8		17			

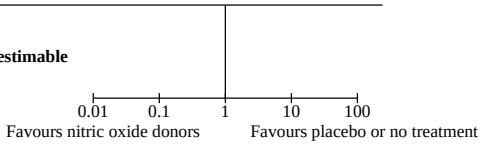
Heterogeneity: Not applicable
Test for overall effect: Z = 1.73 (P = 0.08)
Test for subgroup differences: Not applicable



Analysis 6.9. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

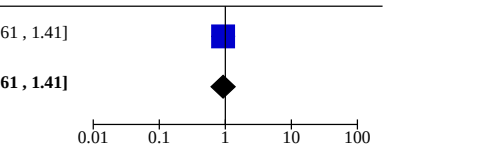
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.10. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Nitric oxide Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 2007	26	74	30	79	100.0%	0.93 [0.61 , 1.41]
Total (95% CI)		**74**		**79**	**100.0%**	**0.93 [0.61 , 1.41]**
Total events:	26		30			

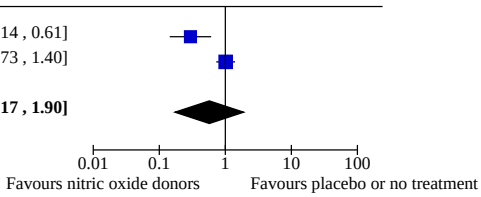
Heterogeneity: Not applicable
Test for overall effect: Z = 0.36 (P = 0.72)
Test for subgroup differences: Not applicable



Analysis 6.11. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Nitric oxide Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Haghighi 2005	8	75	27	75	46.4%	0.30 [0.14 , 0.61]
Smith 2007	36	74	38	79	53.6%	1.01 [0.73 , 1.40]
Total (95% CI)		**149**		**154**	**100.0%**	**0.57 [0.17 , 1.90]**
Total events:	44		65			

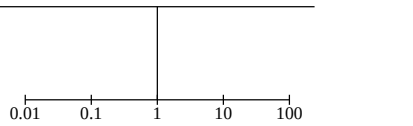
Heterogeneity: Tau² = 0.67; Chi² = 9.23, df = 1 (P = 0.002); I² = 89%
Test for overall effect: Z = 0.91 (P = 0.36)
Test for subgroup differences: Not applicable



Analysis 6.12. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

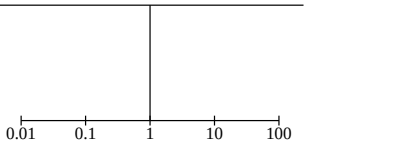
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.13. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 13: Pulmonary oedema

Study or Subgroup	Nitric oxide donors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Smith 1999	0	17	0	16		Not estimable	
Total (95% CI)		**17**		**16**		**Not estimable**	
Total events:	0		0				

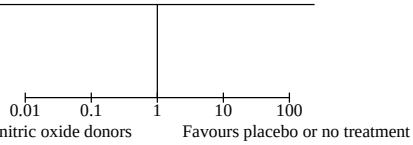
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.14. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

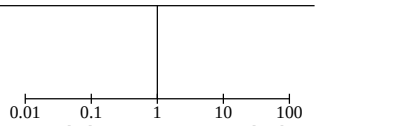
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.15. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

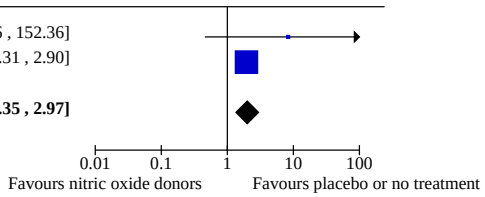
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.16. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 16: Headaches

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Haghighi 2005	4	81	0	75	1.8%	8.34 [0.46 , 152.36]
Smith 2007	42	74	23	79	98.2%	1.95 [1.31 , 2.90]
Total (95% CI)		**155**		**154**	**100.0%**	**2.00 [1.35 , 2.97]**
Total events:	46		23			

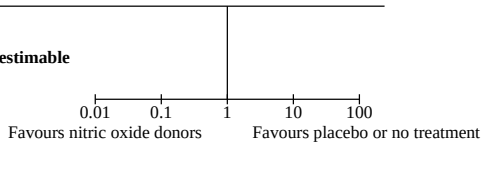
Heterogeneity: Tau² = 0.00; Chi² = 0.94, df = 1 (P = 0.33); I² = 0%
Test for overall effect: Z = 3.46 (P = 0.0005)
Test for subgroup differences: Not applicable



Analysis 6.17. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 17: Nausea or vomiting

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

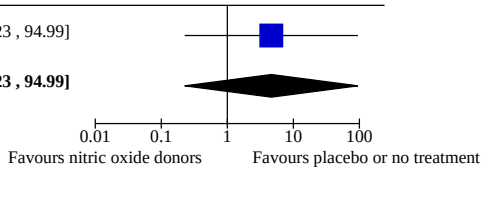
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.18. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 18: Tachycardia

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Haghighi 2005	2	81	0	75	100.0%	4.63 [0.23 , 94.99]
Total (95% CI)		**81**		**75**	**100.0%**	**4.63 [0.23 , 94.99]**
Total events:	2		0			

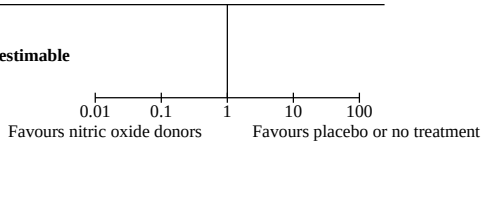
Heterogeneity: Not applicable
Test for overall effect: Z = 1.00 (P = 0.32)
Test for subgroup differences: Not applicable



Analysis 6.19. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

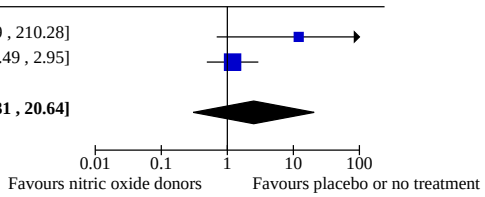
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.20. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 20: Maternal hypotension

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Haghighi 2005	6	81	0	75	32.0%	12.05 [0.69 , 210.28]
Smith 2007	9	74	8	79	68.0%	1.20 [0.49 , 2.95]
Total (95% CI)		**155**		**154**	**100.0%**	**2.51 [0.31 , 20.64]**
Total events:	15		8			

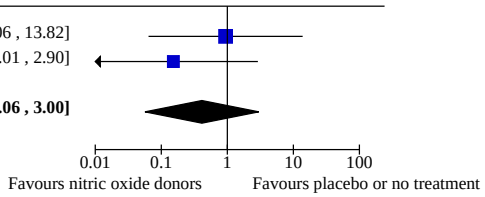
Heterogeneity: Tau² = 1.49; Chi² = 2.27, df = 1 (P = 0.13); I² = 56%
Test for overall effect: Z = 0.86 (P = 0.39)
Test for subgroup differences: Not applicable



Analysis 6.21. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 21: Perinatal death

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	1	17	1	16	54.6%	0.94 [0.06 , 13.82]
Smith 2007	0	74	3	79	45.4%	0.15 [0.01 , 2.90]
Total (95% CI)		**91**		**95**	**100.0%**	**0.41 [0.06 , 3.00]**
Total events:	1		4			

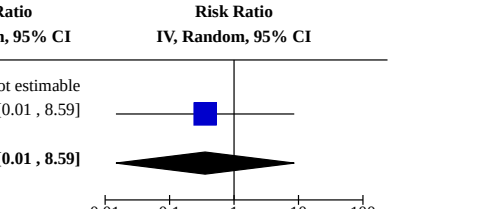
Heterogeneity: Tau² = 0.00; Chi² = 0.80, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 0.88 (P = 0.38)
Test for subgroup differences: Not applicable



Analysis 6.22. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 22: Stillbirth

Study or Subgroup	Nitric oxide donors Events	Nitric oxide donors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	0	17	0	16		Not estimable
Smith 2007	0	74	1	79	100.0%	0.36 [0.01 , 8.59]
Total (95% CI)		**91**		**95**	**100.0%**	**0.36 [0.01 , 8.59]**
Total events:	0		1			

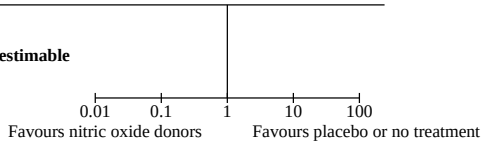
Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)
Test for subgroup differences: Not applicable



Analysis 6.23. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Nitric oxide Events	Nitric oxide Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

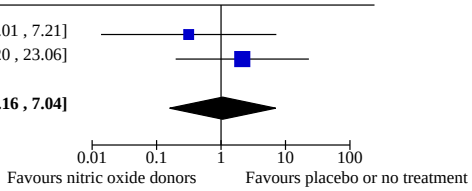
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 6.24. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Nitric oxide donors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	0	17	1	16	36.6%	0.31 [0.01 , 7.21]
Smith 2007	2	74	1	79	63.4%	2.14 [0.20 , 23.06]
Total (95% CI)		**91**		**95**	**100.0%**	**1.06 [0.16 , 7.04]**
Total events:	2		2			

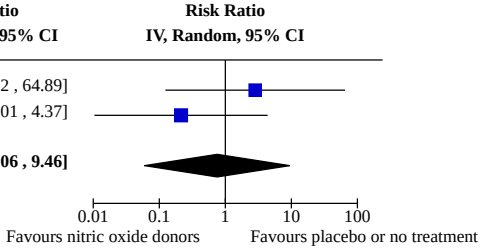
Heterogeneity: Tau² = 0.00; Chi² = 0.91, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 0.06 (P = 0.95)
Test for subgroup differences: Not applicable



Analysis 6.25. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Nitric oxide Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	1	17	0	16	48.7%	2.83 [0.12 , 64.89]
Smith 2007	0	74	2	79	51.3%	0.21 [0.01 , 4.37]
Total (95% CI)		**91**		**95**	**100.0%**	**0.75 [0.06 , 9.46]**
Total events:	1		2			

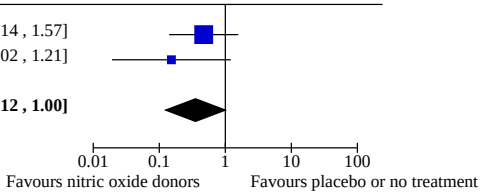
Heterogeneity: Tau² = 0.88; Chi² = 1.36, df = 1 (P = 0.24); I² = 26%
Test for overall effect: Z = 0.22 (P = 0.82)
Test for subgroup differences: Not applicable



Analysis 6.26. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 26: Respiratory morbidity

Study or Subgroup	Nitric oxide Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Smith 1999	3	17	6	16	74.7%	0.47 [0.14 , 1.57]
Smith 2007	1	74	7	79	25.3%	0.15 [0.02 , 1.21]
Total (95% CI)		**91**		**95**	**100.0%**	**0.35 [0.12 , 1.00]**
Total events:	4		13			

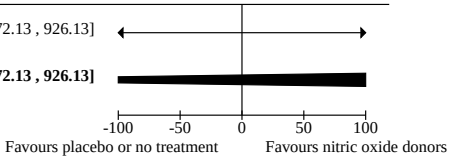
Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 1.95 (P = 0.05)
Test for subgroup differences: Not applicable



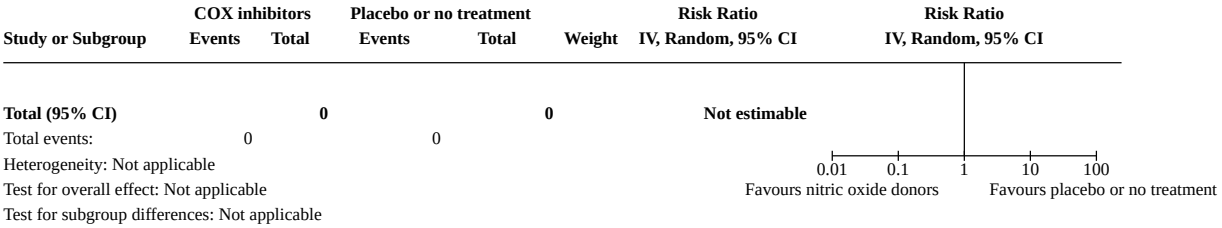
Analysis 6.27. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 27: Mean birthweight

Study or Subgroup	Nitric oxide Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Smith 1999	2543	934	17	2216	821	16	100.0%	327.00 [-272.13 , 926.13]
Total (95% CI)			**17**			**16**	**100.0%**	**327.00 [-272.13 , 926.13]**

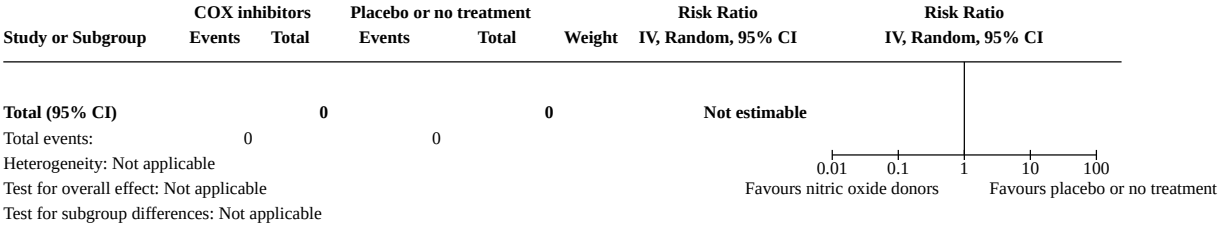
Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.28)
Test for subgroup differences: Not applicable



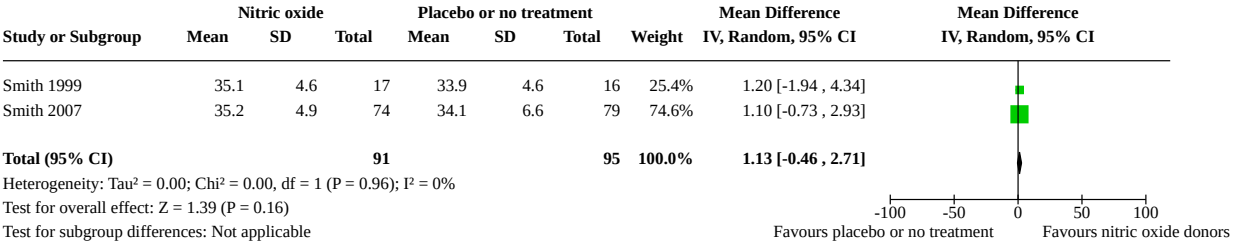
Analysis 6.28. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 28: Birthweight < 2000 g



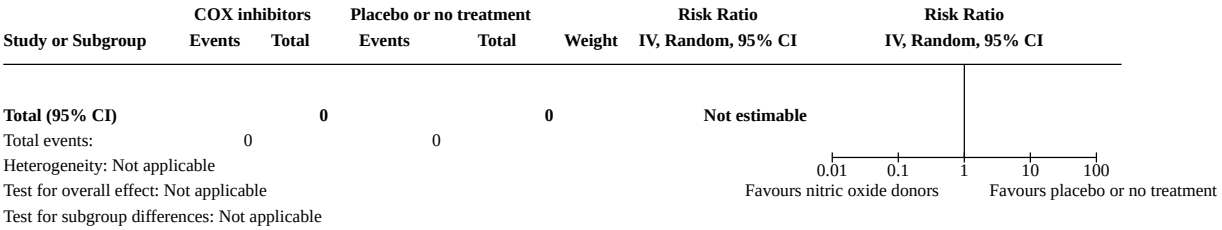
Analysis 6.29. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 29: Birthweight < 2500 g



Analysis 6.30. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 30: Gestational age at birth



Analysis 6.31. Comparison 6: Nitric oxide donors vs placebo or no treatment, Outcome 31: Neonatal infection



Comparison 7. Combinations of tocolytics vs placebo or no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Delay in birth by 48 hours	1	54	Risk Ratio (IV, Random, 95% CI)	1.05 [0.84, 1.31]
7.2 Delay in birth by 7 days	1	54	Risk Ratio (IV, Random, 95% CI)	0.92 [0.67, 1.28]

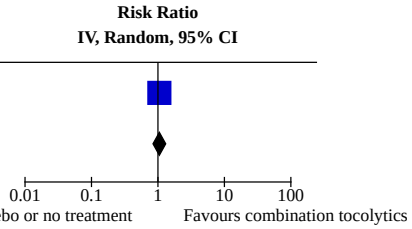
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.3 Neonatal death before 28 days	1	54	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.4 Pregnancy prolongation (time from trial entry to birth in days)	1	54	Mean Difference (IV, Random, 95% CI)	-6.10 [-13.54, 1.34]
7.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.7 Cessation of treatment due to adverse effects	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.11 Birth before 37 weeks' gestation	1	54	Risk Ratio (IV, Random, 95% CI)	1.32 [0.90, 1.95]
7.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.21 Perinatal death	1	54	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.22 Stillbirth	1	54	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.23 Neonatal death before 7 days	1	54	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.24 Neurodevelopmental morbidity	1	54	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.25 Gastrointestinal morbidity	1	54	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.26 Respiratory morbidity	1	54	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.27 Mean birthweight	1	54	Mean Difference (IV, Random, 95% CI)	-287.00 [-562.65, -11.35]
7.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
7.30 Gestational age at birth	1	54	Mean Difference (IV, Random, 95% CI)	-0.80 [-1.87, 0.27]
7.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 7.1. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Combination Events	Combination Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	21	24	25	30	100.0%	1.05 [0.84 , 1.31]
Total (95% CI)		**24**		**30**	**100.0%**	**1.05 [0.84 , 1.31]**
Total events:	21		25			

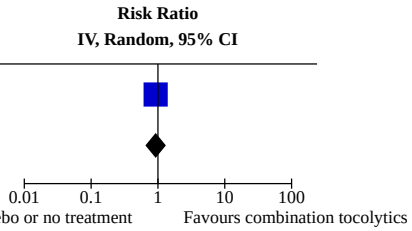
Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.66)
Test for subgroup differences: Not applicable



Analysis 7.2. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Combination Events	Combination Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	17	24	23	30	100.0%	0.92 [0.67 , 1.28]
Total (95% CI)		**24**		**30**	**100.0%**	**0.92 [0.67 , 1.28]**
Total events:	17		23			

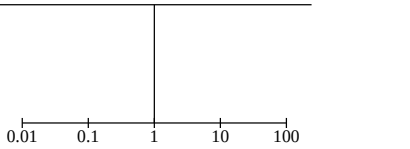
Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)
Test for subgroup differences: Not applicable



Analysis 7.3. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Combination Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	0	24	0	30		Not estimable
Total (95% CI)		**24**		**30**		**Not estimable**
Total events:	0		0			

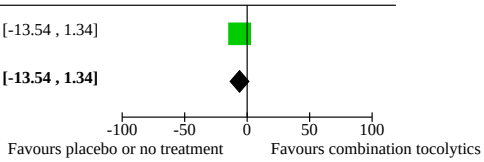
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.4. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Combination Mean	SD	Total	Placebo or no treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
How 2006	17.8	12	24	23.9	15.9	30	100.0%	-6.10 [-13.54 , 1.34]
Total (95% CI)			**24**			**30**	**100.0%**	**-6.10 [-13.54 , 1.34]**

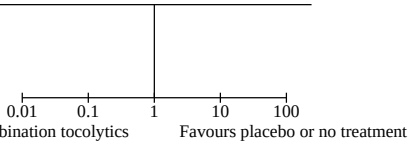
Heterogeneity: Not applicable
Test for overall effect: Z = 1.61 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 7.5. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

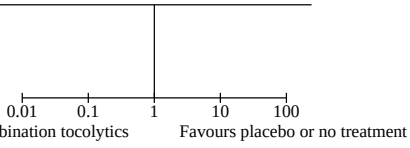
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.6. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

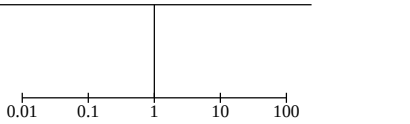
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.7. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

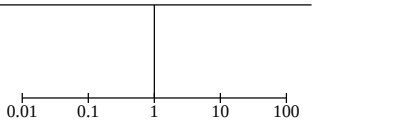
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.8. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

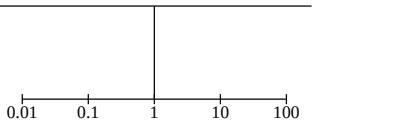
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.9. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

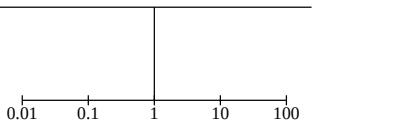
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.10. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

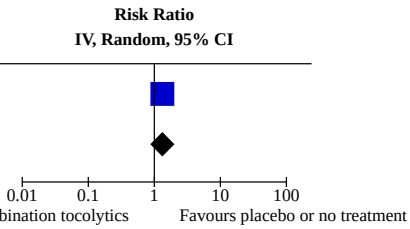
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.11. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Combination Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	18	24	17	30	100.0%	1.32 [0.90 , 1.95]
Total (95% CI)		**24**		**30**	**100.0%**	**1.32 [0.90 , 1.95]**
Total events:	18		17			

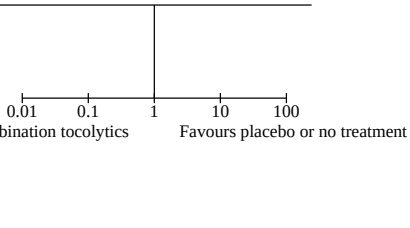
Heterogeneity: Not applicable
Test for overall effect: Z = 1.41 (P = 0.16)
Test for subgroup differences: Not applicable



Analysis 7.12. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

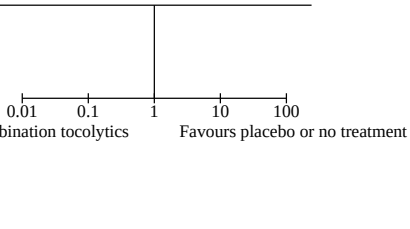
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.13. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 13: Pulmonary oedema

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

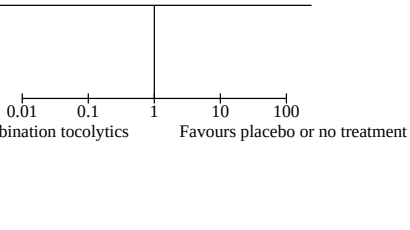
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.14. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

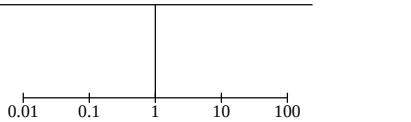
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.15. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

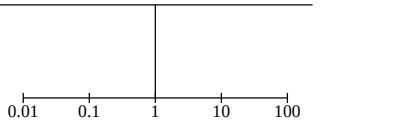
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.16. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 16: Headaches

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

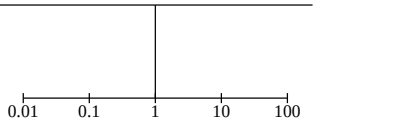
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.17. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 17: Nausea or vomiting

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

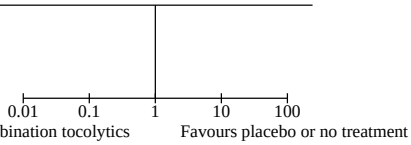
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.18. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 18: Tachycardia

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

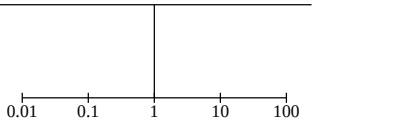
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.19. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

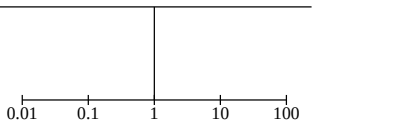
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.20. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 20: Maternal hypotension

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

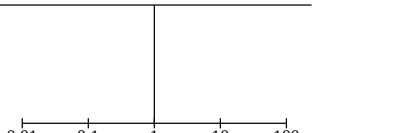
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.21. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 21: Perinatal death

Study or Subgroup	Combination Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	0	24	0	30		Not estimable
Total (95% CI)		**24**		**30**		**Not estimable**
Total events:	0		0			

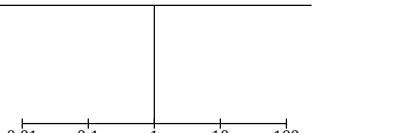
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.22. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 22: Stillbirth

Study or Subgroup	Combination Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	0	24	0	30		Not estimable
Total (95% CI)		**24**		**30**		**Not estimable**
Total events:	0		0			

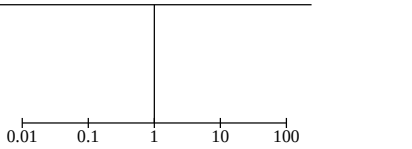
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.23. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Combination Events	Combination Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	0	24	0	30		Not estimable
Total (95% CI)		**24**		**30**		**Not estimable**
Total events:	0		0			

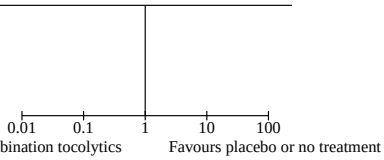
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.24. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Combinations of tocolytics Events	Combinations of tocolytics Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	0	24	0	30		Not estimable
Total (95% CI)		**24**		**30**		**Not estimable**
Total events:	0		0			

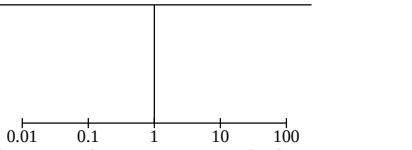
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 7.25. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Combination Events	Combination Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	0	24	0	30		Not estimable
Total (95% CI)		**24**		**30**		**Not estimable**
Total events:	0		0			

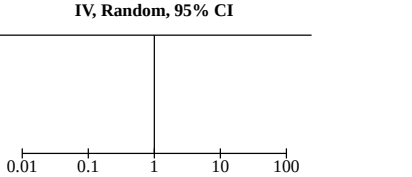
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



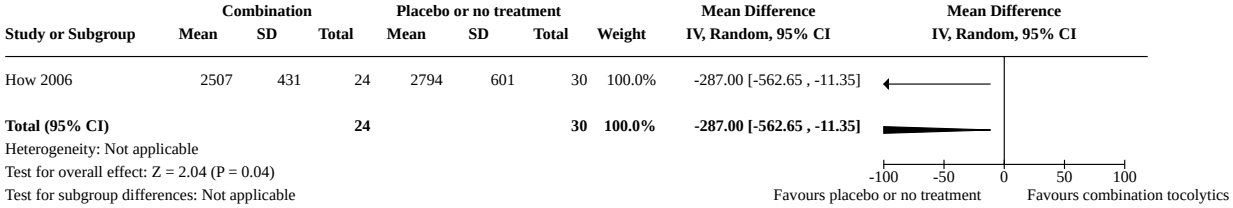
Analysis 7.26. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 26: Respiratory morbidity

Study or Subgroup	Combination Events	Combination Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
How 2006	0	24	0	30		Not estimable
Total (95% CI)		**24**		**30**		**Not estimable**
Total events:	0		0			

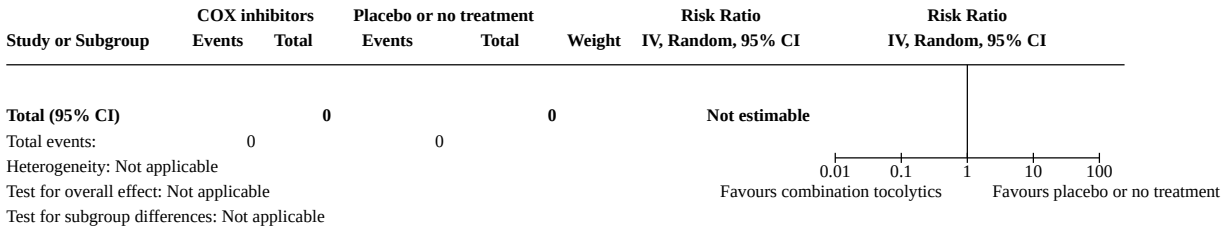
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



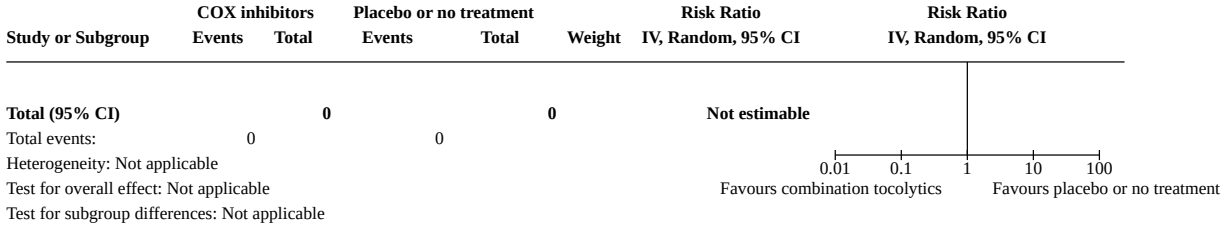
Analysis 7.27. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 27: Mean birthweight



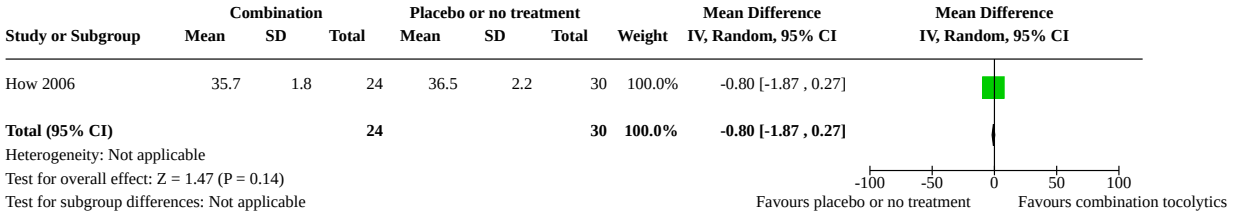
Analysis 7.28. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 28: Birthweight < 2000 g



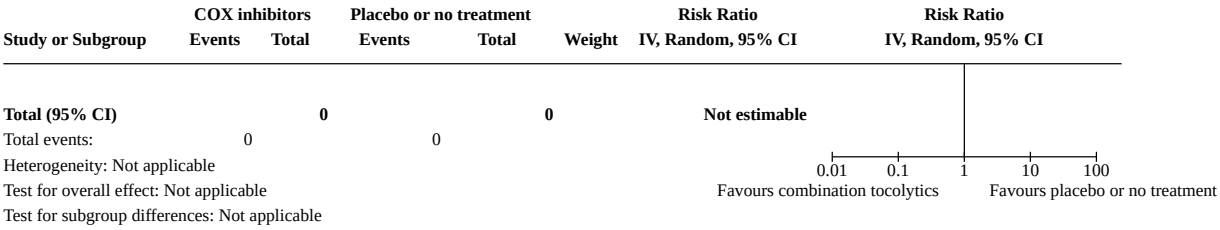
Analysis 7.29. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 29: Birthweight < 2500 g



Analysis 7.30. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 30: Gestational age at birth



Analysis 7.31. Comparison 7: Combinations of tocolytics vs placebo or no treatment, Outcome 31: Neonatal infection



Comparison 8. Betamimetics vs calcium channel blockers

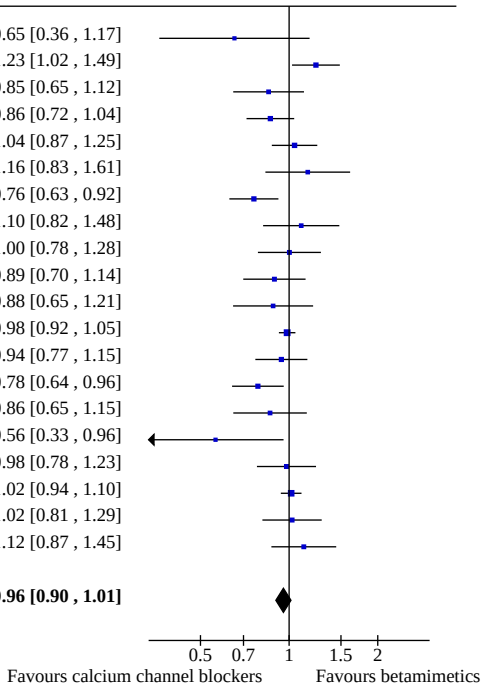
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Delay in birth by 48 hours	20	1649	Risk Ratio (IV, Random, 95% CI)	0.96 [0.90, 1.01]
8.2 Delay in birth by 7 days	13	1092	Risk Ratio (IV, Random, 95% CI)	0.95 [0.86, 1.03]
8.3 Neonatal death before 28 days	17	1216	Risk Ratio (IV, Random, 95% CI)	1.22 [0.68, 2.20]
8.4 Pregnancy prolongation (time from trial entry to birth in days)	12	887	Mean Difference (IV, Random, 95% CI)	-3.91 [-7.03, -0.79]
8.5 Serious adverse effects of drugs	18	1556	Risk Ratio (IV, Random, 95% CI)	4.25 [1.32, 13.66]
8.6 Maternal infection	1	49	Risk Ratio (IV, Random, 95% CI)	0.22 [0.01, 4.46]
8.7 Cessation of treatment due to adverse effects	18	1422	Risk Ratio (IV, Random, 95% CI)	4.35 [2.05, 9.25]
8.8 Birth before 28 weeks' gestation	1	91	Risk Ratio (IV, Random, 95% CI)	7.80 [0.41, 146.74]
8.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.10 Birth before 34 weeks' gestation	8	794	Risk Ratio (IV, Random, 95% CI)	1.25 [1.09, 1.44]
8.11 Birth before 37 weeks' gestation	14	1098	Risk Ratio (IV, Random, 95% CI)	1.11 [1.00, 1.23]
8.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
8.13 Pulmonary oedema	7	622	Risk Ratio (IV, Random, 95% CI)	3.39 [0.83, 13.79]
8.14 Dyspnoea	5	374	Risk Ratio (IV, Random, 95% CI)	5.59 [1.25, 25.07]
8.15 Palpitations	12	903	Risk Ratio (IV, Random, 95% CI)	5.18 [3.60, 7.44]
8.16 Headaches	16	1187	Risk Ratio (IV, Random, 95% CI)	0.66 [0.43, 1.03]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.17 Nausea or vomiting	13	991	Risk Ratio (IV, Random, 95% CI)	3.43 [2.22, 5.30]
8.18 Tachycardia	10	596	Risk Ratio (IV, Random, 95% CI)	3.55 [1.80, 7.01]
8.19 Maternal cardiac arrhythmias	1	66	Risk Ratio (IV, Random, 95% CI)	5.00 [0.25, 100.32]
8.20 Maternal hypotension	14	1046	Risk Ratio (IV, Random, 95% CI)	1.56 [0.76, 3.24]
8.21 Perinatal death	19	1391	Risk Ratio (IV, Random, 95% CI)	1.33 [0.81, 2.18]
8.22 Stillbirth	15	1135	Risk Ratio (IV, Random, 95% CI)	1.85 [0.38, 8.98]
8.23 Neonatal death before 7 days	17	1226	Risk Ratio (IV, Random, 95% CI)	1.31 [0.70, 2.48]
8.24 Neurodevelopmental morbidity	8	654	Risk Ratio (IV, Random, 95% CI)	1.80 [1.14, 2.85]
8.25 Gastrointestinal morbidity	6	551	Risk Ratio (IV, Random, 95% CI)	4.79 [1.05, 21.90]
8.26 Respiratory morbidity	15	1191	Risk Ratio (IV, Random, 95% CI)	1.44 [1.08, 1.92]
8.27 Mean birthweight	19	1434	Mean Difference (IV, Random, 95% CI)	-126.47 [-207.03, -45.91]
8.28 Birthweight < 2000 g	1	53	Risk Ratio (IV, Random, 95% CI)	1.74 [1.04, 2.91]
8.29 Birthweight < 2500 g	5	292	Risk Ratio (IV, Random, 95% CI)	1.14 [0.92, 1.40]
8.30 Gestational age at birth	13	1098	Mean Difference (IV, Random, 95% CI)	-0.76 [-1.14, -0.38]
8.31 Neonatal infection	8	686	Risk Ratio (IV, Random, 95% CI)	1.31 [0.86, 2.00]

Analysis 8.1. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	9	23	18	30	0.9%	0.65 [0.36 , 1.17]
Cararach 2006	37	39	30	39	6.1%	1.23 [1.02 , 1.49]
Ferguson 1990	23	33	27	33	3.5%	0.85 [0.65 , 1.12]
Ganla 1999	38	50	44	50	6.1%	0.86 [0.72 , 1.04]
Garcia-Velasco 1998	24	26	23	26	6.5%	1.04 [0.87 , 1.25]
George 1991	10	11	11	14	2.6%	1.16 [0.83 , 1.61]
Jaju 2011	41	60	54	60	5.9%	0.76 [0.63 , 0.92]
Koks 1998	31	47	33	55	3.1%	1.10 [0.82 , 1.48]
Kose 1995	17	21	42	52	4.2%	1.00 [0.78 , 1.28]
Kupferminc 1993	26	35	30	36	4.3%	0.89 [0.70 , 1.14]
Laohapojanart 2007	15	20	17	20	2.9%	0.88 [0.65 , 1.21]
Mawaldi 2008	90	95	76	79	13.1%	0.98 [0.92 , 1.05]
Padovani 2015	28	34	28	32	5.5%	0.94 [0.77 , 1.15]
Papatsonis 1997	48	77	74	93	5.5%	0.78 [0.64 , 0.96]
Raymajhi 2003	21	30	26	32	3.3%	0.86 [0.65 , 1.15]
Read 1986	9	20	16	20	1.1%	0.56 [0.33 , 0.96]
Trabelsi 2008	18	21	21	24	4.6%	0.98 [0.78 , 1.23]
Valdes 2012	63	66	62	66	12.1%	1.02 [0.94 , 1.10]
Van De Water 2008	33	43	36	48	4.6%	1.02 [0.81 , 1.29]
Weerakul 2002	34	44	31	45	4.0%	1.12 [0.87 , 1.45]
Total (95% CI)		**795**		**854**	**100.0%**	**0.96 [0.90 , 1.01]**
Total events:	615		699			

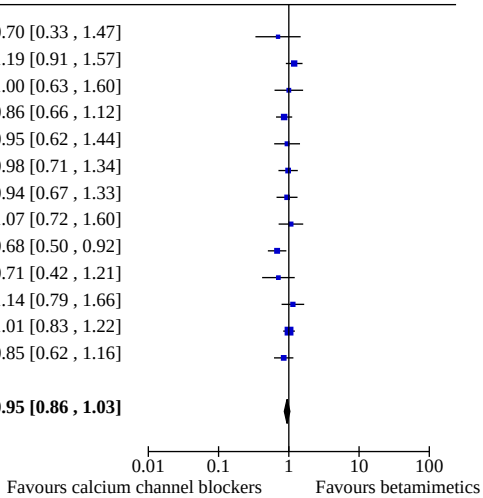
Heterogeneity: Tau² = 0.01; Chi² = 32.01, df = 19 (P = 0.03); I² = 41%
Test for overall effect: Z = 1.48 (P = 0.14)
Test for subgroup differences: Not applicable



Analysis 8.2. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	7	23	13	30	1.5%	0.70 [0.33 , 1.47]
Cararach 2006	31	39	26	39	10.8%	1.19 [0.91 , 1.57]
Ferguson 1990	17	33	17	33	3.7%	1.00 [0.63 , 1.60]
Jaju 2011	36	60	42	60	11.5%	0.86 [0.66 , 1.12]
Koks 1998	21	47	26	55	4.5%	0.95 [0.62 , 1.44]
Kose 1995	15	21	38	52	8.1%	0.98 [0.71 , 1.34]
Kupferminc 1993	22	35	24	36	6.8%	0.94 [0.67 , 1.33]
Laohapojanart 2007	12	16	14	20	5.0%	1.07 [0.72 , 1.60]
Papatsonis 1997	33	78	59	95	8.8%	0.68 [0.50 , 0.92]
Raymajhi 2003	12	30	18	32	2.8%	0.71 [0.42 , 1.21]
Trabelsi 2008	16	21	16	24	5.9%	1.14 [0.79 , 1.66]
Valdes 2012	50	64	45	58	22.5%	1.01 [0.83 , 1.22]
Van De Water 2008	25	43	33	48	8.0%	0.85 [0.62 , 1.16]
Total (95% CI)		**510**		**582**	**100.0%**	**0.95 [0.86 , 1.03]**
Total events:	297		371			

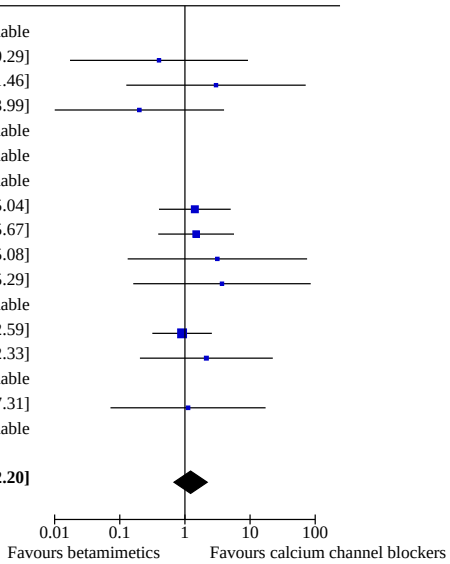
Heterogeneity: Tau² = 0.00; Chi² = 11.87, df = 12 (P = 0.46); I² = 0%
Test for overall effect: Z = 1.23 (P = 0.22)
Test for subgroup differences: Not applicable



Analysis 8.3. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	0	23	0	30		Not estimable
Bracero 1991	0	19	1	23	3.5%	0.40 [0.02 , 9.29]
Cararach 2006	1	39	0	39	3.4%	3.00 [0.13 , 71.46]
Ferguson 1990	0	28	2	28	3.8%	0.20 [0.01 , 3.99]
Garcia-Velasco 1998	0	26	0	26		Not estimable
George 1991	0	11	0	14		Not estimable
Janky 1990	0	32	0	30		Not estimable
Koks 1998	5	59	4	67	21.4%	1.42 [0.40 , 5.04]
Kose 1995	3	21	5	52	19.2%	1.49 [0.39 , 5.67]
Kupferminc 1993	1	39	0	41	3.4%	3.15 [0.13 , 75.08]
Laohapojanart 2007	1	16	0	20	3.5%	3.71 [0.16 , 85.29]
Padovani 2015	0	34	0	32		Not estimable
Papatsonis 1997	6	90	7	95	31.0%	0.90 [0.32 , 2.59]
Raymajhi 2003	2	30	1	32	6.2%	2.13 [0.20 , 22.33]
Read 1986	0	20	0	20		Not estimable
Van De Water 2008	1	43	1	48	4.6%	1.12 [0.07 , 17.31]
Weerakul 2002	0	44	0	45		Not estimable
Total (95% CI)		**574**		**642**	**100.0%**	**1.22 [0.68 , 2.20]**
Total events:	20		21			

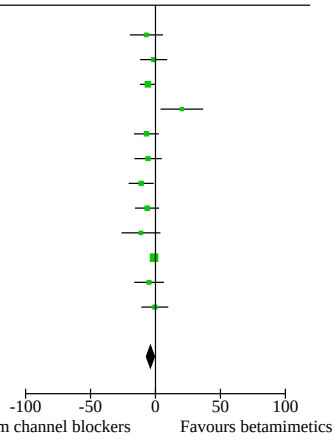
Heterogeneity: Tau² = 0.00; Chi² = 3.69, df = 9 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.67 (P = 0.50)
Test for subgroup differences: Not applicable



Analysis 8.4. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Betamimetics Mean	Betamimetics SD	Betamimetics Total	Calcium channel blockers Mean	Calcium channel blockers SD	Calcium channel blockers Total	Weight	Mean Difference IV, Random, 95% CI
Bracero 1991	21	21	19	28	21	23	4.9%	-7.00 [-19.76 , 5.76]
Cararach 2006	28	21.6	39	29.4	25.1	39	6.8%	-1.40 [-11.79 , 8.99]
Ganla 1999	16.5	14.5	50	22.4	15.6	50	14.0%	-5.90 [-11.80 , 0.00]
Garcia-Velasco 1998	64	36.8	26	43.7	21.6	26	3.2%	20.30 [3.90 , 36.70]
Janky 1990	35	15.6	32	42	21.9	30	7.8%	-7.00 [-16.52 , 2.52]
Kose 1995	15.8	19.5	21	21.5	23.7	52	6.7%	-5.70 [-16.24 , 4.84]
Padovani 2015	12	18.5	34	23	21.5	32	7.6%	-11.00 [-20.70 , -1.30]
Raymajhi 2003	19.2	17.8	30	25.7	19.5	32	8.1%	-6.50 [-15.79 , 2.79]
Read 1986	25.1	25.5	20	36.3	22.8	20	3.8%	-11.20 [-26.19 , 3.79]
Valdes 2012	25.6	6.7	66	26.7	6.4	66	24.5%	-1.10 [-3.34 , 1.14]
Van De Water 2008	30.1	27.7	43	35	27.7	48	5.9%	-4.90 [-16.30 , 6.50]
Weerakul 2002	27	25.7	44	27.5	24.1	45	6.9%	-0.50 [-10.86 , 9.86]
Total (95% CI)			**424**			**463**	**100.0%**	**-3.91 [-7.03 , -0.79]**

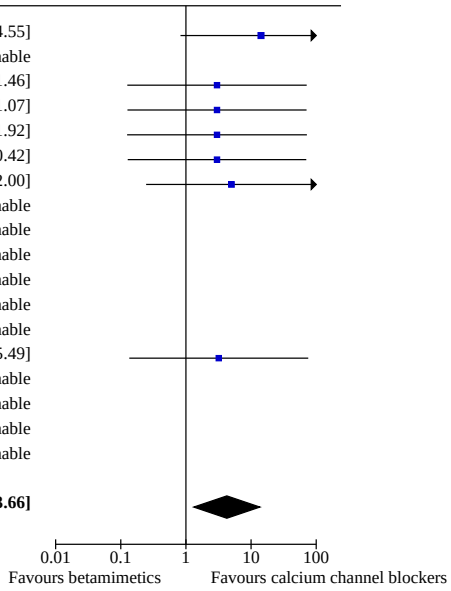
Heterogeneity: Tau² = 9.07; Chi² = 17.21, df = 11 (P = 0.10); I² = 36%
Test for overall effect: Z = 2.45 (P = 0.01)
Test for subgroup differences: Not applicable



Analysis 8.5. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	5	23	0	30	16.9%	14.21 [0.83 , 244.55]
Bracero 1991	0	23	0	26		Not estimable
Cararach 2006	1	39	0	39	13.6%	3.00 [0.13 , 71.46]
Ferguson 1990	1	33	0	33	13.6%	3.00 [0.13 , 71.07]
Ganla 1999	1	50	0	50	13.5%	3.00 [0.13 , 71.92]
Garcia-Velasco 1998	1	26	0	26	13.7%	3.00 [0.13 , 70.42]
Jaju 2011	2	60	0	60	15.0%	5.00 [0.25 , 102.00]
Jannet 1997	0	43	0	43		Not estimable
Kose 1995	0	21	0	52		Not estimable
Laohapojanart 2007	0	20	0	20		Not estimable
Mawaldi 2008	0	95	0	79		Not estimable
Padovani 2015	0	34	0	32		Not estimable
Papatsonis 1997	0	90	0	95		Not estimable
Raymajhi 2003	1	30	0	32	13.7%	3.19 [0.14 , 75.49]
Read 1986	0	20	0	20		Not estimable
Valdes 2012	0	66	0	66		Not estimable
Van De Water 2008	0	43	0	48		Not estimable
Weerakul 2002	0	44	0	45		Not estimable
Total (95% CI)		**760**		**796**	**100.0%**	**4.25 [1.32 , 13.66]**
Total events:	12		0			

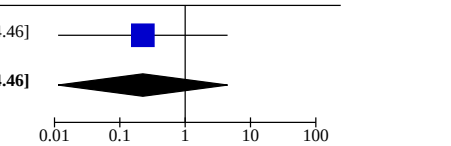
Heterogeneity: Tau² = 0.00; Chi² = 0.92, df = 6 (P = 0.99); I² = 0%
Test for overall effect: Z = 2.43 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 8.6. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 6: Maternal infection

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Bracero 1991	0	23	2	26	100.0%	0.23 [0.01 , 4.46]
Total (95% CI)		**23**		**26**	**100.0%**	**0.23 [0.01 , 4.46]**
Total events:	0		2			

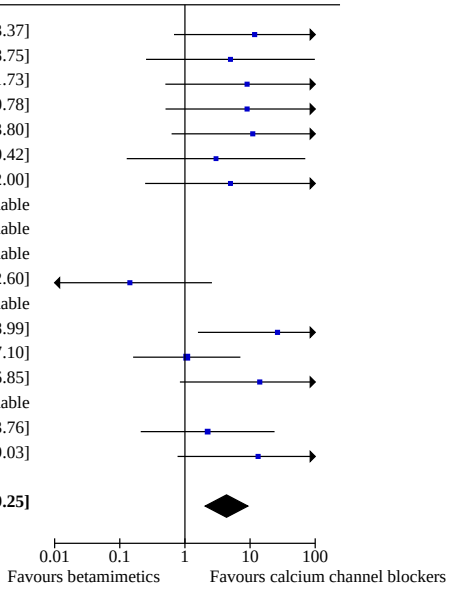
Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)
Test for subgroup differences: Not applicable



Analysis 8.7. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	5	28	0	30	7.0%	11.76 [0.68 , 203.37]
Bracero 1991	2	23	0	23	6.4%	5.00 [0.25 , 98.75]
Cararach 2006	4	39	0	39	6.8%	9.00 [0.50 , 161.73]
Ferguson 1990	4	33	0	33	6.8%	9.00 [0.50 , 160.78]
Ganla 1999	5	50	0	50	6.9%	11.00 [0.62 , 193.80]
Garcia-Velasco 1998	1	26	0	26	5.7%	3.00 [0.13 , 70.42]
Jaju 2011	2	60	0	60	6.3%	5.00 [0.25 , 102.00]
Janky 1990	0	32	0	30		Not estimable
Koks 1998	0	24	0	32		Not estimable
Kupferminc 1993	0	35	0	36		Not estimable
Laohapojanart 2007	0	20	3	20	6.8%	0.14 [0.01 , 2.60]
Padovani 2015	0	34	0	32		Not estimable
Papatsonis 1997	12	90	0	95	7.2%	26.37 [1.58 , 438.99]
Raymajhi 2003	2	30	2	32	15.8%	1.07 [0.16 , 7.10]
Trabelsi 2008	6	23	0	25	7.1%	14.08 [0.84 , 236.85]
Valdes 2012	0	66	0	66		Not estimable
Van De Water 2008	2	43	1	48	10.2%	2.23 [0.21 , 23.76]
Weerakul 2002	6	44	0	45	7.0%	13.29 [0.77 , 229.03]
Total (95% CI)		**700**		**722**	**100.0%**	**4.35 [2.05 , 9.25]**
Total events:	51		6			

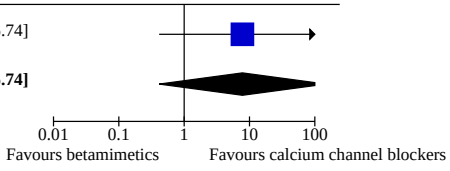
Heterogeneity: Tau² = 0.00; Chi² = 12.01, df = 12 (P = 0.45); I² = 0%
Test for overall effect: Z = 3.82 (P = 0.0001)
Test for subgroup differences: Not applicable



Analysis 8.8. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Van De Water 2008	3	43	0	48	100.0%	7.80 [0.41 , 146.74]
Total (95% CI)		**43**		**48**	**100.0%**	**7.80 [0.41 , 146.74]**
Total events:	3		0			

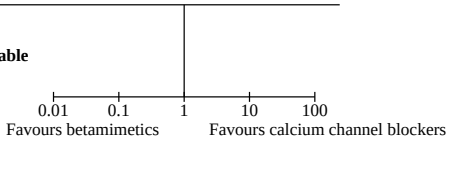
Heterogeneity: Not applicable
Test for overall effect: Z = 1.37 (P = 0.17)
Test for subgroup differences: Not applicable



Analysis 8.9. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

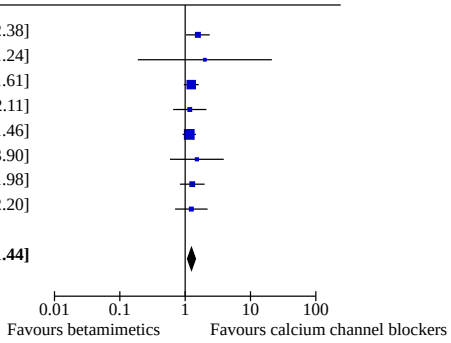
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 8.10. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	18	23	15	30	11.3%	1.57 [1.03 , 2.38]
Jannet 1997	2	43	1	43	0.4%	2.00 [0.19 , 21.24]
Koks 1998	36	47	34	55	28.8%	1.24 [0.95 , 1.61]
Padovani 2015	15	34	12	32	5.7%	1.18 [0.65 , 2.11]
Papatsonis 1997	58	90	53	95	35.3%	1.16 [0.91 , 1.46]
Valdes 2012	10	64	6	58	2.2%	1.51 [0.59 , 3.90]
Van De Water 2008	23	43	20	48	10.3%	1.28 [0.83 , 1.98]
Weerakul 2002	17	44	14	45	6.0%	1.24 [0.70 , 2.20]
Total (95% CI)		**388**		**406**	**100.0%**	**1.25 [1.09 , 1.44]**
Total events:	179		155			

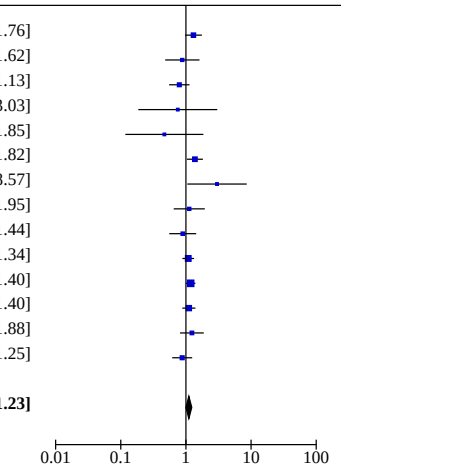
Heterogeneity: Tau² = 0.00; Chi² = 1.91, df = 7 (P = 0.96); I² = 0%
Test for overall effect: Z = 3.12 (P = 0.002)
Test for subgroup differences: Not applicable



Analysis 8.11. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	20	23	20	30	9.3%	1.30 [0.97 , 1.76]
Cararach 2006	13	39	14	37	2.7%	0.88 [0.48 , 1.62]
Ferguson 1990	19	33	24	33	6.9%	0.79 [0.55 , 1.13]
Garcia-Velasco 1998	3	26	4	26	0.5%	0.75 [0.19 , 3.03]
George 1991	2	10	6	14	0.5%	0.47 [0.12 , 1.85]
Jaju 2011	44	60	32	60	10.2%	1.38 [1.04 , 1.82]
Jannet 1997	12	43	4	43	0.9%	3.00 [1.05 , 8.57]
Kose 1995	10	21	22	52	3.2%	1.13 [0.65 , 1.95]
Laohapojanart 2007	10	16	14	20	4.2%	0.89 [0.55 , 1.44]
Padovani 2015	30	34	26	32	15.7%	1.09 [0.88 , 1.34]
Papatsonis 1997	64	78	66	95	19.9%	1.18 [1.00 , 1.40]
Raymajhi 2003	26	30	25	32	13.6%	1.11 [0.88 , 1.40]
Valdes 2012	30	64	22	58	5.3%	1.24 [0.81 , 1.88]
Weerakul 2002	24	44	28	45	7.1%	0.88 [0.62 , 1.25]
Total (95% CI)		**521**		**577**	**100.0%**	**1.11 [1.00 , 1.23]**
Total events:	307		307			

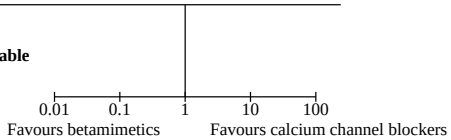
Heterogeneity: Tau² = 0.01; Chi² = 15.87, df = 13 (P = 0.26); I² = 18%
Test for overall effect: Z = 1.96 (P = 0.05)
Test for subgroup differences: Not applicable



Analysis 8.12. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 12: Maternal death

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

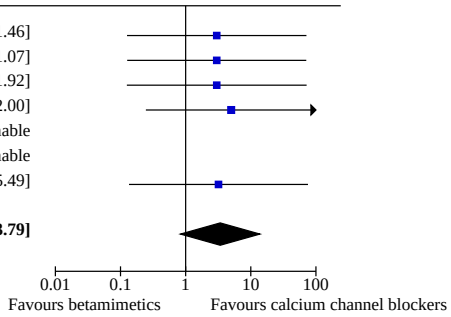
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 8.13. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 13: Pulmonary oedema

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cararach 2006	1	39	0	39	19.6%	3.00 [0.13 , 71.46]
Ferguson 1990	1	33	0	33	19.6%	3.00 [0.13 , 71.07]
Ganla 1999	1	50	0	50	19.5%	3.00 [0.13 , 71.92]
Jaju 2011	2	60	0	60	21.6%	5.00 [0.25 , 102.00]
Kose 1995	0	104	0	52		Not estimable
Laohapojanart 2007	0	20	0	20		Not estimable
Raymajhi 2003	1	30	0	32	19.7%	3.19 [0.14 , 75.49]
Total (95% CI)		**336**		**286**	**100.0%**	**3.39 [0.83 , 13.79]**
Total events:	6		0			

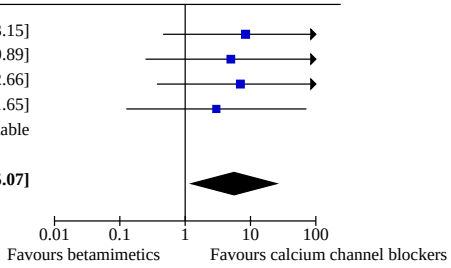
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 4 (P = 1.00); I² = 0%
Test for overall effect: Z = 1.71 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 8.14. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 14: Dyspnoea

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bracero 1991	3	19	0	23	26.7%	8.40 [0.46 , 153.15]
Cararach 2006	2	39	0	39	24.9%	5.00 [0.25 , 100.89]
Jaju 2011	3	60	0	60	26.0%	7.00 [0.37 , 132.66]
Jannet 1997	1	43	0	43	22.4%	3.00 [0.13 , 71.65]
Trabelsi 2008	0	23	0	25		Not estimable
Total (95% CI)		**184**		**190**	**100.0%**	**5.59 [1.25 , 25.07]**
Total events:	9		0			

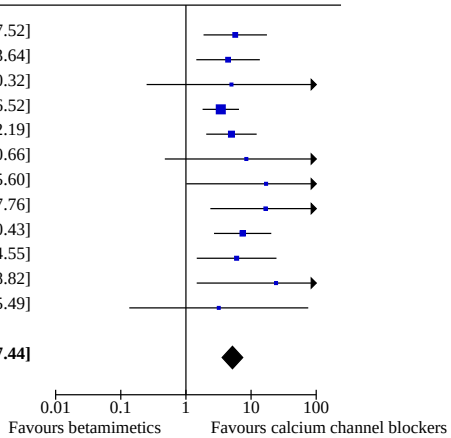
Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 3 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.25 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 8.15. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 15: Palpitations

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	16	28	3	30	10.5%	5.71 [1.86 , 17.52]
Bracero 1991	11	19	3	23	10.4%	4.44 [1.44 , 13.64]
Ferguson 1990	2	33	0	33	1.5%	5.00 [0.25 , 100.32]
Garcia-Velasco 1998	24	26	7	26	31.8%	3.43 [1.80 , 6.52]
Jaju 2011	25	60	5	60	16.6%	5.00 [2.05 , 12.19]
Janky 1990	4	32	0	30	1.6%	8.45 [0.47 , 150.66]
Jannet 1997	8	43	0	43	1.7%	17.00 [1.01 , 285.60]
Koks 1998	13	21	1	27	3.5%	16.71 [2.37 , 117.76]
Kose 1995	12	21	4	52	12.9%	7.43 [2.70 , 20.43]
Kupferminc 1993	12	30	2	30	6.6%	6.00 [1.47 , 24.55]
Mawaldi 2008	14	95	0	79	1.7%	24.17 [1.46 , 398.82]
Raymajhi 2003	1	30	0	32	1.3%	3.19 [0.14 , 75.49]
Total (95% CI)		**438**		**465**	**100.0%**	**5.18 [3.60 , 7.44]**
Total events:	142		25			

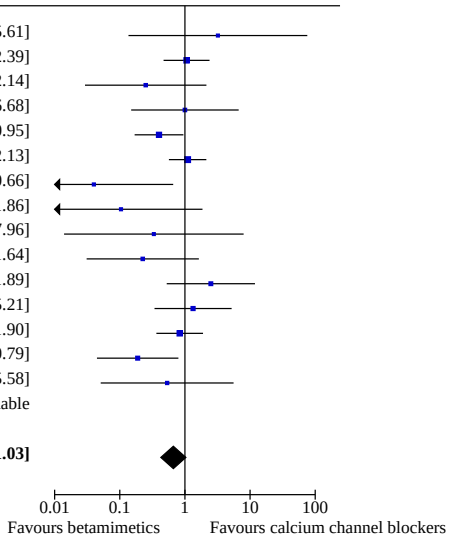
Heterogeneity: Tau² = 0.00; Chi² = 5.65, df = 11 (P = 0.90); I² = 0%
Test for overall effect: Z = 8.88 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 8.16. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 16: Headaches

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	1	28	0	30	1.8%	3.21 [0.14 , 75.61]
Bracero 1991	7	19	8	23	13.7%	1.06 [0.47 , 2.39]
Cararach 2006	1	39	4	39	3.6%	0.25 [0.03 , 2.14]
Ferguson 1990	2	33	2	33	4.5%	1.00 [0.15 , 6.68]
Ganla 1999	6	50	15	50	12.9%	0.40 [0.17 , 0.95]
Garcia-Velasco 1998	11	26	10	26	16.2%	1.10 [0.57 , 2.13]
Jaju 2011	0	60	12	60	2.3%	0.04 [0.00 , 0.66]
Janky 1990	0	32	4	30	2.2%	0.10 [0.01 , 1.86]
Jannet 1997	0	43	1	43	1.8%	0.33 [0.01 , 7.96]
Kose 1995	1	21	11	52	4.1%	0.23 [0.03 , 1.64]
Kupferminc 1993	5	30	2	30	6.1%	2.50 [0.53 , 11.89]
Laohapojanart 2007	4	20	3	20	7.4%	1.33 [0.34 , 5.21]
Mawaldi 2008	10	95	10	79	13.5%	0.83 [0.36 , 1.90]
Padovani 2015	2	34	10	32	6.9%	0.19 [0.04 , 0.79]
Raymajhi 2003	1	30	2	32	3.1%	0.53 [0.05 , 5.58]
Trabelsi 2008	0	23	0	25		Not estimable
Total (95% CI)		**583**		**604**	**100.0%**	**0.66 [0.43 , 1.03]**
Total events:	51		94			

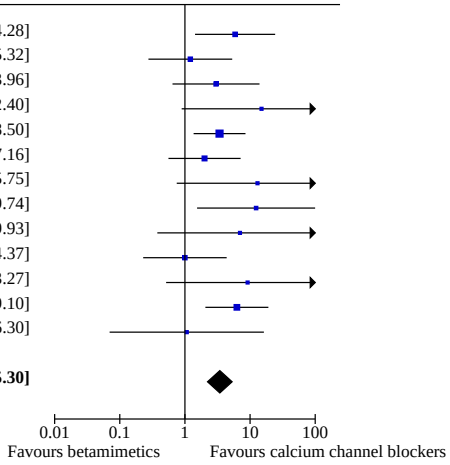
Heterogeneity: Tau² = 0.20; Chi² = 20.23, df = 14 (P = 0.12); I² = 31%
Test for overall effect: Z = 1.82 (P = 0.07)
Test for subgroup differences: Not applicable



Analysis 8.17. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 17: Nausea or vomiting

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	11	28	2	30	9.4%	5.89 [1.43 , 24.28]
Bracero 1991	3	19	3	23	8.6%	1.21 [0.28 , 5.32]
Cararach 2006	6	39	2	39	8.0%	3.00 [0.64 , 13.96]
Ferguson 1990	7	33	0	33	2.4%	15.00 [0.89 , 252.40]
Ganla 1999	17	50	5	50	22.4%	3.40 [1.36 , 8.50]
Garcia-Velasco 1998	6	26	3	26	11.6%	2.00 [0.56 , 7.16]
Jaju 2011	6	60	0	60	2.3%	13.00 [0.75 , 225.75]
Kose 1995	5	21	1	52	4.3%	12.38 [1.54 , 99.74]
Kupferminc 1993	3	30	0	30	2.2%	7.00 [0.38 , 129.93]
Laohapojanart 2007	3	20	3	20	8.7%	1.00 [0.23 , 4.37]
Mawaldi 2008	5	95	0	79	2.3%	9.17 [0.51 , 163.27]
Padovani 2015	20	34	3	32	15.2%	6.27 [2.06 , 19.10]
Raymajhi 2003	1	30	1	32	2.5%	1.07 [0.07 , 16.30]
Total (95% CI)		**485**		**506**	**100.0%**	**3.43 [2.22 , 5.30]**
Total events:	93		23			

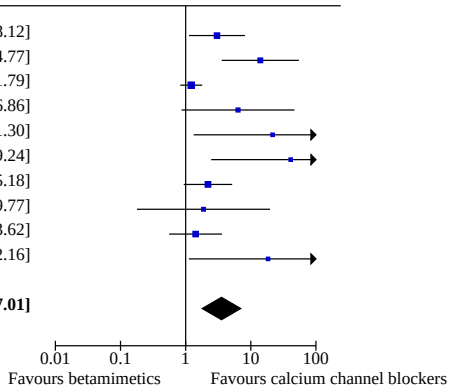
Heterogeneity: Tau² = 0.00; Chi² = 11.71, df = 12 (P = 0.47); I² = 0%
Test for overall effect: Z = 5.57 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 8.18. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 18: Tachycardia

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Bracero 1991	10	19	4	23	14.0%	3.03 [1.13 , 8.12]
Cararach 2006	28	39	2	39	11.0%	14.00 [3.58 , 54.77]
Ganla 1999	28	50	23	50	18.6%	1.22 [0.83 , 1.79]
George 1991	5	11	1	14	7.3%	6.36 [0.86 , 46.86]
Janky 1990	11	32	0	30	4.6%	21.61 [1.33 , 351.30]
Kose 1995	8	21	0	52	4.5%	40.95 [2.47 , 679.24]
Laohapojanart 2007	11	20	5	20	15.1%	2.20 [0.93 , 5.18]
Padovani 2015	2	34	1	32	5.9%	1.88 [0.18 , 19.77]
Raymajhi 2003	8	30	6	32	14.4%	1.42 [0.56 , 3.62]
Trabelsi 2008	8	23	0	25	4.6%	18.42 [1.12 , 302.16]
Total (95% CI)		**279**		**317**	**100.0%**	**3.55 [1.80 , 7.01]**
Total events:	119		42			

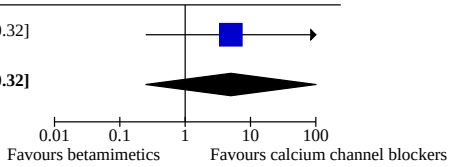
Heterogeneity: Tau² = 0.61; Chi² = 26.06, df = 9 (P = 0.002); I² = 65%
Test for overall effect: Z = 3.65 (P = 0.0003)
Test for subgroup differences: Not applicable



Analysis 8.19. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Ferguson 1990	2	33	0	33	100.0%	5.00 [0.25 , 100.32]
Total (95% CI)		**33**		**33**	**100.0%**	**5.00 [0.25 , 100.32]**
Total events:	2		0			

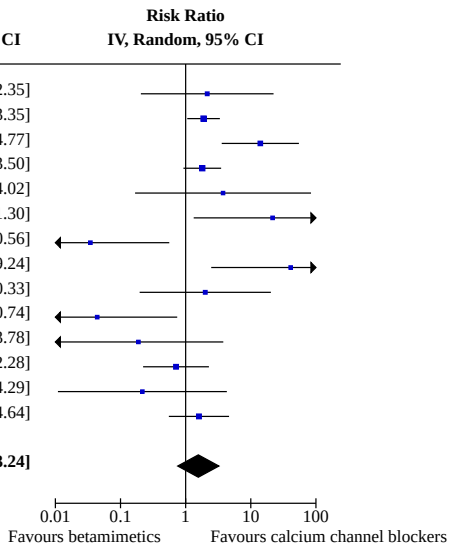
Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)
Test for subgroup differences: Not applicable



Analysis 8.20. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 20: Maternal hypotension

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	2	28	1	30	5.8%	2.14 [0.21 , 22.35]
Bracero 1991	14	19	9	23	13.3%	1.88 [1.06 , 3.35]
Cararach 2006	28	39	2	39	9.6%	14.00 [3.58 , 54.77]
Ganla 1999	18	50	10	50	13.0%	1.80 [0.92 , 3.50]
George 1991	1	11	0	14	4.0%	3.75 [0.17 , 84.02]
Janky 1990	11	32	0	30	4.6%	21.61 [1.33 , 351.30]
Jannet 1997	0	43	14	43	4.6%	0.03 [0.00 , 0.56]
Kose 1995	8	21	0	52	4.6%	40.95 [2.47 , 679.24]
Laohapojanart 2007	2	20	1	20	5.9%	2.00 [0.20 , 20.33]
Mawaldi 2008	0	95	9	79	4.5%	0.04 [0.00 , 0.74]
Padovani 2015	0	34	2	32	4.2%	0.19 [0.01 , 3.78]
Raymajhi 2003	4	30	6	32	10.6%	0.71 [0.22 , 2.28]
Trabelsi 2008	0	23	2	25	4.2%	0.22 [0.01 , 4.29]
Valdes 2012	8	66	5	66	11.1%	1.60 [0.55 , 4.64]
Total (95% CI)		**511**		**535**	**100.0%**	**1.56 [0.76 , 3.24]**
Total events:	96		61			

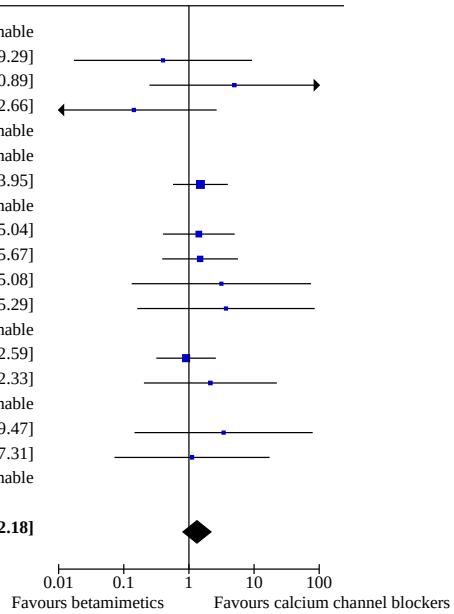
Heterogeneity: Tau² = 0.95; Chi² = 37.71, df = 13 (P = 0.0003); I² = 66%
Test for overall effect: Z = 1.21 (P = 0.23)
Test for subgroup differences: Not applicable



Analysis 8.21. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 21: Perinatal death

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	0	23	0	30		Not estimable
Bracero 1991	0	19	1	23	2.5%	0.40 [0.02 , 9.29]
Cararach 2006	2	39	0	39	2.7%	5.00 [0.25 , 100.89]
Ferguson 1990	0	33	3	33	2.9%	0.14 [0.01 , 2.66]
Garcia-Velasco 1998	0	26	0	26		Not estimable
George 1991	0	11	0	14		Not estimable
Jaju 2011	9	60	6	60	26.0%	1.50 [0.57 , 3.95]
Janky 1990	0	32	0	30		Not estimable
Koks 1998	5	59	4	67	15.2%	1.42 [0.40 , 5.04]
Kose 1995	3	21	5	52	13.6%	1.49 [0.39 , 5.67]
Kupferminc 1993	1	39	0	41	2.4%	3.15 [0.13 , 75.08]
Laohapojanart 2007	1	16	0	20	2.5%	3.71 [0.16 , 85.29]
Padovani 2015	0	32	0	34		Not estimable
Papatsonis 1997	6	90	7	95	22.1%	0.90 [0.32 , 2.59]
Raymajhi 2003	2	30	1	32	4.4%	2.13 [0.20 , 22.33]
Read 1986	0	20	0	20		Not estimable
Trabelsi 2008	1	21	0	24	2.5%	3.41 [0.15 , 79.47]
Van De Water 2008	1	43	1	48	3.3%	1.12 [0.07 , 17.31]
Weerakul 2002	0	44	0	45		Not estimable
Total (95% CI)		**658**		**733**	**100.0%**	**1.33 [0.81 , 2.18]**
Total events:	31		28			

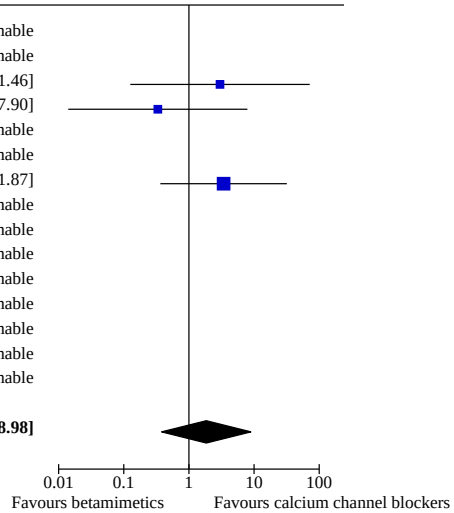
Heterogeneity: Tau² = 0.00; Chi² = 5.36, df = 11 (P = 0.91); I² = 0%
Test for overall effect: Z = 1.12 (P = 0.26)
Test for subgroup differences: Not applicable



Analysis 8.22. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 22: Stillbirth

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	0	23	0	30		Not estimable
Bracero 1991	0	19	0	23		Not estimable
Cararach 2006	1	39	0	39	24.9%	3.00 [0.13 , 71.46]
Ferguson 1990	0	33	1	33	25.0%	0.33 [0.01 , 7.90]
Garcia-Velasco 1998	0	26	0	26		Not estimable
Janky 1990	0	32	0	30		Not estimable
Koks 1998	3	59	1	67	50.1%	3.41 [0.36 , 31.87]
Kose 1995	0	21	0	52		Not estimable
Kupferminc 1993	0	39	0	41		Not estimable
Laohapojanart 2007	0	16	0	20		Not estimable
Papatsonis 1997	0	90	0	95		Not estimable
Raymajhi 2003	0	30	0	32		Not estimable
Read 1986	0	20	0	20		Not estimable
Van De Water 2008	0	43	0	48		Not estimable
Weerakul 2002	0	44	0	45		Not estimable
Total (95% CI)		**534**		**601**	**100.0%**	**1.85 [0.38 , 8.98]**
Total events:	4		2			

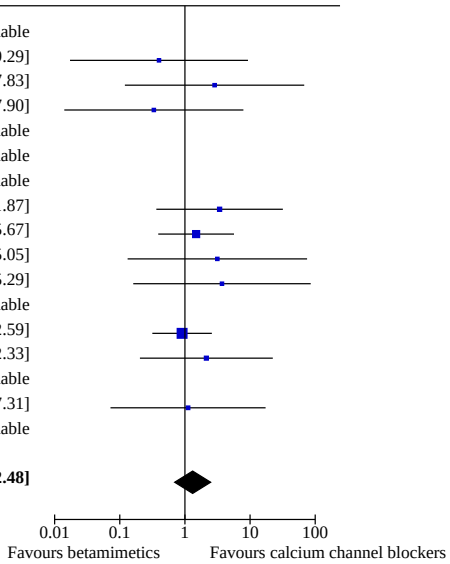
Heterogeneity: Tau² = 0.00; Chi² = 1.50, df = 2 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.76 (P = 0.45)
Test for subgroup differences: Not applicable



Analysis 8.23. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	0	23	0	30		Not estimable
Bracero 1991	0	19	1	23	4.1%	0.40 [0.02 , 9.29]
Cararach 2006	1	39	0	37	4.0%	2.85 [0.12 , 67.83]
Ferguson 1990	0	33	1	33	4.0%	0.33 [0.01 , 7.90]
Garcia-Velasco 1998	0	26	0	26		Not estimable
George 1991	0	11	0	14		Not estimable
Janky 1990	0	32	0	30		Not estimable
Koks 1998	3	59	1	67	8.1%	3.41 [0.36 , 31.87]
Kose 1995	3	21	5	52	22.5%	1.49 [0.39 , 5.67]
Kupferminc 1993	1	40	0	42	4.0%	3.15 [0.13 , 75.05]
Laohapojanart 2007	1	16	0	20	4.1%	3.71 [0.16 , 85.29]
Padovani 2015	0	34	0	32		Not estimable
Papatsonis 1997	6	90	7	95	36.5%	0.90 [0.32 , 2.59]
Raymajhi 2003	2	30	1	32	7.3%	2.13 [0.20 , 22.33]
Read 1986	0	20	0	20		Not estimable
Van De Water 2008	1	43	1	48	5.4%	1.12 [0.07 , 17.31]
Weerakul 2002	0	44	0	45		Not estimable
Total (95% CI)		**580**		**646**	**100.0%**	**1.31 [0.70 , 2.48]**
Total events:	18		17			

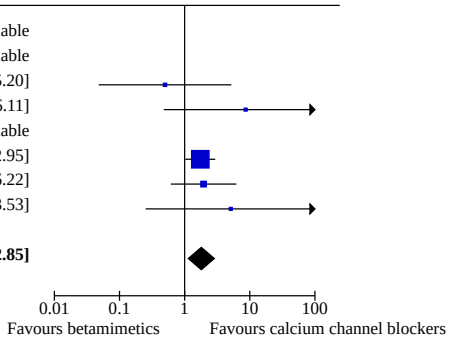
Heterogeneity: Tau² = 0.00; Chi² = 3.60, df = 9 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.84 (P = 0.40)
Test for subgroup differences: Not applicable



Analysis 8.24. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Betamimetics Events	Betamimetics Total	Calcium channel blockers Events	Calcium channel blockers Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	0	23	0	30		Not estimable
Cararach 2006	0	39	0	39		Not estimable
Ferguson 1990	1	28	2	28	3.9%	0.50 [0.05 , 5.20]
Laohapojanart 2007	3	16	0	20	2.5%	8.65 [0.48 , 156.11]
Padovani 2015	0	34	0	32		Not estimable
Papatsonis 1997	28	90	17	95	75.5%	1.74 [1.02 , 2.95]
Van De Water 2008	7	43	4	48	15.8%	1.95 [0.61 , 6.22]
Weerakul 2002	2	44	0	45	2.3%	5.11 [0.25 , 103.53]
Total (95% CI)		**317**		**337**	**100.0%**	**1.80 [1.14 , 2.85]**
Total events:	41		23			

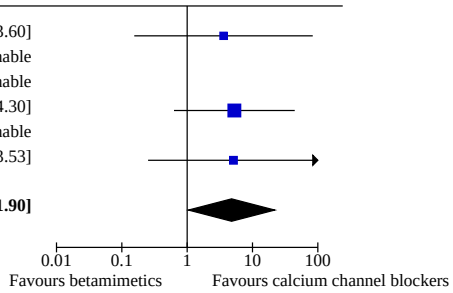
Heterogeneity: Tau² = 0.00; Chi² = 2.78, df = 4 (P = 0.60); I² = 0%
Test for overall effect: Z = 2.51 (P = 0.01)
Test for subgroup differences: Not applicable



Analysis 8.25. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bracero 1991	1	19	0	23	23.4%	3.60 [0.16 , 83.60]
Cararach 2006	0	39	0	39		Not estimable
Padovani 2015	0	34	0	32		Not estimable
Papatsonis 1997	5	90	1	95	51.1%	5.28 [0.63 , 44.30]
Van De Water 2008	0	43	0	48		Not estimable
Weerakul 2002	2	44	0	45	25.5%	5.11 [0.25 , 103.53]
Total (95% CI)		**269**		**282**	**100.0%**	**4.79 [1.05 , 21.90]**
Total events:	8		1			

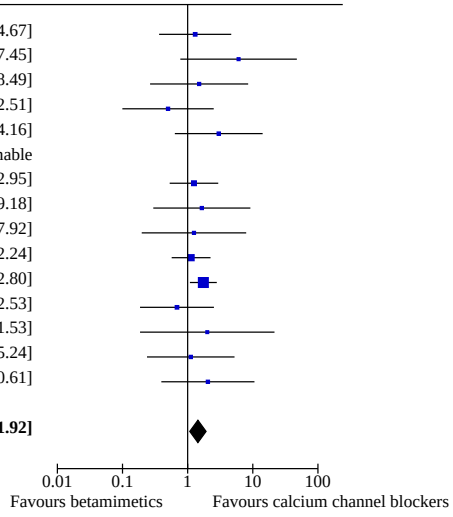
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 2 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.02 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 8.26. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 26: Respiratory morbidity

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	4	23	4	30	5.1%	1.30 [0.36 , 4.67]
Bracero 1991	5	19	1	23	2.0%	6.05 [0.77 , 47.45]
Cararach 2006	3	39	2	39	2.8%	1.50 [0.27 , 8.49]
Ferguson 1990	2	28	4	28	3.2%	0.50 [0.10 , 2.51]
Ganla 1999	6	50	2	50	3.4%	3.00 [0.64 , 14.16]
George 1991	0	11	0	14		Not estimable
Jaju 2011	10	60	8	60	11.2%	1.25 [0.53 , 2.95]
Kose 1995	2	21	3	52	2.8%	1.65 [0.30 , 9.18]
Laohapojanart 2007	2	16	2	20	2.4%	1.25 [0.20 , 7.92]
Padovani 2015	12	34	10	32	17.6%	1.13 [0.57 , 2.24]
Papatsonis 1997	33	90	20	95	36.7%	1.74 [1.08 , 2.80]
Trabelsi 2008	3	21	5	24	4.9%	0.69 [0.19 , 2.53]
Valdes 2012	2	66	1	66	1.5%	2.00 [0.19 , 21.53]
Van De Water 2008	3	43	3	48	3.5%	1.12 [0.24 , 5.24]
Weerakul 2002	4	44	2	45	3.1%	2.05 [0.39 , 10.61]
Total (95% CI)		**565**		**626**	**100.0%**	**1.44 [1.08 , 1.92]**
Total events:	91		67			

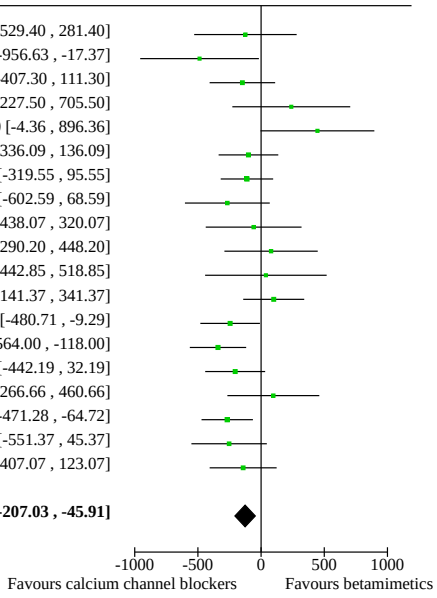
Heterogeneity: Tau² = 0.00; Chi² = 7.24, df = 13 (P = 0.89); I² = 0%
Test for overall effect: Z = 2.47 (P = 0.01)
Test for subgroup differences: Not applicable



Analysis 8.27. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 27: Mean birthweight

Study or Subgroup	Betamimetics Mean	SD	Total	Calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Al Qattan 2000	2078	711	23	2202	790	30	3.3%	-124.00 [-529.40 , 281.40]
Bracero 1991	2336	781	19	2823	763	23	2.5%	-487.00 [-956.63 , -17.37]
Cararach 2006	2722	676	39	2870	475	39	6.4%	-148.00 [-407.30 , 111.30]
Ferguson 1990	2467	901	28	2228	880	28	2.6%	239.00 [-227.50 , 705.50]
Garcia-Velasco 1998	3100	694	26	2654	944	26	2.7%	446.00 [-4.36 , 896.36]
Janky 1990	2900	474	32	3000	474	30	7.2%	-100.00 [-336.09 , 136.09]
Jannet 1997	3019	494	43	3131	488	43	8.3%	-112.00 [-319.55 , 95.55]
Koks 1998	1696	930	59	1963	991	67	4.4%	-267.00 [-602.59 , 68.59]
Kose 1995	2688	716	21	2747	822	52	3.6%	-59.00 [-438.07 , 320.07]
Kupferminc 1993	2471	738	30	2392	721	30	3.8%	79.00 [-290.20 , 448.20]
Laohapojanart 2007	2368	731	16	2330	732	20	2.4%	38.00 [-442.85 , 518.85]
Padovani 2015	2500	500	34	2400	500	32	7.0%	100.00 [-141.37 , 341.37]
Papatsonis 1997	1875	707	90	2120	920	95	7.2%	-245.00 [-480.71 , -9.29]
Raymajhi 2003	2042	413	30	2383	482	32	7.7%	-341.00 [-564.00 , -118.00]
Read 1986	3020	326	20	3225	432	20	7.1%	-205.00 [-442.19 , 32.19]
Trabelsi 2008	2747	525	21	2650	715	24	3.9%	97.00 [-266.66 , 460.66]
Valdes 2012	2784	794	66	3052	282	66	8.5%	-268.00 [-471.28 , -64.72]
Van De Water 2008	2281	725	43	2534	725	48	5.2%	-253.00 [-551.37 , 45.37]
Weerakul 2002	2508	684	44	2650	587	45	6.2%	-142.00 [-407.07 , 123.07]
Total (95% CI)			**684**			**750**	**100.0%**	**-126.47 [-207.03 , -45.91]**

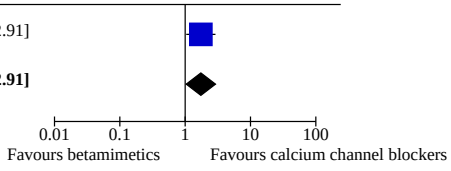
Heterogeneity: Tau² = 9067.56; Chi² = 25.60, df = 18 (P = 0.11); I² = 30%
Test for overall effect: Z = 3.08 (P = 0.002)
Test for subgroup differences: Not applicable



Analysis 8.28. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	16	23	12	30	100.0%	1.74 [1.04 , 2.91]
Total (95% CI)		**23**		**30**	**100.0%**	**1.74 [1.04 , 2.91]**
Total events:	16		12			

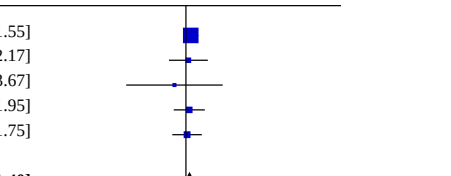
Heterogeneity: Not applicable
Test for overall effect: Z = 2.11 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 8.29. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Qattan 2000	20	23	22	30	59.6%	1.19 [0.91 , 1.55]
Cararach 2006	12	39	11	39	9.0%	1.09 [0.55 , 2.17]
Garcia-Velasco 1998	2	26	3	26	1.5%	0.67 [0.12 , 3.67]
Kose 1995	10	21	22	52	14.1%	1.13 [0.65 , 1.95]
Laohapojanart 2007	10	16	12	20	15.7%	1.04 [0.62 , 1.75]
Total (95% CI)		**125**		**167**	**100.0%**	**1.14 [0.92 , 1.40]**
Total events:	54		70			

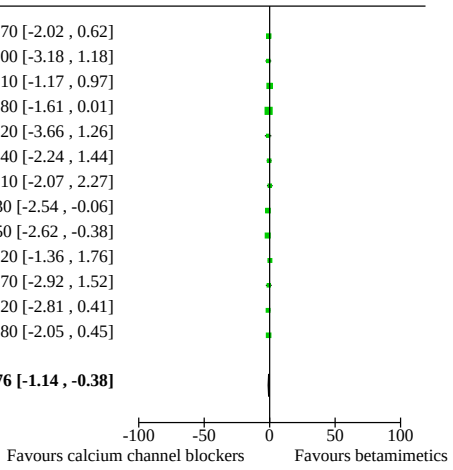
Heterogeneity: Tau² = 0.00; Chi² = 0.59, df = 4 (P = 0.96); I² = 0%
Test for overall effect: Z = 1.20 (P = 0.23)
Test for subgroup differences: Not applicable



Analysis 8.30. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 30: Gestational age at birth

Study or Subgroup	Betamimetics Mean	SD	Total	Calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Al Qattan 2000	29.5	2.3	23	30.2	2.6	30	8.2%	-0.70 [-2.02 , 0.62]
Bracero 1991	35	4	19	36	3	23	3.0%	-1.00 [-3.18 , 1.18]
Cararach 2006	36.1	2.4	39	36.2	2.4	39	12.7%	-0.10 [-1.17 , 0.97]
Jannet 1997	37.6	2.1	43	38.4	1.7	43	22.0%	-0.80 [-1.61 , 0.01]
Koks 1998	31.7	6.9	59	32.9	7.2	67	2.4%	-1.20 [-3.66 , 1.26]
Kose 1995	35.7	3.8	21	36.1	3.2	52	4.2%	-0.40 [-2.24 , 1.44]
Laohapojanart 2007	34.6	3.6	16	34.5	2.9	20	3.0%	0.10 [-2.07 , 2.27]
Papatsonis 1997	32.1	4.1	90	33.4	4.5	95	9.4%	-1.30 [-2.54 , -0.06]
Raymajhi 2003	33.5	2.2	30	35	2.3	32	11.5%	-1.50 [-2.62 , -0.38]
Trabelsi 2008	35.3	2.1	21	35.1	3.2	24	5.9%	0.20 [-1.36 , 1.76]
Valdes 2012	25.5	6.9	66	26.2	6.1	66	2.9%	-0.70 [-2.92 , 1.52]
Van De Water 2008	34.4	4	43	35.6	3.8	48	5.6%	-1.20 [-2.81 , 0.41]
Weerakul 2002	34.9	3.1	44	35.7	2.9	45	9.2%	-0.80 [-2.05 , 0.45]
Total (95% CI)			**514**			**584**	**100.0%**	**-0.76 [-1.14 , -0.38]**

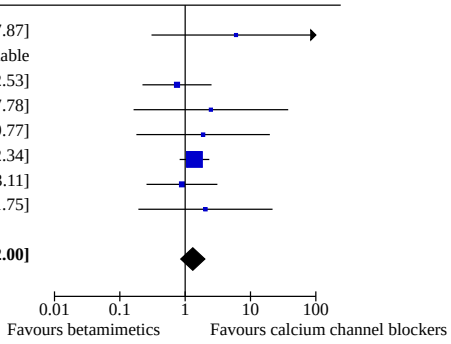
Heterogeneity: Tau² = 0.00; Chi² = 6.56, df = 12 (P = 0.89); I² = 0%
Test for overall effect: Z = 3.94 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 8.31. Comparison 8: Betamimetics vs calcium channel blockers, Outcome 31: Neonatal infection

Study or Subgroup	Betamimetics Events	Total	Calcium channel blockers Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bracero 1991	2	19	0	23	2.0%	6.00 [0.31 , 117.87]
Cararach 2006	0	39	0	39		Not estimable
Janky 1990	4	32	5	30	12.1%	0.75 [0.22 , 2.53]
Kose 1995	1	21	1	52	2.4%	2.48 [0.16 , 37.78]
Padovani 2015	2	34	1	32	3.2%	1.88 [0.18 , 19.77]
Papatsonis 1997	25	90	19	95	65.6%	1.39 [0.82 , 2.34]
Van De Water 2008	4	43	5	48	11.5%	0.89 [0.26 , 3.11]
Weerakul 2002	2	44	1	45	3.2%	2.05 [0.19 , 21.75]
Total (95% CI)		**322**		**364**	**100.0%**	**1.31 [0.86 , 2.00]**
Total events:	40		32			

Heterogeneity: Tau² = 0.00; Chi² = 2.66, df = 6 (P = 0.85); I² = 0%
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable



Comparison 9. Betamimetics vs COX inhibitors

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Delay in birth by 48 hours	2	100	Risk Ratio (IV, Random, 95% CI)	0.84 [0.72, 0.99]
9.2 Delay in birth by 7 days	1	40	Risk Ratio (IV, Random, 95% CI)	0.98 [0.63, 1.51]
9.3 Neonatal death before 28 days	3	114	Risk Ratio (IV, Random, 95% CI)	0.73 [0.09, 5.66]
9.4 Pregnancy prolongation (time from trial entry to birth in days)	2	78	Mean Difference (IV, Random, 95% CI)	-7.07 [-18.16, 4.01]
9.5 Serious adverse effects of drugs	3	120	Risk Ratio (IV, Random, 95% CI)	Not estimable

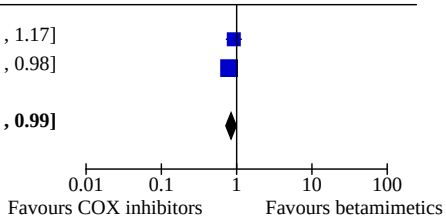
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.7 Cessation of treatment due to adverse effects	2	60	Risk Ratio (IV, Random, 95% CI)	3.63 [0.16, 84.11]
9.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.11 Birth before 37 weeks' gestation	2	80	Risk Ratio (IV, Random, 95% CI)	0.53 [0.28, 0.99]
9.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.13 Pulmonary oedema	2	80	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.14 Dyspnoea	3	120	Risk Ratio (IV, Random, 95% CI)	9.79 [1.30, 73.81]
9.15 Palpitations	2	100	Risk Ratio (IV, Random, 95% CI)	10.10 [2.00, 51.05]
9.16 Headaches	1	40	Risk Ratio (IV, Random, 95% CI)	11.00 [1.53, 78.86]
9.17 Nausea or vomiting	3	120	Risk Ratio (IV, Random, 95% CI)	0.87 [0.47, 1.61]
9.18 Tachycardia	2	80	Risk Ratio (IV, Random, 95% CI)	11.00 [0.69, 175.86]
9.19 Maternal cardiac arrhythmias	1	60	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.20 Maternal hypotension	2	80	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.21 Perinatal death	3	114	Risk Ratio (IV, Random, 95% CI)	0.73 [0.09, 5.66]
9.22 Stillbirth	1	20	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.23 Neonatal death before 7 days	2	69	Risk Ratio (IV, Random, 95% CI)	0.35 [0.01, 8.12]
9.24 Neurodevelopmental morbidity	3	114	Risk Ratio (IV, Random, 95% CI)	0.60 [0.14, 2.59]
9.25 Gastrointestinal morbidity	2	69	Risk Ratio (IV, Random, 95% CI)	0.35 [0.01, 8.12]
9.26 Respiratory morbidity	1	60	Risk Ratio (IV, Random, 95% CI)	0.67 [0.12, 3.71]
9.27 Mean birthweight	2	94	Mean Difference (IV, Random, 95% CI)	-192.87 [-590.66, 204.92]
9.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
9.30 Gestational age at birth	2	89	Mean Difference (IV, Random, 95% CI)	-1.55 [-3.49, 0.40]
9.31 Neonatal infection	2	69	Risk Ratio (IV, Random, 95% CI)	1.04 [0.07, 15.73]

Analysis 9.1. Comparison 9: Betamimetics vs COX inhibitors, Outcome 1: Delay in birth by 48 hours

	Betamimetics		COX inhibitors			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Besinger 1991	15	18	20	22	41.9%	0.92 [0.72 , 1.17]	
Kurki 1991b	23	30	29	30	58.1%	0.79 [0.64 , 0.98]	
Total (95% CI)		**48**		**52**	**100.0%**	**0.84 [0.72 , 0.99]**	
Total events:	38		49				

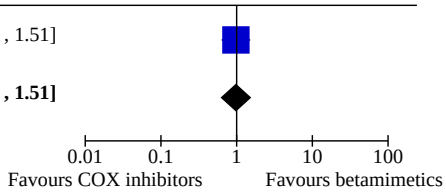
Heterogeneity: Tau² = 0.00; Chi² = 0.78, df = 1 (P = 0.38); I² = 0%
Test for overall effect: Z = 2.11 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 9.2. Comparison 9: Betamimetics vs COX inhibitors, Outcome 2: Delay in birth by 7 days

	Betamimetics		COX inhibitors			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Besinger 1991	12	18	15	22	100.0%	0.98 [0.63 , 1.51]	
Total (95% CI)		**18**		**22**	**100.0%**	**0.98 [0.63 , 1.51]**	
Total events:	12		15				

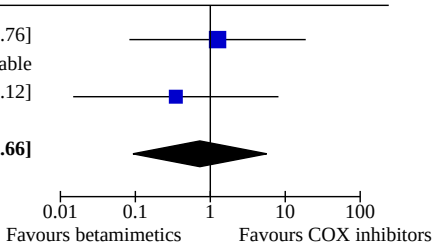
Heterogeneity: Not applicable
Test for overall effect: Z = 0.10 (P = 0.92)
Test for subgroup differences: Not applicable



Analysis 9.3. Comparison 9: Betamimetics vs COX inhibitors, Outcome 3: Neonatal death before 28 days

	Betamimetics		COX inhibitors			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Besinger 1991	1	20	1	25	57.5%	1.25 [0.08 , 18.76]	
Kramer 1999	0	10	0	10		Not estimable	
Kurki 1991b	0	24	1	25	42.5%	0.35 [0.01 , 8.12]	
Total (95% CI)		**54**		**60**	**100.0%**	**0.73 [0.09 , 5.66]**	
Total events:	1		2				

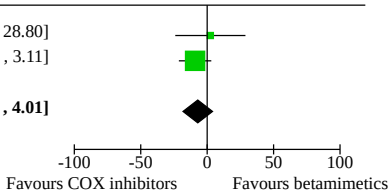
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.76)
Test for subgroup differences: Not applicable



Analysis 9.4. Comparison 9: Betamimetics vs COX inhibitors, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Betamimetics Mean	SD	Total	COX inhibitors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Besinger 1991	27.9	44.9	18	25.5	39.1	22	17.6%	2.40 [-24.00 , 28.80]
Kurki 1991b	55.9	16.4	16	65	22	22	82.4%	-9.10 [-21.31 , 3.11]
Total (95% CI)			**34**			**44**	**100.0%**	**-7.07 [-18.16 , 4.01]**

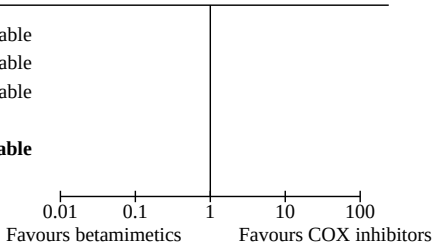
Heterogeneity: Tau² = 0.00; Chi² = 0.60, df = 1 (P = 0.44); I² = 0%
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable



Analysis 9.5. Comparison 9: Betamimetics vs COX inhibitors, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	0	18	0	22		Not estimable
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	0	30	0	30		Not estimable
Total (95% CI)		**58**		**62**		**Not estimable**
Total events:	0		0			

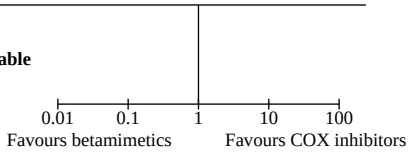
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.6. Comparison 9: Betamimetics vs COX inhibitors, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

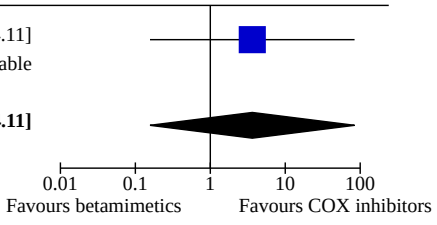
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.7. Comparison 9: Betamimetics vs COX inhibitors, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	1	18	0	22	100.0%	3.63 [0.16 , 84.11]
Kramer 1999	0	10	0	10		Not estimable
Total (95% CI)		**28**		**32**	**100.0%**	**3.63 [0.16 , 84.11]**
Total events:	1		0			

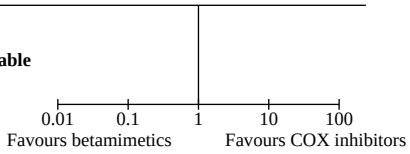
Heterogeneity: Not applicable
Test for overall effect: Z = 0.80 (P = 0.42)
Test for subgroup differences: Not applicable



Analysis 9.8. Comparison 9: Betamimetics vs COX inhibitors, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

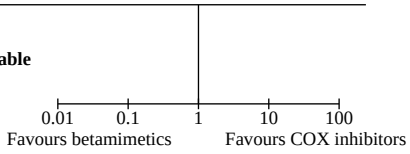
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.9. Comparison 9: Betamimetics vs COX inhibitors, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

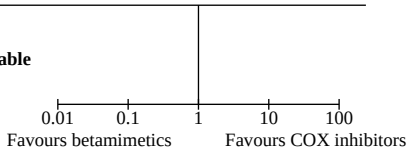
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.10. Comparison 9: Betamimetics vs COX inhibitors, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

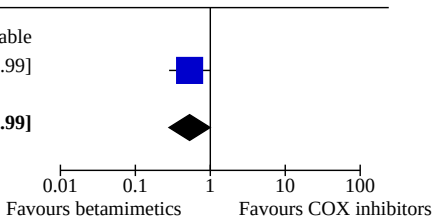
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.11. Comparison 9: Betamimetics vs COX inhibitors, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Betamimetics Events	Betamimetics Total	COX inhibitors Events	COX inhibitors Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	9	30	17	30	100.0%	0.53 [0.28 , 0.99]
Total (95% CI)		**40**		**40**	**100.0%**	**0.53 [0.28 , 0.99]**
Total events:	9		17			

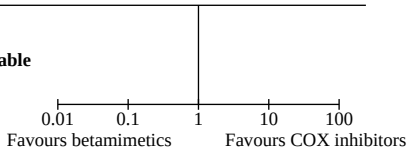
Heterogeneity: Not applicable
Test for overall effect: Z = 1.98 (P = 0.05)
Test for subgroup differences: Not applicable



Analysis 9.12. Comparison 9: Betamimetics vs COX inhibitors, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

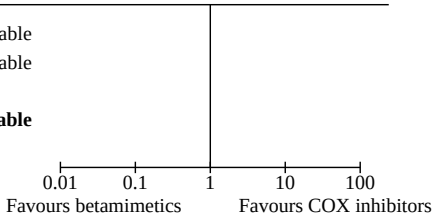
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.13. Comparison 9: Betamimetics vs COX inhibitors, Outcome 13: Pulmonary oedema

Study or Subgroup	Betamimetics Events	Betamimetics Total	COX inhibitors Events	COX inhibitors Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	0	30	0	30		Not estimable
Total (95% CI)		**40**		**40**		**Not estimable**
Total events:	0		0			

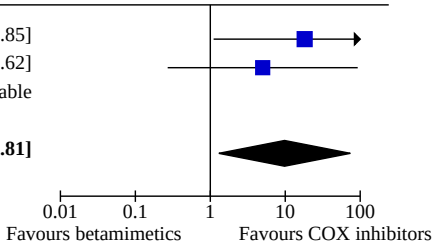
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.14. Comparison 9: Betamimetics vs COX inhibitors, Outcome 14: Dyspnoea

Study or Subgroup	Betamimetics Events	Betamimetics Total	COX inhibitors Events	COX inhibitors Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	7	18	0	22	52.1%	18.16 [1.11 , 297.85]
Kramer 1999	2	10	0	10	47.9%	5.00 [0.27 , 92.62]
Kurki 1991b	0	30	0	30		Not estimable
Total (95% CI)		**58**		**62**	**100.0%**	**9.79 [1.30 , 73.81]**
Total events:	9		0			

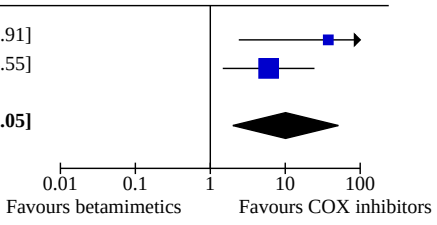
Heterogeneity: Tau² = 0.00; Chi² = 0.39, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 2.21 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 9.15. Comparison 9: Betamimetics vs COX inhibitors, Outcome 15: Palpitations

Study or Subgroup	Betamimetics Events	Betamimetics Total	COX inhibitors Events	COX inhibitors Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	15	18	0	22	28.4%	37.53 [2.40 , 586.91]
Kurki 1991b	12	30	2	30	71.6%	6.00 [1.47 , 24.55]
Total (95% CI)		**48**		**52**	**100.0%**	**10.10 [2.00 , 51.05]**
Total events:	27		2			

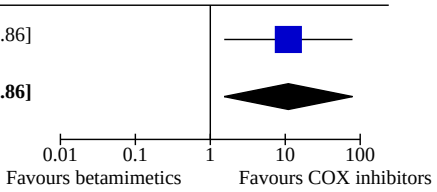
Heterogeneity: Tau² = 0.44; Chi² = 1.35, df = 1 (P = 0.24); I² = 26%
Test for overall effect: Z = 2.80 (P = 0.005)
Test for subgroup differences: Not applicable



Analysis 9.16. Comparison 9: Betamimetics vs COX inhibitors, Outcome 16: Headaches

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	9	18	1	22	100.0%	11.00 [1.53 , 78.86]
Total (95% CI)		**18**		**22**	**100.0%**	**11.00 [1.53 , 78.86]**
Total events:	9		1			

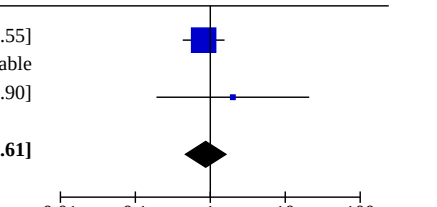
Heterogeneity: Not applicable
Test for overall effect: Z = 2.39 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 9.17. Comparison 9: Betamimetics vs COX inhibitors, Outcome 17: Nausea or vomiting

Study or Subgroup	Betamimetic Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	8	18	12	22	93.0%	0.81 [0.43 , 1.55]
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	2	30	1	30	7.0%	2.00 [0.19 , 20.90]
Total (95% CI)		**58**		**62**	**100.0%**	**0.87 [0.47 , 1.61]**
Total events:	10		13			

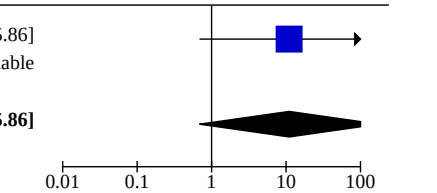
Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 1 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.45 (P = 0.65)
Test for subgroup differences: Not applicable



Analysis 9.18. Comparison 9: Betamimetics vs COX inhibitors, Outcome 18: Tachycardia

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	5	10	0	10	100.0%	11.00 [0.69 , 175.86]
Kurki 1991b	0	30	0	30		Not estimable
Total (95% CI)		**40**		**40**	**100.0%**	**11.00 [0.69 , 175.86]**
Total events:	5		0			

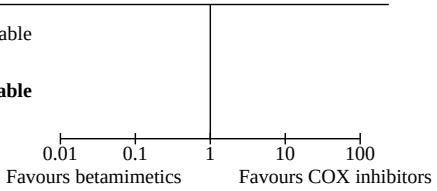
Heterogeneity: Not applicable
Test for overall effect: Z = 1.70 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 9.19. Comparison 9: Betamimetics vs COX inhibitors, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kurki 1991b	0	30	0	30		Not estimable
Total (95% CI)		**30**		**30**		**Not estimable**
Total events:	0		0			

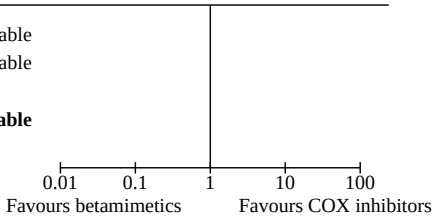
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.20. Comparison 9: Betamimetics vs COX inhibitors, Outcome 20: Maternal hypotension

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	0	30	0	30		Not estimable
Total (95% CI)		**40**		**40**		**Not estimable**
Total events:	0		0			

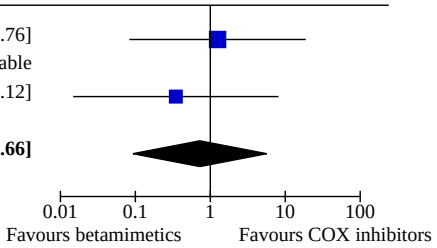
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.21. Comparison 9: Betamimetics vs COX inhibitors, Outcome 21: Perinatal death

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	1	20	1	25	57.5%	1.25 [0.08 , 18.76]
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	0	24	1	25	42.5%	0.35 [0.01 , 8.12]
Total (95% CI)		**54**		**60**	**100.0%**	**0.73 [0.09 , 5.66]**
Total events:	1		2			

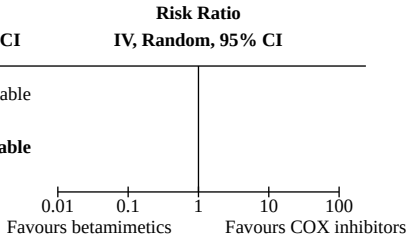
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.76)
Test for subgroup differences: Not applicable



Analysis 9.22. Comparison 9: Betamimetics vs COX inhibitors, Outcome 22: Stillbirth

Study or Subgroup	COX inhibitors Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	0	10	0	10		Not estimable
Total (95% CI)		**10**		**10**		**Not estimable**
Total events:	0		0			

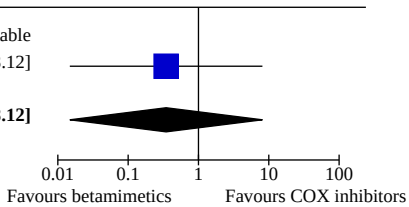
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.23. Comparison 9: Betamimetics vs COX inhibitors, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Combination Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	0	24	1	25	100.0%	0.35 [0.01 , 8.12]
Total (95% CI)		**34**		**35**	**100.0%**	**0.35 [0.01 , 8.12]**
Total events:	0		1			

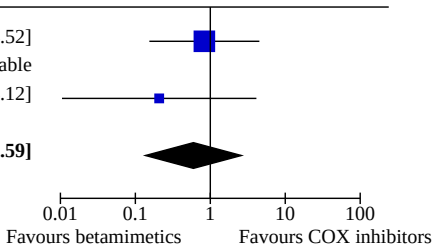
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 9.24. Comparison 9: Betamimetics vs COX inhibitors, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Besinger 1991	2	20	3	25	75.7%	0.83 [0.15 , 4.52]
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	0	24	2	25	24.3%	0.21 [0.01 , 4.12]
Total (95% CI)		**54**		**60**	**100.0%**	**0.60 [0.14 , 2.59]**
Total events:	2		5			

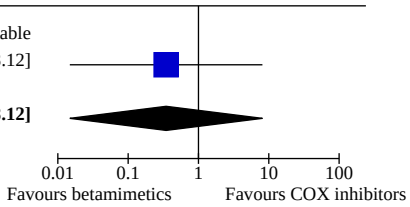
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 9.25. Comparison 9: Betamimetics vs COX inhibitors, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Combination Events	Total	Placebo or no treatment Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	0	24	1	25	100.0%	0.35 [0.01 , 8.12]
Total (95% CI)		**34**		**35**	**100.0%**	**0.35 [0.01 , 8.12]**
Total events:	0		1			

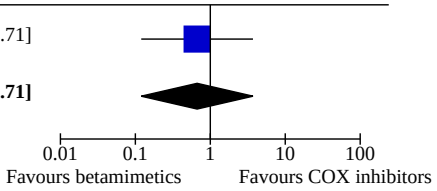
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 9.26. Comparison 9: Betamimetics vs COX inhibitors, Outcome 26: Respiratory morbidity

Study or Subgroup	Betamimetics Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kurki 1991b	2	30	3	30	100.0%	0.67 [0.12 , 3.71]
Total (95% CI)		**30**		**30**	**100.0%**	**0.67 [0.12 , 3.71]**
Total events:	2		3			

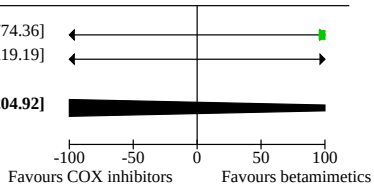
Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.64)
Test for subgroup differences: Not applicable



Analysis 9.27. Comparison 9: Betamimetics vs COX inhibitors, Outcome 27: Mean birthweight

Study or Subgroup	Betamimetics Mean	SD	Total	COX inhibitors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Besinger 1991	2189	1104	20	2090	1202	25	32.6%	99.00 [-576.36 , 774.36]
Kurki 1991b	2558	746	24	2892	870	25	67.4%	-334.00 [-787.19 , 119.19]
Total (95% CI)			**44**			**50**	**100.0%**	**-192.87 [-590.66 , 204.92]**

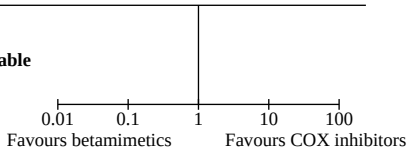
Heterogeneity: Tau² = 7645.94; Chi² = 1.09, df = 1 (P = 0.30); I² = 8%
Test for overall effect: Z = 0.95 (P = 0.34)
Test for subgroup differences: Not applicable



Analysis 9.28. Comparison 9: Betamimetics vs COX inhibitors, Outcome 28: Birthweight < 2000 g

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

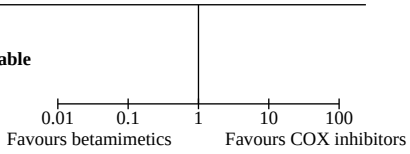
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.29. Comparison 9: Betamimetics vs COX inhibitors, Outcome 29: Birthweight < 2500 g

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

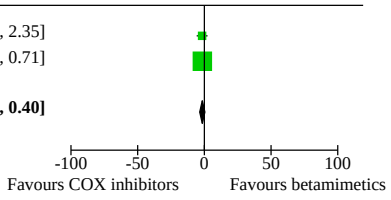
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 9.30. Comparison 9: Betamimetics vs COX inhibitors, Outcome 30: Gestational age at birth

Study or Subgroup	Betamimetics Mean	Betamimetics SD	Betamimetics Total	COX inhibitors Mean	COX inhibitors SD	COX inhibitors Total	Weight	Mean Difference IV, Random, 95% CI
Besinger 1991	33.8	7.1	18	35.5	5.7	22	22.9%	-1.70 [-5.75 , 2.35]
Kurki 1991b	35.2	3.9	24	36.7	4	25	77.1%	-1.50 [-3.71 , 0.71]
Total (95% CI)			**42**			**47**	**100.0%**	**-1.55 [-3.49 , 0.40]**

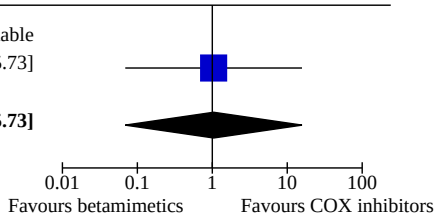
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.56 (P = 0.12)
Test for subgroup differences: Not applicable



Analysis 9.31. Comparison 9: Betamimetics vs COX inhibitors, Outcome 31: Neonatal infection

Study or Subgroup	Betamimetics Events	Betamimetics Total	COX inhibitors Events	COX inhibitors Total	Weight	Risk Ratio IV, Random, 95% CI
Kramer 1999	0	10	0	10		Not estimable
Kurki 1991b	1	24	1	25	100.0%	1.04 [0.07 , 15.73]
Total (95% CI)		**34**		**35**	**100.0%**	**1.04 [0.07 , 15.73]**
Total events:	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)
Test for subgroup differences: Not applicable



Comparison 10. Betamimetics vs nitric oxide donors

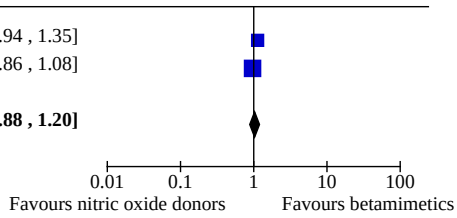
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Delay in birth by 48 hours	2	370	Risk Ratio (IV, Random, 95% CI)	1.03 [0.88, 1.20]
10.2 Delay in birth by 7 days	4	629	Risk Ratio (IV, Random, 95% CI)	1.00 [0.89, 1.12]
10.3 Neonatal death before 28 days	2	427	Risk Ratio (IV, Random, 95% CI)	1.28 [0.21, 7.89]
10.4 Pregnancy prolongation (time from trial entry to birth in days)	2	365	Mean Difference (IV, Random, 95% CI)	-4.15 [-15.90, 7.60]
10.5 Serious adverse effects of drugs	3	559	Risk Ratio (IV, Random, 95% CI)	2.91 [0.12, 70.50]
10.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.7 Cessation of treatment due to adverse effects	3	394	Risk Ratio (IV, Random, 95% CI)	2.79 [0.05, 145.73]
10.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.9 Birth before 32 weeks' gestation	1	233	Risk Ratio (IV, Random, 95% CI)	1.00 [0.54, 1.84]
10.10 Birth before 34 weeks' gestation	2	365	Risk Ratio (IV, Random, 95% CI)	1.40 [0.70, 2.79]
10.11 Birth before 37 weeks' gestation	4	627	Risk Ratio (IV, Random, 95% CI)	1.26 [0.92, 1.72]
10.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.13 Pulmonary oedema	1	191	Risk Ratio (IV, Random, 95% CI)	2.91 [0.12, 70.50]
10.14 Dyspnoea	2	217	Risk Ratio (IV, Random, 95% CI)	10.45 [2.13, 51.30]
10.15 Palpitations	3	349	Risk Ratio (IV, Random, 95% CI)	11.11 [2.61, 47.27]
10.16 Headaches	3	349	Risk Ratio (IV, Random, 95% CI)	0.24 [0.06, 0.93]
10.17 Nausea or vomiting	3	349	Risk Ratio (IV, Random, 95% CI)	1.91 [0.85, 4.31]
10.18 Tachycardia	2	323	Risk Ratio (IV, Random, 95% CI)	31.40 [9.12, 108.19]
10.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.21 Perinatal death	3	559	Risk Ratio (IV, Random, 95% CI)	1.98 [0.67, 5.86]
10.22 Stillbirth	1	191	Risk Ratio (IV, Random, 95% CI)	2.91 [0.12, 70.50]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.24 Neurodevelopmental morbidity	1	236	Risk Ratio (IV, Random, 95% CI)	4.14 [0.90, 19.08]
10.25 Gastrointestinal morbidity	1	236	Risk Ratio (IV, Random, 95% CI)	1.03 [0.45, 2.39]
10.26 Respiratory morbidity	1	236	Risk Ratio (IV, Random, 95% CI)	1.03 [0.43, 2.51]
10.27 Mean birthweight	1	132	Mean Difference (IV, Random, 95% CI)	-481.00 [-766.78, -195.22]
10.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
10.29 Birthweight < 2500 g	1	132	Risk Ratio (IV, Random, 95% CI)	2.28 [1.34, 3.88]
10.30 Gestational age at birth	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
10.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 10.1. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 1: Delay in birth by 48 hours

	Betamimetics		Nitric oxide donors			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bisits 2004	83	117	76	121	40.6%	1.13 [0.94 , 1.35]	
Wani 2004	57	65	61	67	59.4%	0.96 [0.86 , 1.08]	
Total (95% CI)		**182**		**188**	**100.0%**	**1.03 [0.88 , 1.20]**	
Total events:	140		137				

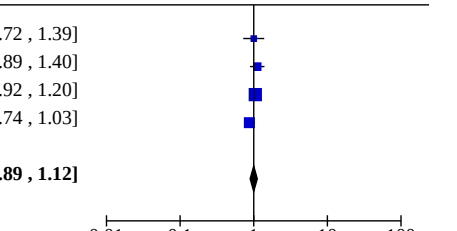
Heterogeneity: Tau² = 0.01; Chi² = 2.11, df = 1 (P = 0.15); I² = 53%
Test for overall effect: Z = 0.35 (P = 0.73)
Test for subgroup differences: Not applicable



Analysis 10.2. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 2: Delay in birth by 7 days

	Betamimetics		Nitric oxide donors			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bisits 1998	11	13	11	13	10.2%	1.00 [0.72 , 1.39]	
Bisits 2004	69	117	64	121	19.3%	1.11 [0.89 , 1.40]	
Lees 1999	97	120	87	113	40.4%	1.05 [0.92 , 1.20]	
Wani 2004	49	65	58	67	30.1%	0.87 [0.74 , 1.03]	
Total (95% CI)		**315**		**314**	**100.0%**	**1.00 [0.89 , 1.12]**	
Total events:	226		220				

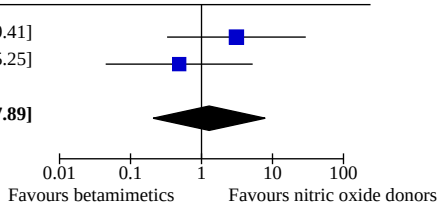
Heterogeneity: Tau² = 0.00; Chi² = 4.01, df = 3 (P = 0.26); I² = 25%
Test for overall effect: Z = 0.02 (P = 0.99)
Test for subgroup differences: Not applicable



Analysis 10.3. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 2004	3	116	1	120	52.4%	3.10 [0.33 , 29.41]
Lees 1999	1	97	2	94	47.6%	0.48 [0.04 , 5.25]
Total (95% CI)		**213**		**214**	**100.0%**	**1.28 [0.21 , 7.89]**
Total events:	4		3			

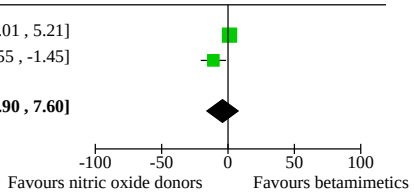
Heterogeneity: Tau² = 0.33; Chi² = 1.23, df = 1 (P = 0.27); I² = 19%
Test for overall effect: Z = 0.27 (P = 0.79)
Test for subgroup differences: Not applicable



Analysis 10.4. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Betamimetics Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Lees 1999	36.9	16	120	35.8	16	113	56.6%	1.10 [-3.01 , 5.21]
Wani 2004	38	28	65	49	28	67	43.4%	-11.00 [-20.55 , -1.45]
Total (95% CI)			**185**			**180**	**100.0%**	**-4.15 [-15.90 , 7.60]**

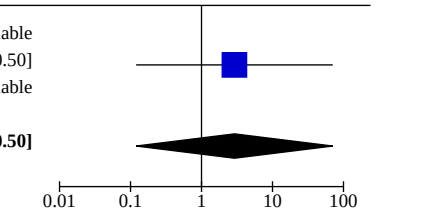
Heterogeneity: Tau² = 59.12; Chi² = 5.20, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 10.5. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 2004	0	116	0	120		Not estimable
Lees 1999	1	97	0	94	100.0%	2.91 [0.12 , 70.50]
Wani 2004	0	65	0	67		Not estimable
Total (95% CI)		**278**		**281**	**100.0%**	**2.91 [0.12 , 70.50]**
Total events:	1		0			

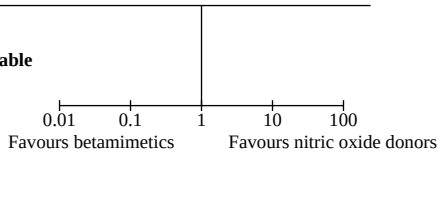
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 10.6. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 6: Maternal infection

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

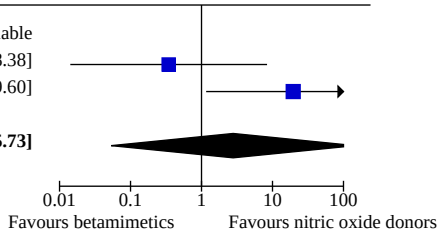
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.7. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 1998	0	13	0	13		Not estimable
Bisits 2004	0	116	1	120	48.2%	0.34 [0.01 , 8.38]
Wani 2004	9	65	0	67	51.8%	19.58 [1.16 , 329.60]
Total (95% CI)		**194**		**200**	**100.0%**	**2.79 [0.05 , 145.73]**
Total events:	9		1			

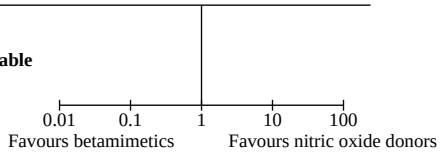
Heterogeneity: Tau² = 5.80; Chi² = 3.45, df = 1 (P = 0.06); I² = 71%
Test for overall effect: Z = 0.51 (P = 0.61)
Test for subgroup differences: Not applicable



Analysis 10.8. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

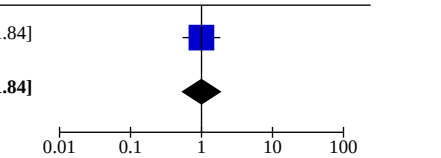
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.9. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lees 1999	18	120	17	113	100.0%	1.00 [0.54 , 1.84]
Total (95% CI)		**120**		**113**	**100.0%**	**1.00 [0.54 , 1.84]**
Total events:	18		17			

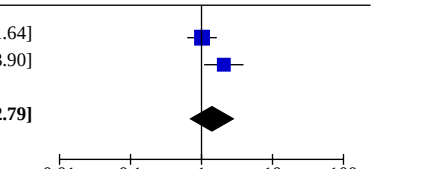
Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)
Test for subgroup differences: Not applicable



Analysis 10.10. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lees 1999	27	120	25	113	54.6%	1.02 [0.63 , 1.64]
Wani 2004	22	65	11	67	45.4%	2.06 [1.09 , 3.90]
Total (95% CI)		**185**		**180**	**100.0%**	**1.40 [0.70 , 2.79]**
Total events:	49		36			

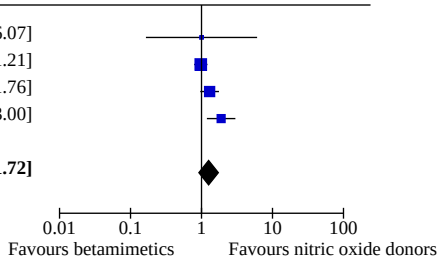
Heterogeneity: Tau² = 0.17; Chi² = 3.01, df = 1 (P = 0.08); I² = 67%
Test for overall effect: Z = 0.96 (P = 0.34)
Test for subgroup differences: Not applicable



Analysis 10.11. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 1998	2	13	2	13	2.9%	1.00 [0.16 , 6.07]
Bisits 2004	67	116	71	120	39.7%	0.98 [0.79 , 1.21]
Lees 1999	58	120	42	113	33.6%	1.30 [0.96 , 1.76]
Wani 2004	33	65	18	67	23.8%	1.89 [1.19 , 3.00]
Total (95% CI)		**314**		**313**	**100.0%**	**1.26 [0.92 , 1.72]**
Total events:	160		133			

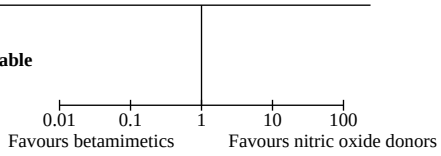
Heterogeneity: Tau² = 0.05; Chi² = 7.32, df = 3 (P = 0.06); I² = 59%
Test for overall effect: Z = 1.43 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 10.12. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 12: Maternal death

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

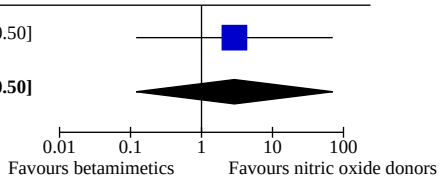
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.13. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 13: Pulmonary oedema

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lees 1999	1	97	0	94	100.0%	2.91 [0.12 , 70.50]
Total (95% CI)		**97**		**94**	**100.0%**	**2.91 [0.12 , 70.50]**
Total events:	1		0			

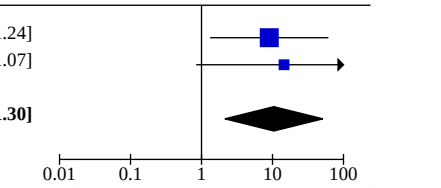
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 10.14. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 14: Dyspnoea

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 1998	9	13	1	13	68.8%	9.00 [1.32 , 61.24]
Lees 1999	7	97	0	94	31.2%	14.54 [0.84 , 251.07]
Total (95% CI)		**110**		**107**	**100.0%**	**10.45 [2.13 , 51.30]**
Total events:	16		1			

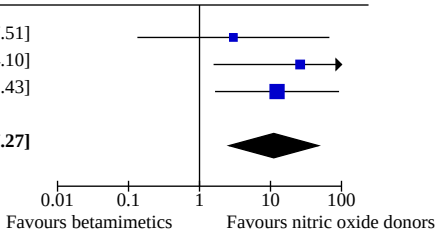
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 2.89 (P = 0.004)
Test for subgroup differences: Not applicable



Analysis 10.15. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 15: Palpitations

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 1998	1	13	0	13	21.6%	3.00 [0.13 , 67.51]
Lees 1999	13	97	0	94	26.6%	26.17 [1.58 , 434.10]
Wani 2004	12	65	1	67	51.8%	12.37 [1.66 , 92.43]
Total (95% CI)		**175**		**174**	**100.0%**	**11.11 [2.61 , 47.27]**
Total events:	26		1			

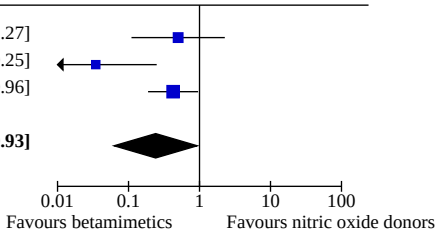
Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 3.26 (P = 0.001)
Test for subgroup differences: Not applicable



Analysis 10.16. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 16: Headaches

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 1998	2	13	4	13	31.5%	0.50 [0.11 , 2.27]
Lees 1999	1	97	28	94	24.6%	0.03 [0.00 , 0.25]
Wani 2004	7	65	17	67	43.9%	0.42 [0.19 , 0.96]
Total (95% CI)		**175**		**174**	**100.0%**	**0.24 [0.06 , 0.93]**
Total events:	10		49			

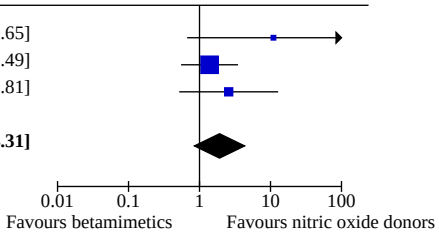
Heterogeneity: Tau² = 0.91; Chi² = 5.67, df = 2 (P = 0.06); I² = 65%
Test for overall effect: Z = 2.07 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 10.17. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 17: Nausea or vomiting

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 1998	5	13	0	13	8.3%	11.00 [0.67 , 180.65]
Lees 1999	10	97	7	94	67.3%	1.38 [0.55 , 3.49]
Wani 2004	5	65	2	67	24.4%	2.58 [0.52 , 12.81]
Total (95% CI)		**175**		**174**	**100.0%**	**1.91 [0.85 , 4.31]**
Total events:	20		9			

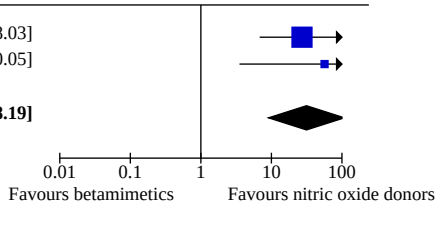
Heterogeneity: Tau² = 0.03; Chi² = 2.10, df = 2 (P = 0.35); I² = 5%
Test for overall effect: Z = 1.57 (P = 0.12)
Test for subgroup differences: Not applicable



Analysis 10.18. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 18: Tachycardia

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lees 1999	56	97	2	94	80.2%	27.13 [6.82 , 108.03]
Wani 2004	27	65	0	67	19.8%	56.67 [3.53 , 910.05]
Total (95% CI)		**162**		**161**	**100.0%**	**31.40 [9.12 , 108.19]**
Total events:	83		2			

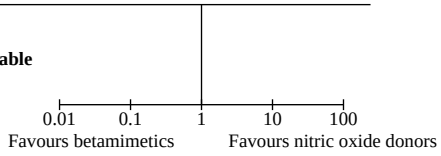
Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 5.46 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 10.19. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

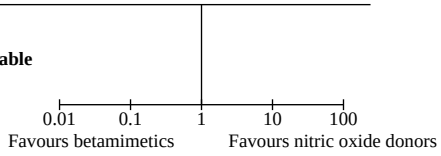
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.20. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 20: Maternal hypotension

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

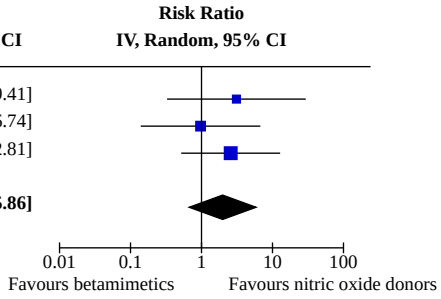
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.21. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 21: Perinatal death

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 2004	3	116	1	120	23.2%	3.10 [0.33 , 29.41]
Lees 1999	2	97	2	94	31.2%	0.97 [0.14 , 6.74]
Wani 2004	5	65	2	67	45.6%	2.58 [0.52 , 12.81]
Total (95% CI)		**278**		**281**	**100.0%**	**1.98 [0.67 , 5.86]**
Total events:	10		5			

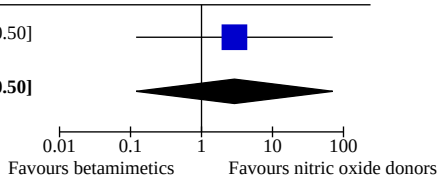
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.78$, df = 2 (P = 0.68); $I^2 = 0\%$
Test for overall effect: Z = 1.24 (P = 0.22)
Test for subgroup differences: Not applicable



Analysis 10.22. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 22: Stillbirth

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lees 1999	1	97	0	94	100.0%	2.91 [0.12 , 70.50]
Total (95% CI)		**97**		**94**	**100.0%**	**2.91 [0.12 , 70.50]**
Total events:	1		0			

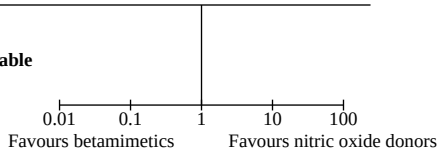
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 10.23. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

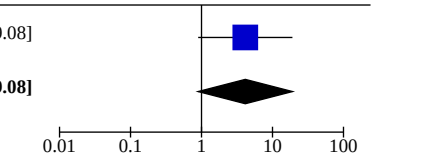
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.24. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 2004	8	116	2	120	100.0%	4.14 [0.90 , 19.08]
Total (95% CI)		**116**		**120**	**100.0%**	**4.14 [0.90 , 19.08]**
Total events:	8		2			

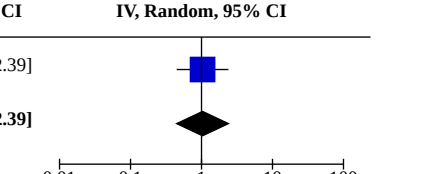
Heterogeneity: Not applicable
Test for overall effect: Z = 1.82 (P = 0.07)
Test for subgroup differences: Not applicable



Analysis 10.25. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 2004	10	116	10	120	100.0%	1.03 [0.45 , 2.39]
Total (95% CI)		**116**		**120**	**100.0%**	**1.03 [0.45 , 2.39]**
Total events:	10		10			

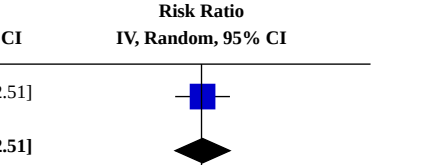
Heterogeneity: Not applicable
Test for overall effect: Z = 0.08 (P = 0.94)
Test for subgroup differences: Not applicable



Analysis 10.26. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 26: Respiratory morbidity

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bisits 2004	9	116	9	120	100.0%	1.03 [0.43 , 2.51]
Total (95% CI)		**116**		**120**	**100.0%**	**1.03 [0.43 , 2.51]**
Total events:	9		9			

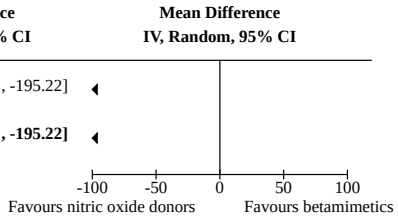
Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.94)
Test for subgroup differences: Not applicable



Analysis 10.27. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 27: Mean birthweight

Study or Subgroup	Betamimetics Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Wani 2004	2532	839	65	3013	836	67	100.0%	-481.00 [-766.78 , -195.22]
Total (95% CI)			**65**			**67**	**100.0%**	**-481.00 [-766.78 , -195.22]**

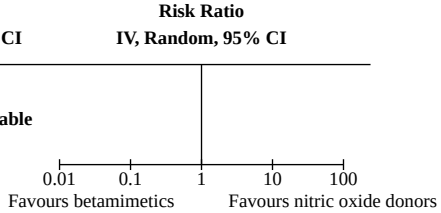
Heterogeneity: Not applicable
Test for overall effect: Z = 3.30 (P = 0.0010)
Test for subgroup differences: Not applicable



Analysis 10.28. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

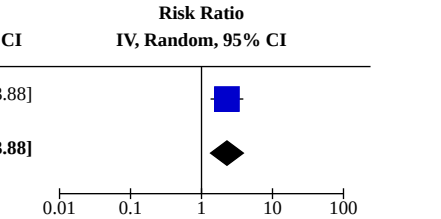
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.29. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Betamimetics Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Wani 2004	31	65	14	67	100.0%	2.28 [1.34 , 3.88]
Total (95% CI)		**65**		**67**	**100.0%**	**2.28 [1.34 , 3.88]**
Total events:	31		14			

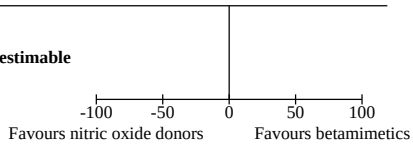
Heterogeneity: Not applicable
Test for overall effect: Z = 3.05 (P = 0.002)
Test for subgroup differences: Not applicable



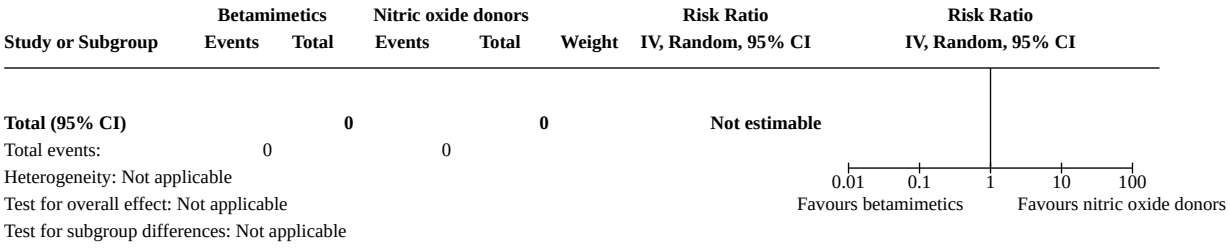
Analysis 10.30. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 30: Gestational age at birth

Study or Subgroup	Betamimetics Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 10.31. Comparison 10: Betamimetics vs nitric oxide donors, Outcome 31: Neonatal infection

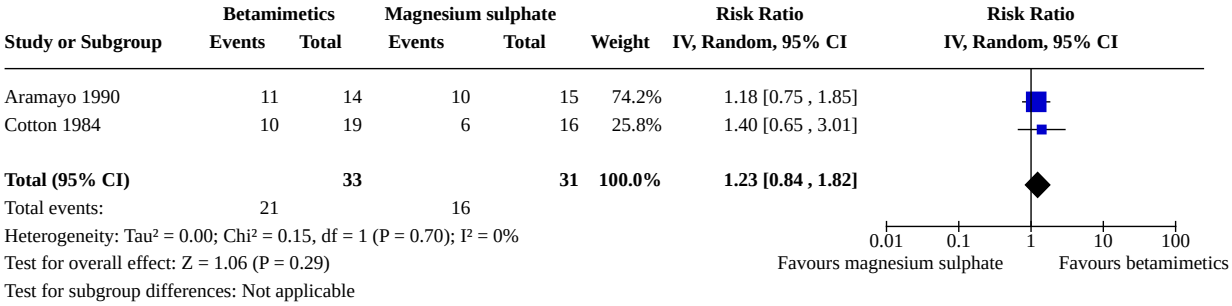


Comparison 11. Betamimetics vs magnesium sulphate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.1 Delay in birth by 48 hours	2	64	Risk Ratio (IV, Random, 95% CI)	1.23 [0.84, 1.82]
11.2 Delay in birth by 7 days	2	64	Risk Ratio (IV, Random, 95% CI)	1.35 [0.71, 2.56]
11.3 Neonatal death before 28 days	2	89	Risk Ratio (IV, Random, 95% CI)	0.57 [0.07, 4.42]
11.4 Pregnancy prolongation (time from trial entry to birth in days)	2	91	Mean Difference (IV, Random, 95% CI)	9.13 [4.93, 13.34]
11.5 Serious adverse effects of drugs	1	57	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.6 Maternal infection	1	35	Risk Ratio (IV, Random, 95% CI)	2.11 [0.47, 9.42]
11.7 Cessation of treatment due to adverse effects	2	106	Risk Ratio (IV, Random, 95% CI)	4.25 [0.22, 82.57]
11.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.11 Birth before 37 weeks' gestation	4	219	Risk Ratio (IV, Random, 95% CI)	1.09 [0.53, 2.21]
11.12 Maternal death	2	92	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.13 Pulmonary oedema	2	92	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.18 Tachycardia	1	35	Risk Ratio (IV, Random, 95% CI)	4.25 [0.22, 82.57]
11.19 Maternal cardiac arrhythmias	1	35	Risk Ratio (IV, Random, 95% CI)	2.55 [0.11, 58.60]
11.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.21 Perinatal death	2	89	Risk Ratio (IV, Random, 95% CI)	0.57 [0.07, 4.42]
11.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
11.23 Neonatal death before 7 days	1	54	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.84]
11.24 Neurodevelopmental morbidity	2	89	Risk Ratio (IV, Random, 95% CI)	2.41 [0.82, 7.07]
11.25 Gastrointestinal morbidity	2	89	Risk Ratio (IV, Random, 95% CI)	0.72 [0.09, 5.58]
11.26 Respiratory morbidity	2	88	Risk Ratio (IV, Random, 95% CI)	0.87 [0.46, 1.67]
11.27 Mean birthweight	3	145	Mean Difference (IV, Random, 95% CI)	144.92 [-27.73, 317.58]
11.28 Birthweight < 2000 g	1	35	Risk Ratio (IV, Random, 95% CI)	0.91 [0.60, 1.38]
11.29 Birthweight < 2500 g	2	66	Risk Ratio (IV, Random, 95% CI)	1.01 [0.86, 1.19]
11.30 Gestational age at birth	2	89	Mean Difference (IV, Random, 95% CI)	0.87 [-1.38, 3.12]
11.31 Neonatal infection	1	35	Risk Ratio (IV, Random, 95% CI)	2.95 [0.71, 12.24]

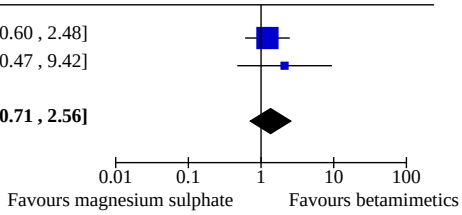
Analysis 11.1. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 1: Delay in birth by 48 hours



Analysis 11.2. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Aramayo 1990	8	14	7	15	81.8%	1.22 [0.60 , 2.48]
Cotton 1984	5	19	2	16	18.2%	2.11 [0.47 , 9.42]
Total (95% CI)		**33**		**31**	**100.0%**	**1.35 [0.71 , 2.56]**
Total events:	13		9			

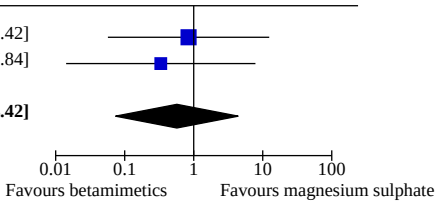
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.92 (P = 0.36)
Test for subgroup differences: Not applicable



Analysis 11.3. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	1	19	1	16	57.9%	0.84 [0.06 , 12.42]
Pezzati 2001	0	27	1	27	42.1%	0.33 [0.01 , 7.84]
Total (95% CI)		**46**		**43**	**100.0%**	**0.57 [0.07 , 4.42]**
Total events:	1		2			

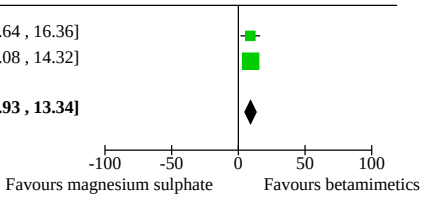
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 0.54 (P = 0.59)
Test for subgroup differences: Not applicable



Analysis 11.4. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Betamimetics Mean	SD	Total	Magnesium sulphate Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cotton 1984	12	14.9	19	3	6	15	32.6%	9.00 [1.64 , 16.36]
Wang 2000	25.1	10.6	32	15.9	9.1	25	67.4%	9.20 [4.08 , 14.32]
Total (95% CI)			**51**			**40**	**100.0%**	**9.13 [4.93 , 13.34]**

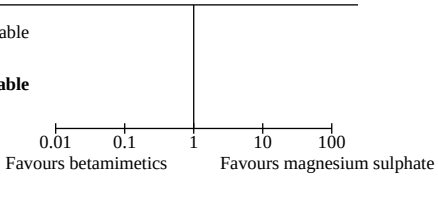
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%
Test for overall effect: Z = 4.26 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 11.5. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Wang 2000	0	32	0	25		Not estimable
Total (95% CI)		**32**		**25**		**Not estimable**
Total events:	0		0			

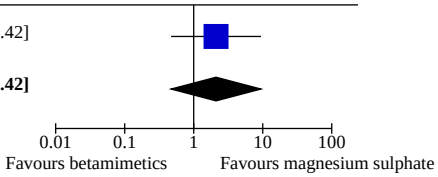
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.6. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 6: Maternal infection

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	5	19	2	16	100.0%	2.11 [0.47 , 9.42]
Total (95% CI)		**19**		**16**	**100.0%**	**2.11 [0.47 , 9.42]**
Total events:	5		2			

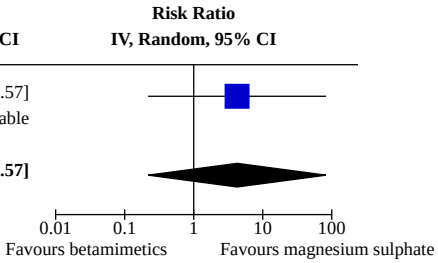
Heterogeneity: Not applicable
Test for overall effect: Z = 0.97 (P = 0.33)
Test for subgroup differences: Not applicable



Analysis 11.7. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	19	0	16	100.0%	4.25 [0.22 , 82.57]
Wang 2000	0	36	0	35		Not estimable
Total (95% CI)		**55**		**51**	**100.0%**	**4.25 [0.22 , 82.57]**
Total events:	2		0			

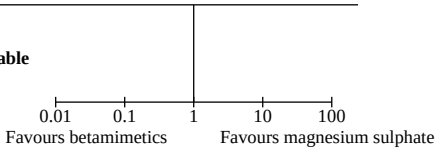
Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)
Test for subgroup differences: Not applicable



Analysis 11.8. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

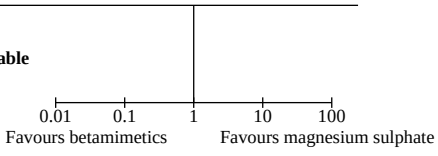
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.9. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

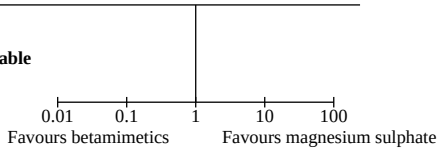
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.10. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

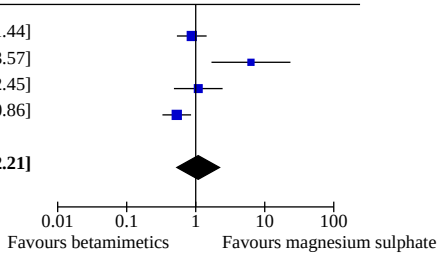
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.11. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Aramayo 1990	9	14	11	15	29.9%	0.88 [0.53 , 1.44]
Cotton 1984	15	19	2	16	15.9%	6.32 [1.69 , 23.57]
Miller 1982	7	15	6	14	24.0%	1.09 [0.48 , 2.45]
Zhu 1996	17	64	31	62	30.2%	0.53 [0.33 , 0.86]
Total (95% CI)		**112**		**107**	**100.0%**	**1.09 [0.53 , 2.21]**
Total events:	48		50			

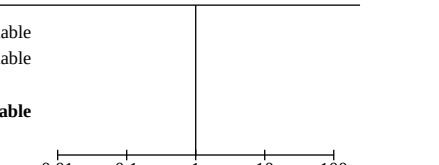
Heterogeneity: Tau² = 0.37; Chi² = 12.94, df = 3 (P = 0.005); I² = 77%
Test for overall effect: Z = 0.23 (P = 0.82)
Test for subgroup differences: Not applicable



Analysis 11.12. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 12: Maternal death

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	0	19	0	16		Not estimable
Wang 2000	0	32	0	25		Not estimable
Total (95% CI)		**51**		**41**		**Not estimable**
Total events:	0		0			

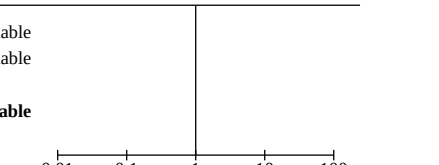
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.13. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 13: Pulmonary oedema

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	0	19	0	16		Not estimable
Wang 2000	0	32	0	25		Not estimable
Total (95% CI)		**51**		**41**		**Not estimable**
Total events:	0		0			

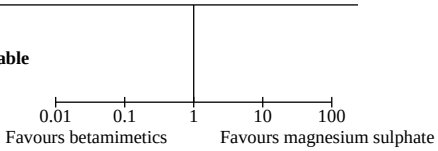
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.14. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 14: Dyspnoea

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

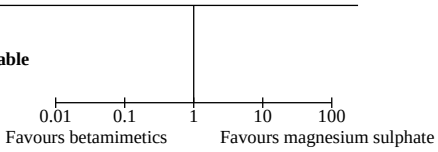
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.15. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 15: Palpitations

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

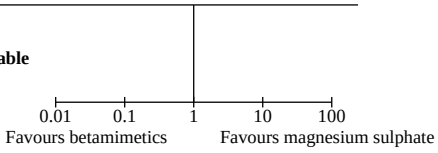
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.16. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 16: Headaches

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

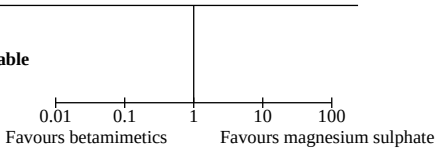
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.17. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 17: Nausea or vomiting

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

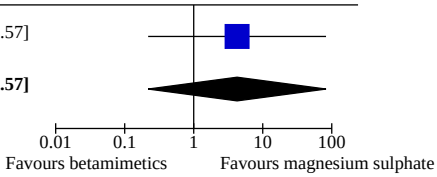
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.18. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 18: Tachycardia

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	19	0	16	100.0%	4.25 [0.22 , 82.57]
Total (95% CI)		**19**		**16**	**100.0%**	**4.25 [0.22 , 82.57]**
Total events:	2		0			

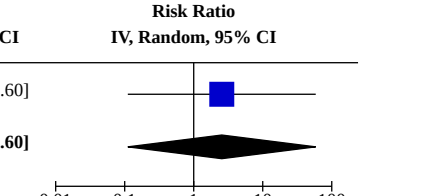
Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)
Test for subgroup differences: Not applicable



Analysis 11.19. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	1	19	0	16	100.0%	2.55 [0.11 , 58.60]
Total (95% CI)		**19**		**16**	**100.0%**	**2.55 [0.11 , 58.60]**
Total events:	1		0			

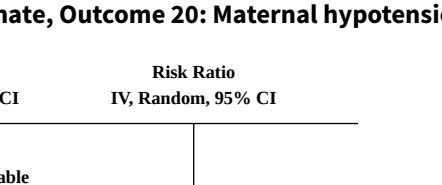
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)
Test for subgroup differences: Not applicable



Analysis 11.20. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 20: Maternal hypotension

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

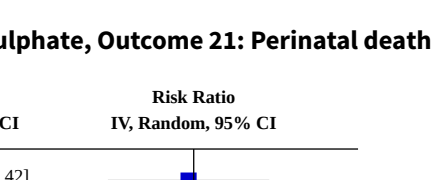
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.21. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 21: Perinatal death

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	1	19	1	16	57.9%	0.84 [0.06 , 12.42]
Pezzati 2001	0	27	1	27	42.1%	0.33 [0.01 , 7.84]
Total (95% CI)		**46**		**43**	**100.0%**	**0.57 [0.07 , 4.42]**
Total events:	1		2			

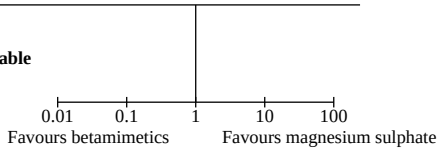
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 0.54 (P = 0.59)
Test for subgroup differences: Not applicable



Analysis 11.22. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 22: Stillbirth

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

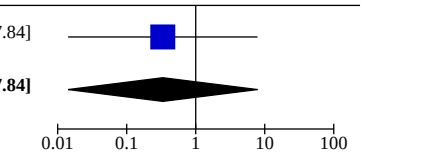
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 11.23. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Pezzati 2001	0	27	1	27	100.0%	0.33 [0.01 , 7.84]
Total (95% CI)		**27**		**27**	**100.0%**	**0.33 [0.01 , 7.84]**
Total events:	0		1			

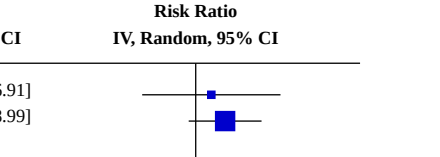
Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)
Test for subgroup differences: Not applicable



Analysis 11.24. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	19	1	16	21.7%	1.68 [0.17 , 16.91]
Pezzati 2001	8	27	3	27	78.3%	2.67 [0.79 , 8.99]
Total (95% CI)		**46**		**43**	**100.0%**	**2.41 [0.82 , 7.07]**
Total events:	10		4			

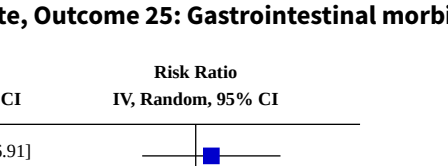
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.12$, df = 1 (P = 0.73); $I^2 = 0\%$
Test for overall effect: Z = 1.61 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 11.25. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	2	19	1	16	60.4%	1.68 [0.17 , 16.91]
Pezzati 2001	0	27	2	27	39.6%	0.20 [0.01 , 3.98]
Total (95% CI)		**46**		**43**	**100.0%**	**0.72 [0.09 , 5.58]**
Total events:	2		3			

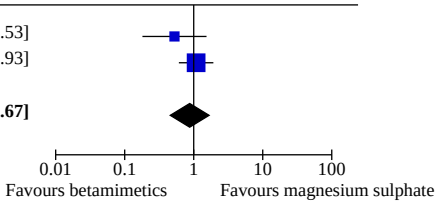
Heterogeneity: $Tau^2 = 0.41$; $Chi^2 = 1.22$, df = 1 (P = 0.27); $I^2 = 18\%$
Test for overall effect: Z = 0.31 (P = 0.76)
Test for subgroup differences: Not applicable



Analysis 11.26. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 26: Respiratory morbidity

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	4	19	6	15	29.7%	0.53 [0.18 , 1.53]
Pezzati 2001	13	27	12	27	70.3%	1.08 [0.61 , 1.93]
Total (95% CI)		**46**		**42**	**100.0%**	**0.87 [0.46 , 1.67]**
Total events:	17		18			

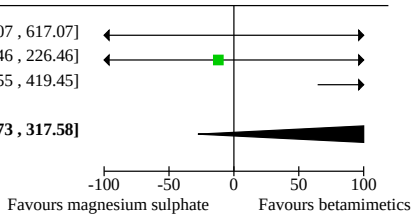
Heterogeneity: Tau² = 0.07; Chi² = 1.36, df = 1 (P = 0.24); I² = 26%
Test for overall effect: Z = 0.41 (P = 0.68)
Test for subgroup differences: Not applicable



Analysis 11.27. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 27: Mean birthweight

Study or Subgroup	Betamimetics Mean	SD	Total	Magnesium sulphate Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cotton 1984	1841	678	19	1651	591	15	14.2%	190.00 [-237.07 , 617.07]
Pezzati 2001	1392	397	27	1404	492	27	35.3%	-12.00 [-250.46 , 226.46]
Wang 2000	2852	360	32	2610	322	25	50.5%	242.00 [64.55 , 419.45]
Total (95% CI)			**78**			**67**	**100.0%**	**144.92 [-27.73 , 317.58]**

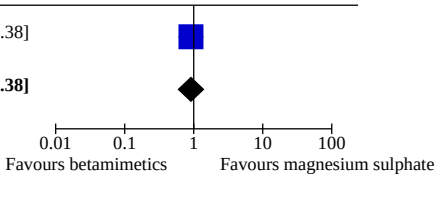
Heterogeneity: Tau² = 7171.93; Chi² = 2.83, df = 2 (P = 0.24); I² = 29%
Test for overall effect: Z = 1.65 (P = 0.10)
Test for subgroup differences: Not applicable



Analysis 11.28. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	13	19	12	16	100.0%	0.91 [0.60 , 1.38]
Total (95% CI)		**19**		**16**	**100.0%**	**0.91 [0.60 , 1.38]**
Total events:	13		12			

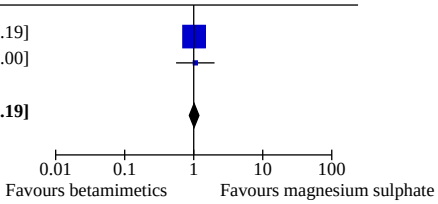
Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)
Test for subgroup differences: Not applicable



Analysis 11.29. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	18	19	15	16	93.8%	1.01 [0.86 , 1.19]
Miller 1982	9	16	8	15	6.2%	1.05 [0.56 , 2.00]
Total (95% CI)		**35**		**31**	**100.0%**	**1.01 [0.86 , 1.19]**
Total events:	27		23			

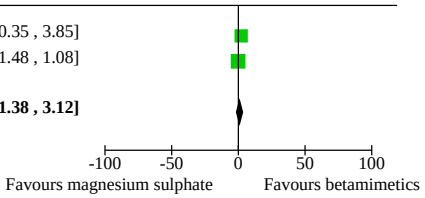
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.16 (P = 0.87)
Test for subgroup differences: Not applicable



Analysis 11.30. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 30: Gestational age at birth

Study or Subgroup	Betamimetics Mean	SD	Total	Magnesium sulphate Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cotton 1984	33.1	3.3	19	31	1.9	16	46.5%	2.10 [0.35 , 3.85]
Pezzati 2001	30.7	2.6	27	30.9	2.2	27	53.5%	-0.20 [-1.48 , 1.08]
Total (95% CI)			**46**			**43**	**100.0%**	**0.87 [-1.38 , 3.12]**

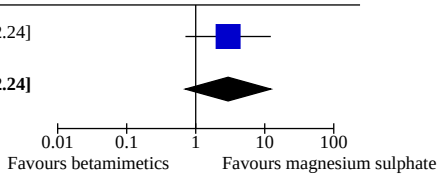
Heterogeneity: Tau² = 2.03; Chi² = 4.31, df = 1 (P = 0.04); I² = 77%
Test for overall effect: Z = 0.76 (P = 0.45)
Test for subgroup differences: Not applicable



Analysis 11.31. Comparison 11: Betamimetics vs magnesium sulphate, Outcome 31: Neonatal infection

Study or Subgroup	Betamimetics Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cotton 1984	7	19	2	16	100.0%	2.95 [0.71 , 12.24]
Total (95% CI)		**19**		**16**	**100.0%**	**2.95 [0.71 , 12.24]**
Total events:	7		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.49 (P = 0.14)
Test for subgroup differences: Not applicable



Comparison 12. Betamimetics vs oxytocin receptor antagonists

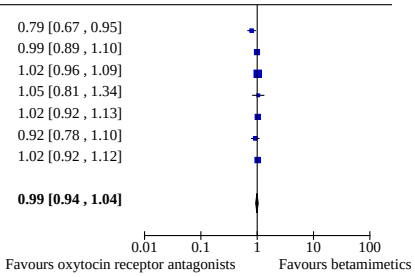
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 Delay in birth by 48 hours	7	1087	Risk Ratio (IV, Random, 95% CI)	0.99 [0.94, 1.04]
12.2 Delay in birth by 7 days	7	1087	Risk Ratio (IV, Random, 95% CI)	0.92 [0.81, 1.05]
12.3 Neonatal death before 28 days	7	1382	Risk Ratio (IV, Random, 95% CI)	1.52 [0.60, 3.87]
12.4 Pregnancy prolongation (time from trial entry to birth in days)	2	206	Mean Difference (IV, Random, 95% CI)	-21.26 [-27.02, -15.50]
12.5 Serious adverse effects of drugs	6	986	Risk Ratio (IV, Random, 95% CI)	1.52 [0.39, 5.94]
12.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.7 Cessation of treatment due to adverse effects	6	1268	Risk Ratio (IV, Random, 95% CI)	17.82 [7.83, 40.54]
12.8 Birth before 28 weeks' gestation	2	324	Risk Ratio (IV, Random, 95% CI)	1.08 [0.63, 1.87]
12.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.10 Birth before 34 weeks' gestation	1	80	Risk Ratio (IV, Random, 95% CI)	1.00 [0.95, 1.05]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.11 Birth before 37 weeks' gestation	1	80	Risk Ratio (IV, Random, 95% CI)	1.00 [0.95, 1.05]
12.12 Maternal death	1	45	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.13 Pulmonary oedema	3	616	Risk Ratio (IV, Random, 95% CI)	1.61 [0.20, 12.95]
12.14 Dyspnoea	5	941	Risk Ratio (IV, Random, 95% CI)	9.77 [3.75, 25.44]
12.15 Palpitations	4	861	Risk Ratio (IV, Random, 95% CI)	8.69 [2.75, 27.48]
12.16 Headaches	6	1243	Risk Ratio (IV, Random, 95% CI)	1.98 [1.40, 2.80]
12.17 Nausea or vomiting	6	1243	Risk Ratio (IV, Random, 95% CI)	1.97 [1.18, 3.30]
12.18 Tachycardia	7	1288	Risk Ratio (IV, Random, 95% CI)	18.28 [8.16, 40.94]
12.19 Maternal cardiac arrhythmias	1	247	Risk Ratio (IV, Random, 95% CI)	0.35 [0.01, 8.44]
12.20 Maternal hypotension	4	861	Risk Ratio (IV, Random, 95% CI)	1.58 [0.60, 4.17]
12.21 Perinatal death	7	1382	Risk Ratio (IV, Random, 95% CI)	1.60 [0.65, 3.92]
12.22 Stillbirth	6	1088	Risk Ratio (IV, Random, 95% CI)	1.80 [0.17, 19.66]
12.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.24 Neurodevelopmental morbidity	5	1196	Risk Ratio (IV, Random, 95% CI)	1.09 [0.67, 1.80]
12.25 Gastrointestinal morbidity	1	292	Risk Ratio (IV, Random, 95% CI)	4.21 [0.27, 66.35]
12.26 Respiratory morbidity	6	1300	Risk Ratio (IV, Random, 95% CI)	0.96 [0.63, 1.46]
12.27 Mean birthweight	7	1176	Mean Difference (IV, Random, 95% CI)	-25.73 [-122.06, 70.60]
12.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
12.29 Birthweight < 2500 g	2	575	Risk Ratio (IV, Random, 95% CI)	1.02 [0.77, 1.36]
12.30 Gestational age at birth	7	1090	Mean Difference (IV, Random, 95% CI)	-0.44 [-1.21, 0.34]
12.31 Neonatal infection	6	1311	Risk Ratio (IV, Random, 95% CI)	1.08 [0.68, 1.72]

Analysis 12.1. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	31	40	39	40	7.3%	0.79 [0.67 , 0.95]
European Atosiban Study 2001	110	129	99	115	16.8%	0.99 [0.89 , 1.10]
French and Australian Atosiban Investigators 2001	115	121	111	119	29.5%	1.02 [0.96 , 1.09]
Lin 2009	19	22	19	23	3.8%	1.05 [0.81 , 1.34]
Moutquin 2000	105	121	107	126	17.1%	1.02 [0.92 , 1.13]
Nonnenmacher 2009	43	54	44	51	7.3%	0.92 [0.78 , 1.10]
Shim 2006	59	63	58	63	18.2%	1.02 [0.92 , 1.12]
Total (95% CI)		**550**		**537**	**100.0%**	**0.99 [0.94 , 1.04]**
Total events:	482		477			

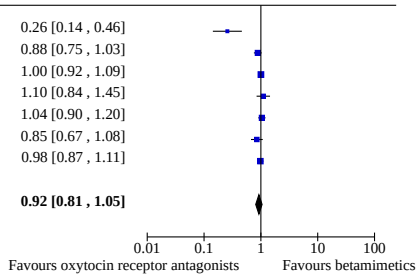
Heterogeneity: Tau² = 0.00; Chi² = 8.26, df = 6 (P = 0.22); I² = 27%
Test for overall effect: Z = 0.40 (P = 0.69)
Test for subgroup differences: Not applicable



Analysis 12.2. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	9	40	35	40	4.0%	0.26 [0.14 , 0.46]
European Atosiban Study 2001	87	129	88	115	16.6%	0.88 [0.75 , 1.03]
French and Australian Atosiban Investigators 2001	109	121	107	119	20.1%	1.00 [0.92 , 1.09]
Lin 2009	19	22	18	23	11.1%	1.10 [0.84 , 1.45]
Moutquin 2000	92	121	92	126	17.1%	1.04 [0.90 , 1.20]
Nonnenmacher 2009	36	54	40	51	12.6%	0.85 [0.67 , 1.08]
Shim 2006	56	63	57	63	18.5%	0.98 [0.87 , 1.11]
Total (95% CI)		**550**		**537**	**100.0%**	**0.92 [0.81 , 1.05]**
Total events:	408		437			

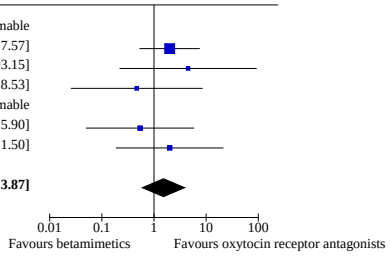
Heterogeneity: Tau² = 0.02; Chi² = 24.66, df = 6 (P = 0.0004); I² = 76%
Test for overall effect: Z = 1.22 (P = 0.22)
Test for subgroup differences: Not applicable



Analysis 12.3. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	0	40	0	40		Not estimable
European Atosiban Study 2001	7	153	3	131	49.3%	2.00 [0.53 , 7.57]
French and Australian Atosiban Investigators 2001	2	143	0	129	9.5%	4.51 [0.22 , 93.15]
Goodwin 1996	0	56	4	238	10.3%	0.47 [0.03 , 8.53]
Lin 2009	0	22	0	23		Not estimable
Moutquin 2000	1	135	2	146	15.3%	0.54 [0.05 , 5.90]
Shim 2006	2	63	1	63	15.5%	2.00 [0.19 , 21.50]
Total (95% CI)		**612**		**770**	**100.0%**	**1.52 [0.60 , 3.87]**
Total events:	12		10			

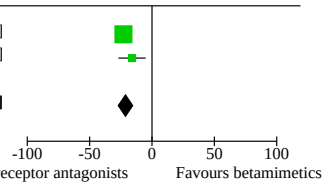
Heterogeneity: Tau² = 0.00; Chi² = 2.06, df = 4 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.88 (P = 0.38)
Test for subgroup differences: Not applicable



Analysis 12.4. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Betamimetics Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cabar 2008	5.3	1.8	40	28.2	15.6	40	76.2%	-22.90 [-27.77 , -18.03]
Shim 2006	4	31.3	63	20	31.3	63	23.8%	-16.00 [-26.93 , -5.07]
Total (95% CI)			**103**			**103**	**100.0%**	**-21.26 [-27.02 , -15.50]**

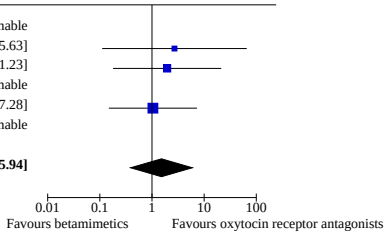
Heterogeneity: Tau² = 5.17; Chi² = 1.28, df = 1 (P = 0.26); I² = 22%
Test for overall effect: Z = 7.23 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 12.5. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	0	40	0	40		Not estimable
European Atosiban Study 2001	1	129	0	116	18.2%	2.70 [0.11 , 65.63]
French and Australian Atosiban Investigators 2001	2	122	1	119	32.6%	1.95 [0.18 , 21.23]
Lin 2009	0	22	0	23		Not estimable
Moutquin 2000	2	121	2	126	49.2%	1.04 [0.15 , 7.28]
Shim 2006	0	65	0	63		Not estimable
Total (95% CI)		**499**		**487**	**100.0%**	**1.52 [0.39 , 5.94]**
Total events:	5		3			

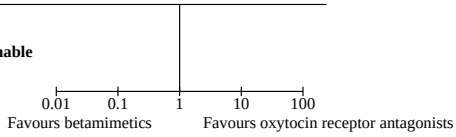
Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 2 (P = 0.86); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable



Analysis 12.6. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 6: Maternal infection

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

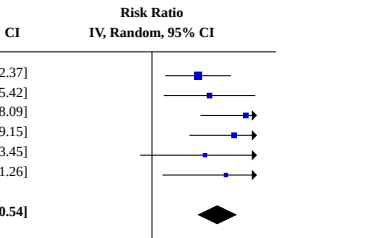
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 12.7. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
European Atosiban Study 2001	17	129	2	116	32.4%	7.64 [1.80 , 32.37]
French and Australian Atosiban Investigators 2001	13	122	1	119	16.6%	12.68 [1.69 , 95.42]
Goodwin 1996	15	58	1	244	16.8%	63.10 [8.51 , 468.09]
Moutquin 2000	36	121	1	126	17.4%	37.49 [5.22 , 269.15]
Nonnenmacher 2009	5	54	0	51	8.2%	10.40 [0.59 , 183.45]
Shim 2006	13	65	0	63	8.6%	26.18 [1.59 , 431.26]
Total (95% CI)		**549**		**719**	**100.0%**	**17.82 [7.83 , 40.54]**
Total events:	99		5			

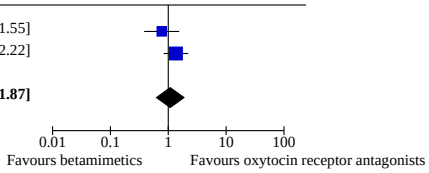
Heterogeneity: Tau² = 0.00; Chi² = 3.71, df = 5 (P = 0.59); I² = 0%
Test for overall effect: Z = 6.87 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 12.8. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	10	40	13	40	40.0%	0.77 [0.38 , 1.55]
European Atosiban Study 2001	32	129	21	115	60.0%	1.36 [0.83 , 2.22]
Total (95% CI)		**169**		**155**	**100.0%**	**1.08 [0.63 , 1.87]**
Total events:	42		34			

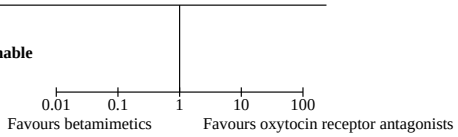
Heterogeneity: Tau² = 0.07; Chi² = 1.71, df = 1 (P = 0.19); I² = 41%
Test for overall effect: Z = 0.28 (P = 0.78)
Test for subgroup differences: Not applicable



Analysis 12.9. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

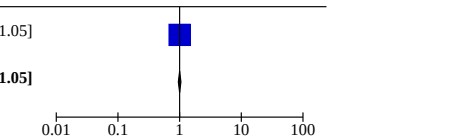
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 12.10. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	40	40	40	40	100.0%	1.00 [0.95 , 1.05]
Total (95% CI)		**40**		**40**	**100.0%**	**1.00 [0.95 , 1.05]**
Total events:	40		40			

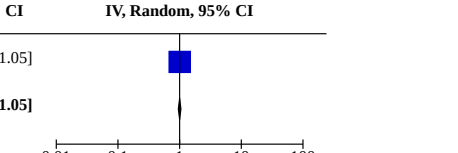
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



Analysis 12.11. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	40	40	40	40	100.0%	1.00 [0.95 , 1.05]
Total (95% CI)		**40**		**40**	**100.0%**	**1.00 [0.95 , 1.05]**
Total events:	40		40			

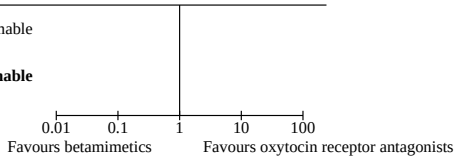
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



Analysis 12.12. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 12: Maternal death

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lin 2009	0	22	0	23		Not estimable
Total (95% CI)		**22**		**23**		**Not estimable**
Total events:	0		0			

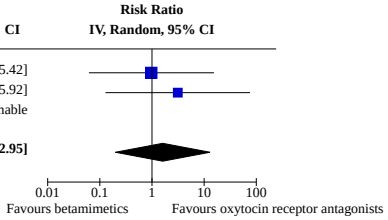
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 12.13. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 13: Pulmonary oedema

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
French and Australian Atosiban Investigators 2001	1	122	1	119	57.2%	0.98 [0.06 , 15.42]
Moutquin 2000	1	121	0	126	42.8%	3.12 [0.13 , 75.92]
Shim 2006	0	65	0	63		Not estimable
Total (95% CI)		**308**		**308**	**100.0%**	**1.61 [0.20 , 12.95]**
Total events:	2		1			

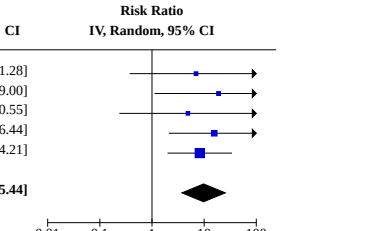
Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 1 (P = 0.59); I² = 0%
Test for overall effect: Z = 0.44 (P = 0.66)
Test for subgroup differences: Not applicable



Analysis 12.14. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 14: Dyspnoea

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	3	40	0	40	10.7%	7.00 [0.37 , 131.28]
European Atosiban Study 2001	10	129	0	116	11.5%	18.90 [1.12 , 319.00]
French and Australian Atosiban Investigators 2001	2	122	0	119	10.0%	4.88 [0.24 , 100.55]
Moutquin 2000	15	121	1	126	22.7%	15.62 [2.10 , 116.44]
Shim 2006	17	65	2	63	45.2%	8.24 [1.98 , 34.21]
Total (95% CI)		**477**		**464**	**100.0%**	**9.77 [3.75 , 25.44]**
Total events:	47		3			

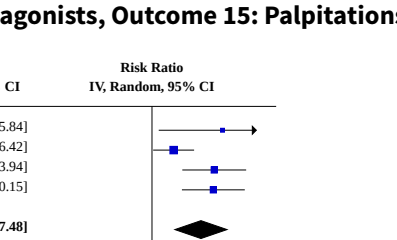
Heterogeneity: Tau² = 0.00; Chi² = 0.73, df = 4 (P = 0.95); I² = 0%
Test for overall effect: Z = 4.67 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 12.15. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 15: Palpitations

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
European Atosiban Study 2001	12	129	0	116	12.1%	22.50 [1.35 , 375.84]
French and Australian Atosiban Investigators 2001	16	122	6	119	34.6%	2.60 [1.05 , 6.42]
Moutquin 2000	30	121	2	126	26.5%	15.62 [3.82 , 63.94]
Shim 2006	31	65	2	63	26.8%	15.02 [3.75 , 60.15]
Total (95% CI)		**437**		**424**	**100.0%**	**8.69 [2.75 , 27.48]**
Total events:	89		10			

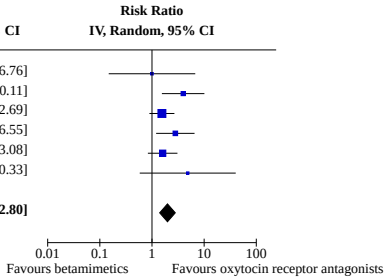
Heterogeneity: Tau² = 0.79; Chi² = 7.57, df = 3 (P = 0.06); I² = 60%
Test for overall effect: Z = 3.68 (P = 0.0002)
Test for subgroup differences: Not applicable



Analysis 12.16. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 16: Headaches

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	2	40	2	40	3.2%	1.00 [0.15 , 6.76]
European Atosiban Study 2001	22	129	5	116	13.3%	3.96 [1.55 , 10.11]
French and Australian Atosiban Investigators 2001	27	122	17	119	37.4%	1.55 [0.89 , 2.69]
Goodwin 1996	8	58	12	244	16.2%	2.80 [1.20 , 6.55]
Moutquin 2000	20	121	13	126	27.1%	1.60 [0.83 , 3.08]
Shim 2006	5	65	1	63	2.6%	4.85 [0.58 , 40.33]
Total (95% CI)		**535**		**708**	**100.0%**	**1.98 [1.40 , 2.80]**
Total events:	84		50			

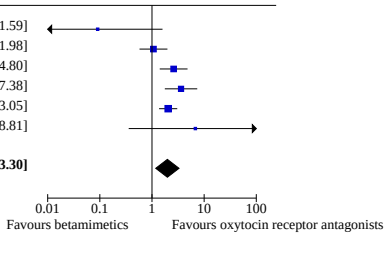
Heterogeneity: Tau² = 0.00; Chi² = 5.08, df = 5 (P = 0.41); I² = 2%
Test for overall effect: Z = 3.89 (P = 0.0001)
Test for subgroup differences: Not applicable



Analysis 12.17. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 17: Nausea or vomiting

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	0	40	5	40	2.9%	0.09 [0.01 , 1.59]
European Atosiban Study 2001	19	129	16	116	22.8%	1.07 [0.58 , 1.98]
French and Australian Atosiban Investigators 2001	32	122	12	119	22.9%	2.60 [1.41 , 4.80]
Goodwin 1996	12	58	14	244	20.5%	3.61 [1.76 , 7.38]
Moutquin 2000	51	121	26	126	28.1%	2.04 [1.37 , 3.05]
Shim 2006	3	65	0	63	2.8%	6.79 [0.36 , 128.81]
Total (95% CI)		**535**		**708**	**100.0%**	**1.97 [1.18 , 3.30]**
Total events:	117		73			

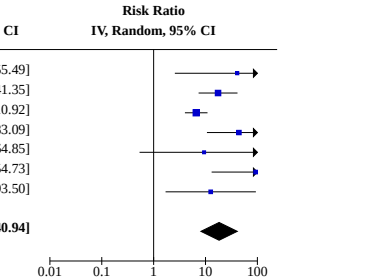
Heterogeneity: Tau² = 0.20; Chi² = 12.45, df = 5 (P = 0.03); I² = 60%
Test for overall effect: Z = 2.59 (P = 0.009)
Test for subgroup differences: Not applicable



Analysis 12.18. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 18: Tachycardia

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	20	40	0	40	6.6%	41.00 [2.56 , 655.49]
European Atosiban Study 2001	97	129	5	116	22.6%	17.44 [7.36 , 41.35]
French and Australian Atosiban Investigators 2001	95	122	14	119	27.3%	6.62 [4.01 , 10.92]
Goodwin 1996	21	58	2	244	15.7%	44.17 [10.66 , 183.09]
Lin 2009	4	22	0	23	6.3%	9.39 [0.54 , 164.85]
Moutquin 2000	89	121	1	126	10.9%	92.68 [13.12 , 654.73]
Shim 2006	13	65	1	63	10.6%	12.60 [1.70 , 93.50]
Total (95% CI)		**557**		**731**	**100.0%**	**18.28 [8.16 , 40.94]**
Total events:	339		23			

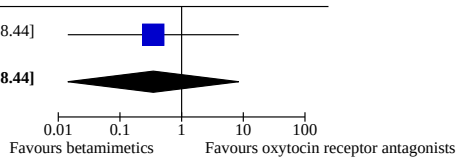
Heterogeneity: Tau² = 0.55; Chi² = 14.18, df = 6 (P = 0.03); I² = 58%
Test for overall effect: Z = 7.06 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 12.19. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Moutquin 2000	0	121	1	126	100.0%	0.35 [0.01 , 8.44]
Total (95% CI)		**121**		**126**	**100.0%**	**0.35 [0.01 , 8.44]**
Total events:	0		1			

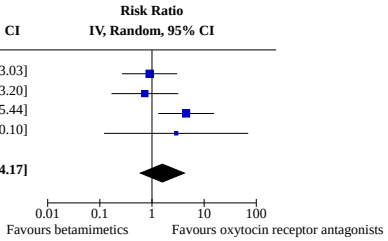
Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.52)
Test for subgroup differences: Not applicable



Analysis 12.20. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 20: Maternal hypotension

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
European Atosiban Study 2001	5	129	5	116	32.9%	0.90 [0.27 , 3.03]
French and Australian Atosiban Investigators 2001	3	122	4	119	26.4%	0.73 [0.17 , 3.20]
Moutquin 2000	13	121	3	126	32.5%	4.51 [1.32 , 15.44]
Shim 2006	1	65	0	63	8.2%	2.91 [0.12 , 70.10]
Total (95% CI)		**437**		**424**	**100.0%**	**1.58 [0.60 , 4.17]**
Total events:	22		12			

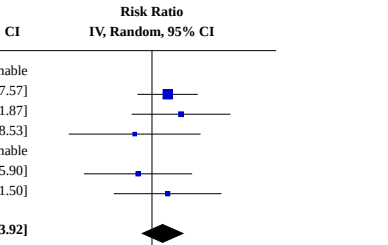
Heterogeneity: Tau² = 0.36; Chi² = 4.81, df = 3 (P = 0.19); I² = 38%
Test for overall effect: Z = 0.93 (P = 0.35)
Test for subgroup differences: Not applicable



Analysis 12.21. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 21: Perinatal death

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	0	40	0	40		Not estimable
European Atosiban Study 2001	7	153	3	131	45.3%	2.00 [0.53 , 7.57]
French and Australian Atosiban Investigators 2001	4	143	1	129	16.9%	3.61 [0.41 , 31.87]
Goodwin 1996	0	56	4	238	9.5%	0.47 [0.03 , 8.53]
Lin 2009	0	22	0	23		Not estimable
Moutquin 2000	1	135	2	146	14.1%	0.54 [0.05 , 5.90]
Shim 2006	2	63	1	63	14.2%	2.00 [0.19 , 21.50]
Total (95% CI)		**612**		**770**	**100.0%**	**1.60 [0.65 , 3.92]**
Total events:	14		11			

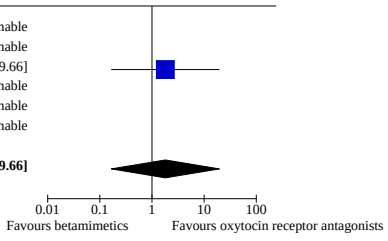
Heterogeneity: Tau² = 0.00; Chi² = 2.16, df = 4 (P = 0.71); I² = 0%
Test for overall effect: Z = 1.03 (P = 0.30)
Test for subgroup differences: Not applicable



Analysis 12.22. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 22: Stillbirth

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Cabar 2008	0	40	0	40		Not estimable
European Atosiban Study 2001	0	153	0	131		Not estimable
French and Australian Atosiban Investigators 2001	2	143	1	129	100.0%	1.80 [0.17 , 19.66]
Lin 2009	0	22	0	23		Not estimable
Moutquin 2000	0	135	0	146		Not estimable
Shim 2006	0	63	0	63		Not estimable
Total (95% CI)		**556**		**532**	**100.0%**	**1.80 [0.17 , 19.66]**
Total events:	2		1			

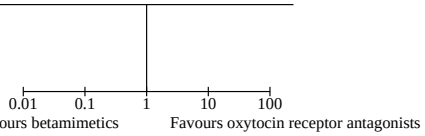
Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)
Test for subgroup differences: Not applicable



Analysis 12.23. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

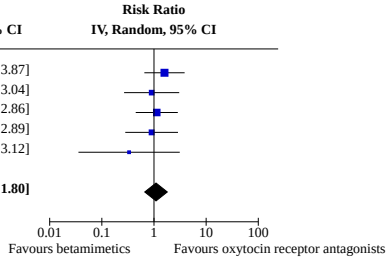
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 12.24. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
European Atosiban Study 2001	13	153	7	131	31.3%	1.59 [0.65 , 3.87]
French and Australian Atosiban Investigators 2001	5	143	5	129	16.7%	0.90 [0.27 , 3.04]
Goodwin 1996	5	44	19	189	28.7%	1.13 [0.45 , 2.86]
Moutquin 2000	5	135	6	146	18.3%	0.90 [0.28 , 2.89]
Shim 2006	1	63	3	63	5.0%	0.33 [0.04 , 3.12]
Total (95% CI)		**538**		**658**	**100.0%**	**1.09 [0.67 , 1.80]**
Total events:	29		40			

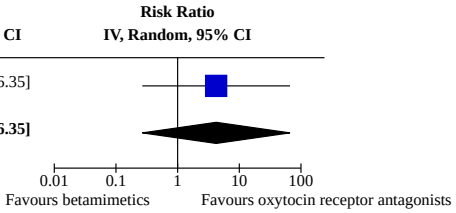
Heterogeneity: Tau² = 0.00; Chi² = 1.97, df = 4 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.35 (P = 0.72)
Test for subgroup differences: Not applicable



Analysis 12.25. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Goodwin 1996	1	56	1	236	100.0%	4.21 [0.27 , 66.35]
Total (95% CI)		**56**		**236**	**100.0%**	**4.21 [0.27 , 66.35]**
Total events:	1		1			

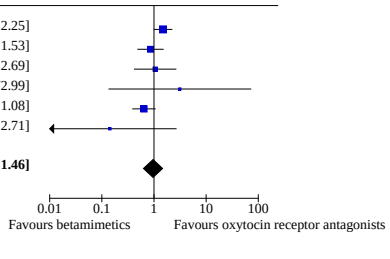
Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)
Test for subgroup differences: Not applicable



Analysis 12.26. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 26: Respiratory morbidity

Study or Subgroup	Betamimetics Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
European Atosiban Study 2001	47	153	27	131	31.4%	1.49 [0.99 , 2.25]
French and Australian Atosiban Investigators 2001	19	143	20	129	24.2%	0.86 [0.48 , 1.53]
Goodwin 1996	5	56	20	236	14.0%	1.05 [0.41 , 2.69]
Lin 2009	1	22	0	23	1.7%	3.13 [0.13 , 72.99]
Moutquin 2000	19	135	32	146	26.8%	0.64 [0.38 , 1.08]
Shim 2006	0	63	3	63	2.0%	0.14 [0.01 , 2.71]
Total (95% CI)		**572**		**728**	**100.0%**	**0.96 [0.63 , 1.46]**
Total events:	91		102			

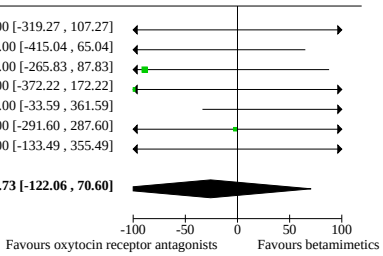
Heterogeneity: Tau² = 0.10; Chi² = 8.88, df = 5 (P = 0.11); I² = 44%
Test for overall effect: Z = 0.19 (P = 0.85)
Test for subgroup differences: Not applicable



Analysis 12.27. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 27: Mean birthweight

Study or Subgroup	Betamimetics Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cabar 2008	2448	439	40	2554	530	40	15.7%	-106.00 [-319.27 , 107.27]
European Atosiban Study 2001	2298	1130	153	2473	930	130	13.1%	-175.00 [-415.04 , 65.04]
French and Australian Atosiban Investigators 2001	2619	743	143	2708	743	129	20.7%	-89.00 [-265.83 , 87.83]
Lin 2009	2800	400	19	2900	500	23	10.6%	-100.00 [-372.22 , 172.22]
Moutquin 2000	2478	759	121	2314	825	126	17.7%	164.00 [-33.59 , 361.59]
Nonnenmacher 2009	2211	756	66	2213	889	60	9.5%	-2.00 [-291.60 , 287.60]
Shim 2006	3017	631	63	2906	763	63	12.7%	111.00 [-133.49 , 355.49]
Total (95% CI)			**605**			**571**	**100.0%**	**-25.73 [-122.06 , 70.60]**

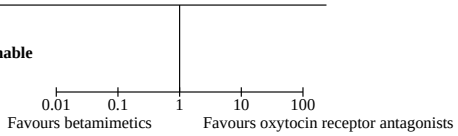
Heterogeneity: Tau² = 3507.19; Chi² = 7.58, df = 6 (P = 0.27); I² = 21%
Test for overall effect: Z = 0.52 (P = 0.60)
Test for subgroup differences: Not applicable



Analysis 12.28. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Betamimetics Events	Betamimetics Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

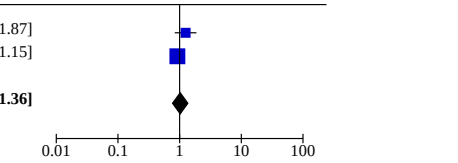
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 12.29. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Betamimetics Events	Betamimetics Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Goodwin 1996	20	56	68	238	34.3%	1.25 [0.83 , 1.87]
Moutquin 2000	68	135	80	146	65.7%	0.92 [0.74 , 1.15]
Total (95% CI)		**191**		**384**	**100.0%**	**1.02 [0.77 , 1.36]**
Total events:	88		148			

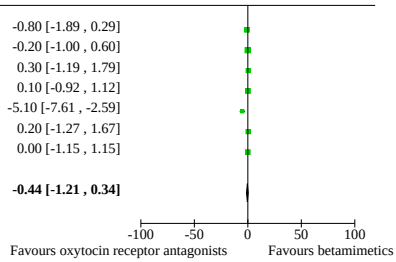
Heterogeneity: Tau² = 0.02; Chi² = 1.70, df = 1 (P = 0.19); I² = 41%
Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable



Analysis 12.30. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 30: Gestational age at birth

Study or Subgroup	Betamimetics Mean	Betamimetics SD	Betamimetics Total	Oxytocin receptor antagonists Mean	Oxytocin receptor antagonists SD	Oxytocin receptor antagonists Total	Weight	Mean Difference IV, Random, 95% CI
European Atosiban Study 2001	34.3	4.5	129	35.1	4.2	115	16.2%	-0.80 [-1.89 , 0.29]
French and Australian Atosiban Investigators 2001	36.3	3.7	143	36.5	3	129	19.0%	-0.20 [-1.00 , 0.60]
Lin 2009	37.4	2.4	19	37.1	2.5	23	12.7%	0.30 [-1.19 , 1.79]
Moutquin 2000	35.2	4	121	35.1	4.2	126	16.8%	0.10 [-0.92 , 1.12]
Neri 2009	30	4.7	25	35.1	4.7	29	6.8%	-5.10 [-7.61 , -2.59]
Nonnenmacher 2009	34.3	3.4	54	34.1	4.2	51	12.9%	0.20 [-1.27 , 1.67]
Shim 2006	37.3	3.1	63	37.3	3.5	63	15.6%	0.00 [-1.15 , 1.15]
Total (95% CI)			**554**			**536**	**100.0%**	**-0.44 [-1.21 , 0.34]**

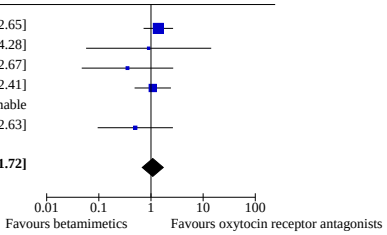
Heterogeneity: Tau² = 0.67; Chi² = 16.78, df = 6 (P = 0.01); I² = 64%
Test for overall effect: Z = 1.09 (P = 0.27)
Test for subgroup differences: Not applicable



Analysis 12.31. Comparison 12: Betamimetics vs oxytocin receptor antagonists, Outcome 31: Neonatal infection

Study or Subgroup	Betamimetics Events	Betamimetics Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
European Atosiban Study 2001	21	153	13	131	50.7%	1.38 [0.72 , 2.65]
French and Australian Atosiban Investigators 2001	1	143	1	129	2.8%	0.90 [0.06 , 14.28]
Goodwin 1996	1	56	12	238	5.3%	0.35 [0.05 , 2.67]
Moutquin 2000	11	135	11	146	33.4%	1.08 [0.48 , 2.41]
Neri 2009	0	25	0	29		Not estimable
Shim 2006	2	63	4	63	7.8%	0.50 [0.09 , 2.63]
Total (95% CI)		**575**		**736**	**100.0%**	**1.08 [0.68 , 1.72]**
Total events:	36		41			

Heterogeneity: Tau² = 0.00; Chi² = 2.57, df = 4 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.33 (P = 0.74)
Test for subgroup differences: Not applicable



Comparison 13. Betamimetics vs combinations of tocolytics

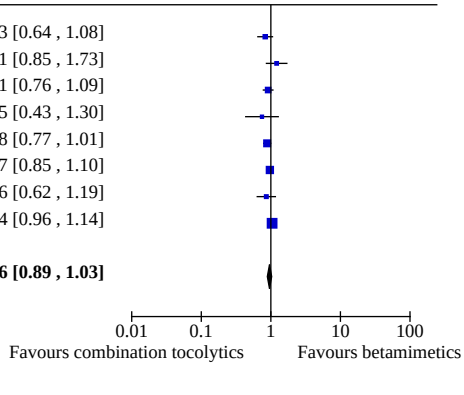
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.1 Delay in birth by 48 hours	8	687	Risk Ratio (IV, Random, 95% CI)	0.96 [0.89, 1.03]
13.2 Delay in birth by 7 days	5	391	Risk Ratio (IV, Random, 95% CI)	0.97 [0.88, 1.08]
13.3 Neonatal death before 28 days	4	296	Risk Ratio (IV, Random, 95% CI)	1.57 [0.53, 4.65]
13.4 Pregnancy prolongation (time from trial entry to birth in days)	4	223	Mean Difference (IV, Random, 95% CI)	0.42 [-8.91, 9.74]
13.5 Serious adverse effects of drugs	5	392	Risk Ratio (IV, Random, 95% CI)	2.90 [0.31, 26.80]
13.6 Maternal infection	2	128	Risk Ratio (IV, Random, 95% CI)	1.16 [0.17, 7.96]
13.7 Cessation of treatment due to adverse effects	9	580	Risk Ratio (IV, Random, 95% CI)	2.36 [0.62, 8.95]
13.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
13.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
13.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
13.11 Birth before 37 weeks' gestation	3	399	Risk Ratio (IV, Random, 95% CI)	1.14 [0.96, 1.36]
13.12 Maternal death	1	131	Risk Ratio (IV, Random, 95% CI)	Not estimable
13.13 Pulmonary oedema	3	315	Risk Ratio (IV, Random, 95% CI)	3.00 [0.13, 71.00]
13.14 Dyspnoea	2	149	Risk Ratio (IV, Random, 95% CI)	4.09 [0.69, 24.17]
13.15 Palpitations	2	191	Risk Ratio (IV, Random, 95% CI)	5.17 [0.84, 31.73]
13.16 Headaches	1	71	Risk Ratio (IV, Random, 95% CI)	2.06 [0.20, 21.68]
13.17 Nausea or vomiting	5	486	Risk Ratio (IV, Random, 95% CI)	0.80 [0.43, 1.50]
13.18 Tachycardia	5	556	Risk Ratio (IV, Random, 95% CI)	1.56 [1.05, 2.30]
13.19 Maternal cardiac arrhythmias	1	106	Risk Ratio (IV, Random, 95% CI)	2.89 [0.12, 69.40]
13.20 Maternal hypotension	4	313	Risk Ratio (IV, Random, 95% CI)	1.70 [0.79, 3.65]
13.21 Perinatal death	6	611	Risk Ratio (IV, Random, 95% CI)	1.60 [0.82, 3.12]
13.22 Stillbirth	4	369	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.23 Neonatal death before 7 days	1	107	Risk Ratio (IV, Random, 95% CI)	Not estimable
13.24 Neurodevelopmental morbidity	1	97	Risk Ratio (IV, Random, 95% CI)	3.76 [0.44, 32.44]
13.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
13.26 Respiratory morbidity	1	70	Risk Ratio (IV, Random, 95% CI)	0.60 [0.24, 1.47]
13.27 Mean birthweight	6	391	Mean Difference (IV, Random, 95% CI)	-70.71 [-193.64, 52.22]
13.28 Birthweight < 2000 g	1	24	Risk Ratio (IV, Random, 95% CI)	1.18 [0.08, 16.78]
13.29 Birthweight < 2500 g	4	360	Risk Ratio (IV, Random, 95% CI)	1.33 [0.92, 1.92]
13.30 Gestational age at birth	3	239	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.76, 0.42]
13.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 13.1. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Betamimetics Events	Betamimetics Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Beall 1985	49	85	32	46	6.6%	0.83 [0.64 , 1.08]
Hatjis 1987	23	32	19	32	3.7%	1.21 [0.85 , 1.73]
Hollander 1987	30	36	31	34	12.6%	0.91 [0.76 , 1.09]
Meyer 1990	10	24	19	34	1.6%	0.75 [0.43 , 1.30]
Morales 1989	45	54	49	52	18.8%	0.88 [0.77 , 1.01]
Surichamorn 2001	32	35	34	36	20.4%	0.97 [0.85 , 1.10]
Tchilinguirian 1984	20	31	27	36	4.6%	0.86 [0.62 , 1.19]
Wilkins 1988	52	54	61	66	31.8%	1.04 [0.96 , 1.14]
Total (95% CI)		**351**		**336**	**100.0%**	**0.96 [0.89 , 1.03]**
Total events:	261		272			

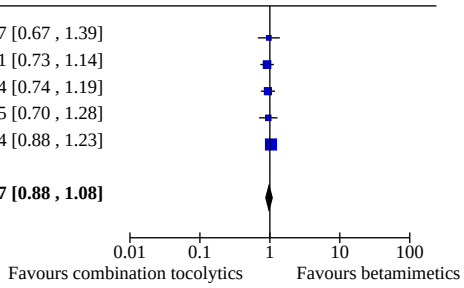
Heterogeneity: Tau² = 0.00; Chi² = 9.00, df = 7 (P = 0.25); I² = 22%
Test for overall effect: Z = 1.22 (P = 0.22)
Test for subgroup differences: Not applicable



Analysis 13.2. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Francioli 1988	9	11	11	13	8.3%	0.97 [0.67 , 1.39]
Hollander 1987	28	36	29	34	21.8%	0.91 [0.73 , 1.14]
Morales 1989	38	54	39	52	19.9%	0.94 [0.74 , 1.19]
Surichamorn 2001	24	35	26	36	11.9%	0.95 [0.70 , 1.28]
Wilkins 1988	45	54	53	66	38.1%	1.04 [0.88 , 1.23]
Total (95% CI)		**190**		**201**	**100.0%**	**0.97 [0.88 , 1.08]**
Total events:	144		158			

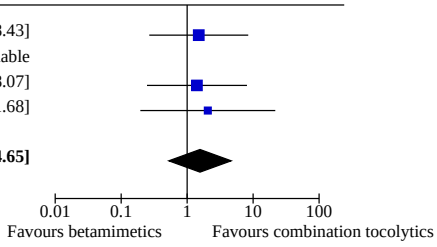
Heterogeneity: Tau² = 0.00; Chi² = 1.00, df = 4 (P = 0.91); I² = 0%
Test for overall effect: Z = 0.52 (P = 0.60)
Test for subgroup differences: Not applicable



Analysis 13.3. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hatjis 1987	3	35	2	35	39.7%	1.50 [0.27 , 8.43]
Meyer 1990	0	24	0	34		Not estimable
Morales 1989	3	50	2	47	38.9%	1.41 [0.25 , 8.07]
Surichamorn 2001	2	35	1	36	21.4%	2.06 [0.20 , 21.68]
Total (95% CI)		**144**		**152**	**100.0%**	**1.57 [0.53 , 4.65]**
Total events:	8		5			

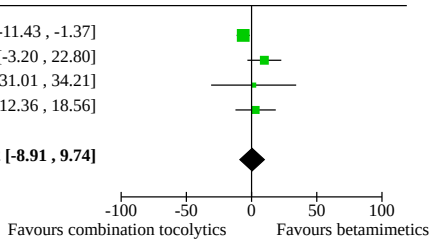
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.81 (P = 0.42)
Test for subgroup differences: Not applicable



Analysis 13.4. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Betamimetics Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ally 1992	20.7	13.6	51	27.1	12.9	56	45.5%	-6.40 [-11.43 , -1.37]
Ferguson 1984	16.8	21.4	14	7	15	20	26.0%	9.80 [-3.20 , 22.80]
Francioli 1988	34	28.9	11	32.4	51.1	13	7.1%	1.60 [-31.01 , 34.21]
Meyer 1990	24.4	32.9	24	21.3	24.1	34	21.5%	3.10 [-12.36 , 18.56]
Total (95% CI)			**100**			**123**	**100.0%**	**0.42 [-8.91 , 9.74]**

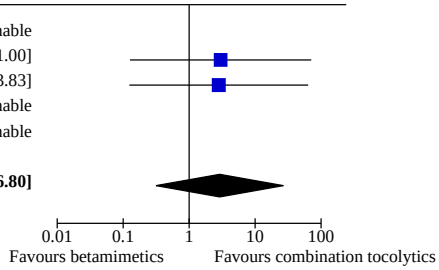
Heterogeneity: Tau² = 43.23; Chi² = 6.09, df = 3 (P = 0.11); I² = 51%
Test for overall effect: Z = 0.09 (P = 0.93)
Test for subgroup differences: Not applicable



Analysis 13.5. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Betamimetics Events	Betamimetics Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Beall 1985	0	85	0	46		Not estimable
Hatjis 1987	1	32	0	32	49.3%	3.00 [0.13 , 71.00]
Miller 1982	1	15	0	14	50.7%	2.81 [0.12 , 63.83]
Morales 1989	0	50	0	47		Not estimable
Surichamorn 2001	0	35	0	36		Not estimable
Total (95% CI)		**217**		**175**	**100.0%**	**2.90 [0.31 , 26.80]**
Total events:	2		0			

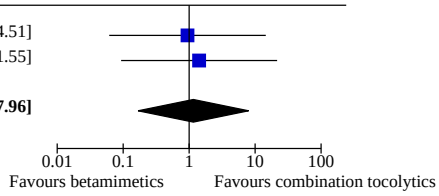
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.98); I² = 0%
Test for overall effect: Z = 0.94 (P = 0.35)
Test for subgroup differences: Not applicable



Analysis 13.6. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 6: Maternal infection

Study or Subgroup	Betamimetics Events	Betamimetics Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Hollander 1987	1	36	1	34	49.8%	0.94 [0.06 , 14.51]
Meyer 1990	1	24	1	34	50.2%	1.42 [0.09 , 21.55]
Total (95% CI)		**60**		**68**	**100.0%**	**1.16 [0.17 , 7.96]**
Total events:	2		2			

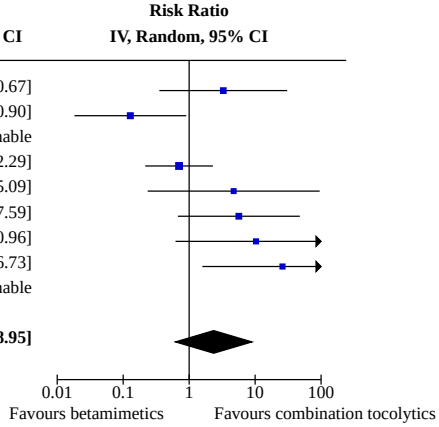
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable



Analysis 13.7. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Betamimetics Events	Betamimetics Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Ally 1992	3	51	1	56	14.4%	3.29 [0.35 , 30.67]
Ferguson 1984	1	17	11	24	16.0%	0.13 [0.02 , 0.90]
Francioli 1988	0	11	0	13		Not estimable
Hatjis 1987	4	36	6	38	20.3%	0.70 [0.22 , 2.29]
Hollander 1987	2	36	0	34	10.9%	4.73 [0.24 , 95.09]
Meyer 1990	4	24	1	34	15.0%	5.67 [0.67 , 47.59]
Miller 1982	5	15	0	14	11.7%	10.31 [0.62 , 170.96]
Morales 1989	13	54	0	52	11.7%	26.02 [1.59 , 426.73]
Surichamorn 2001	0	35	0	36		Not estimable
Total (95% CI)		**279**		**301**	**100.0%**	**2.36 [0.62 , 8.95]**
Total events:	32		19			

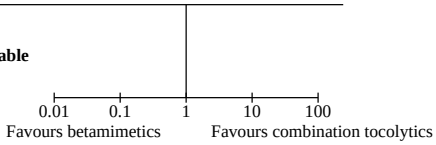
Heterogeneity: Tau² = 1.92; Chi² = 16.03, df = 6 (P = 0.01); I² = 63%
Test for overall effect: Z = 1.26 (P = 0.21)
Test for subgroup differences: Not applicable



Analysis 13.8. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

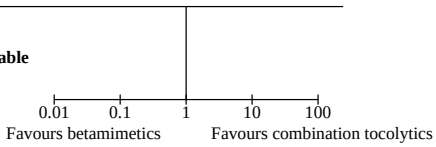
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 13.9. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

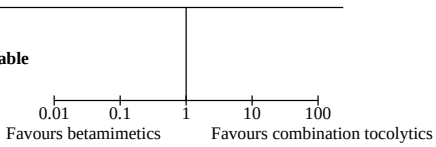
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 13.10. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

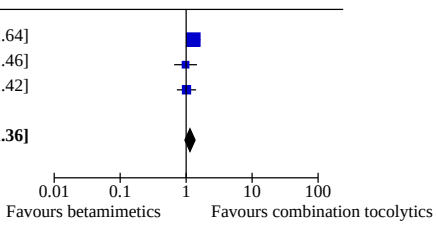
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 13.11. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Gamissans 1982	67	104	52	104	53.1%	1.29 [1.01 , 1.64]
Surichamorn 2001	20	35	21	36	19.6%	0.98 [0.66 , 1.46]
Wilkins 1988	29	54	35	66	27.4%	1.01 [0.72 , 1.42]
Total (95% CI)		**193**		**206**	**100.0%**	**1.14 [0.96 , 1.36]**
Total events:	116		108			

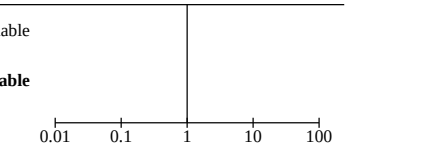
Heterogeneity: Tau² = 0.00; Chi² = 2.04, df = 2 (P = 0.36); I² = 2%
Test for overall effect: Z = 1.48 (P = 0.14)
Test for subgroup differences: Not applicable



Analysis 13.12. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 12: Maternal death

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Beall 1985	0	85	0	46		Not estimable
Total (95% CI)		**85**		**46**		**Not estimable**
Total events:	0		0			

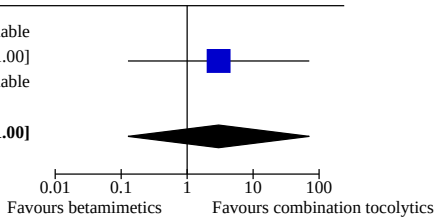
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 13.13. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 13: Pulmonary oedema

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Beall 1985	0	85	0	46		Not estimable
Hatjis 1987	1	32	0	32	100.0%	3.00 [0.13 , 71.00]
Wilkins 1988	0	54	0	66		Not estimable
Total (95% CI)		**171**		**144**	**100.0%**	**3.00 [0.13 , 71.00]**
Total events:	1		0			

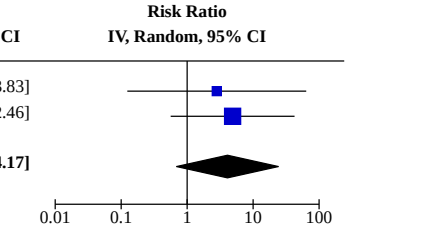
Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)
Test for subgroup differences: Not applicable



Analysis 13.14. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 14: Dyspnoea

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Miller 1982	1	15	0	14	32.4%	2.81 [0.12 , 63.83]
Wilkins 1988	4	54	1	66	67.6%	4.89 [0.56 , 42.46]
Total (95% CI)		**69**		**80**	**100.0%**	**4.09 [0.69 , 24.17]**
Total events:	5		1			

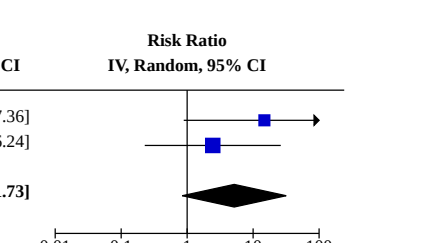
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 1.55 (P = 0.12)
Test for subgroup differences: Not applicable



Analysis 13.15. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 15: Palpitations

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hollander 1987	8	38	0	33	41.6%	14.82 [0.89 , 247.36]
Wilkins 1988	2	54	1	66	58.4%	2.44 [0.23 , 26.24]
Total (95% CI)		**92**		**99**	**100.0%**	**5.17 [0.84 , 31.73]**
Total events:	10		1			

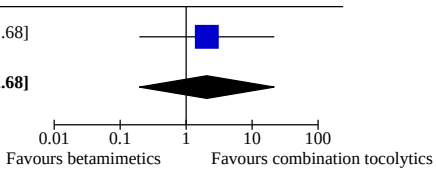
Heterogeneity: Tau² = 0.00; Chi² = 0.92, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 1.77 (P = 0.08)
Test for subgroup differences: Not applicable



Analysis 13.16. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 16: Headaches

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Surichamorn 2001	2	35	1	36	100.0%	2.06 [0.20 , 21.68]
Total (95% CI)		**35**		**36**	**100.0%**	**2.06 [0.20 , 21.68]**
Total events:	2		1			

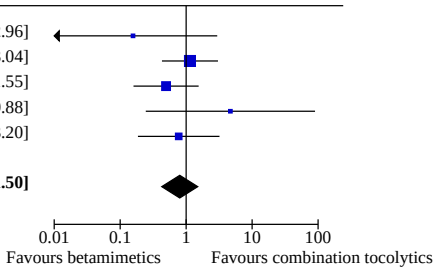
Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable



Analysis 13.17. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 17: Nausea or vomiting

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ally 1992	0	51	3	56	4.5%	0.16 [0.01 , 2.96]
Gamissans 1982	8	104	7	104	41.1%	1.14 [0.43 , 3.04]
Hollander 1987	4	38	7	33	30.4%	0.50 [0.16 , 1.55]
Miller 1982	2	15	0	14	4.5%	4.69 [0.24 , 89.88]
Surichamorn 2001	3	35	4	36	19.4%	0.77 [0.19 , 3.20]
Total (95% CI)		**243**		**243**	**100.0%**	**0.80 [0.43 , 1.50]**
Total events:	17		21			

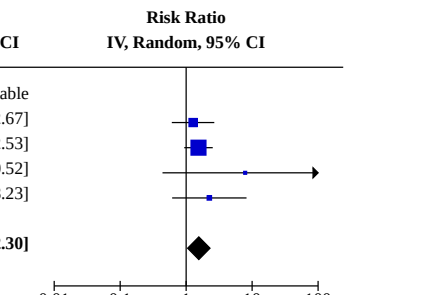
Heterogeneity: Tau² = 0.00; Chi² = 3.75, df = 4 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.70 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 13.18. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 18: Tachycardia

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ally 1992	0	51	0	56		Not estimable
Gamissans 1982	14	104	11	104	27.7%	1.27 [0.61 , 2.67]
Hatjis 1987	20	32	13	32	61.5%	1.54 [0.94 , 2.53]
Hollander 1987	4	38	0	33	1.8%	7.85 [0.44 , 140.52]
Morales 1989	7	54	3	52	9.0%	2.25 [0.61 , 8.23]
Total (95% CI)		**279**		**277**	**100.0%**	**1.56 [1.05 , 2.30]**
Total events:	45		27			

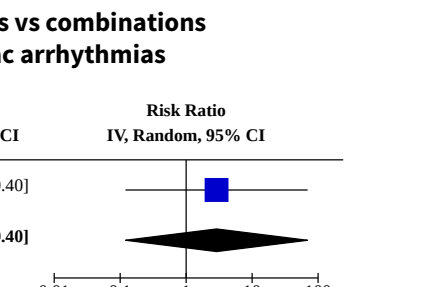
Heterogeneity: Tau² = 0.00; Chi² = 1.80, df = 3 (P = 0.61); I² = 0%
Test for overall effect: Z = 2.22 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 13.19. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Morales 1989	1	54	0	52	100.0%	2.89 [0.12 , 69.40]
Total (95% CI)		**54**		**52**	**100.0%**	**2.89 [0.12 , 69.40]**
Total events:	1		0			

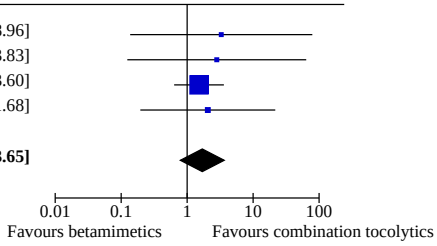
Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 13.20. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 20: Maternal hypotension

Study or Subgroup	Betamimetics Events	Betamimetics Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Ally 1992	1	51	0	56	5.8%	3.29 [0.14 , 78.96]
Miller 1982	1	15	0	14	6.0%	2.81 [0.12 , 63.83]
Morales 1989	11	54	7	52	77.7%	1.51 [0.64 , 3.60]
Surichamorn 2001	2	35	1	36	10.5%	2.06 [0.20 , 21.68]
Total (95% CI)		**155**		**158**	**100.0%**	**1.70 [0.79 , 3.65]**
Total events:	15		8			

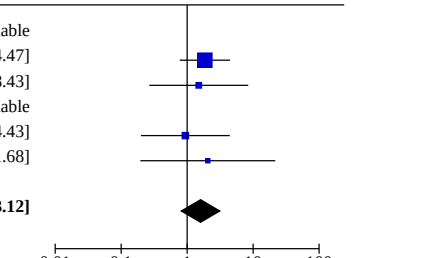
Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 3 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.36 (P = 0.18)
Test for subgroup differences: Not applicable



Analysis 13.21. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 21: Perinatal death

Study or Subgroup	Betamimetics Events	Betamimetics Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Beall 1985	0	55	0	52		Not estimable
Gamissans 1982	13	104	7	104	58.2%	1.86 [0.77 , 4.47]
Hatjis 1987	3	35	2	35	15.0%	1.50 [0.27 , 8.43]
Meyer 1990	0	24	0	34		Not estimable
Morales 1989	3	50	3	47	18.7%	0.94 [0.20 , 4.43]
Surichamorn 2001	2	35	1	36	8.1%	2.06 [0.20 , 21.68]
Total (95% CI)		**303**		**308**	**100.0%**	**1.60 [0.82 , 3.12]**
Total events:	21		13			

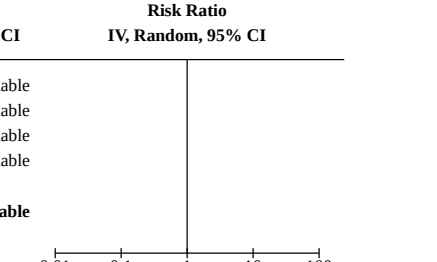
Heterogeneity: Tau² = 0.00; Chi² = 0.61, df = 3 (P = 0.89); I² = 0%
Test for overall effect: Z = 1.37 (P = 0.17)
Test for subgroup differences: Not applicable



Analysis 13.22. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 22: Stillbirth

Study or Subgroup	Betamimetics Events	Betamimetics Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Beall 1985	0	85	0	46		Not estimable
Hatjis 1987	0	35	0	35		Not estimable
Morales 1989	0	50	0	47		Not estimable
Surichamorn 2001	0	35	0	36		Not estimable
Total (95% CI)		**205**		**164**		**Not estimable**
Total events:	0		0			

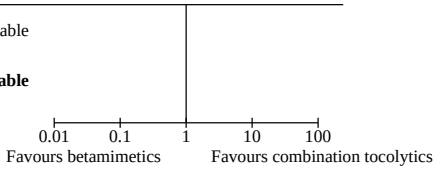
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 13.23. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Beall 1985	0	52	0	55		Not estimable
Total (95% CI)		**52**		**55**		**Not estimable**
Total events:	0		0			

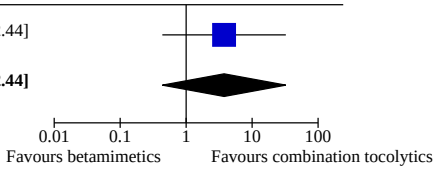
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 13.24. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Morales 1989	4	50	1	47	100.0%	3.76 [0.44 , 32.44]
Total (95% CI)		**50**		**47**	**100.0%**	**3.76 [0.44 , 32.44]**
Total events:	4		1			

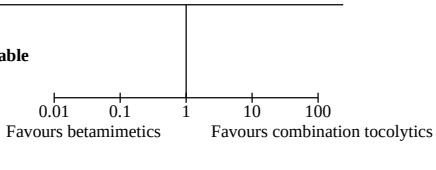
Heterogeneity: Not applicable
Test for overall effect: Z = 1.20 (P = 0.23)
Test for subgroup differences: Not applicable



Analysis 13.25. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

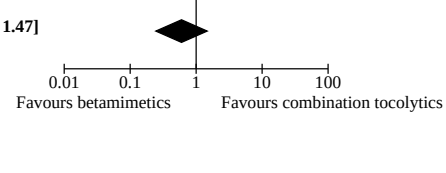
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 13.26. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 26: Respiratory morbidity

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Hatjis 1987	6	35	10	35	100.0%	0.60 [0.24 , 1.47]
Total (95% CI)		**35**		**35**	**100.0%**	**0.60 [0.24 , 1.47]**
Total events:	6		10			

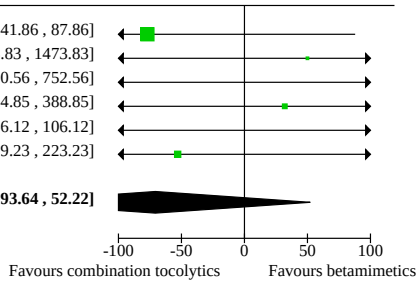
Heterogeneity: Not applicable
Test for overall effect: Z = 1.12 (P = 0.26)
Test for subgroup differences: Not applicable



Analysis 13.27. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 27: Mean birthweight

Study or Subgroup	Betamimetics Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ally 1992	2852	420	51	2929	450	56	55.6%	-77.00 [-241.86 , 87.86]
Francioli 1988	2990	1415	11	2940	2120	13	0.7%	50.00 [-1373.83 , 1473.83]
Hatjis 1987	2191	1537	35	2065	1102	35	3.8%	126.00 [-500.56 , 752.56]
Hollander 1987	2416	696	30	2384	726	31	11.9%	32.00 [-324.85 , 388.85]
Meyer 1990	2281	858	24	2606	776	34	8.1%	-325.00 [-756.12 , 106.12]
Surichamorn 2001	2534	603	35	2587	584	36	19.8%	-53.00 [-329.23 , 223.23]
Total (95% CI)			**186**			**205**	**100.0%**	**-70.71 [-193.64 , 52.22]**

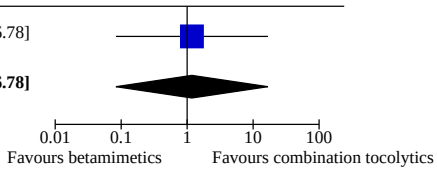
Heterogeneity: Tau² = 0.00; Chi² = 2.08, df = 5 (P = 0.84); I² = 0%
Test for overall effect: Z = 1.13 (P = 0.26)
Test for subgroup differences: Not applicable



Analysis 13.28. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Francioli 1988	1	11	1	13	100.0%	1.18 [0.08 , 16.78]
Total (95% CI)		**11**		**13**	**100.0%**	**1.18 [0.08 , 16.78]**
Total events:	1		1			

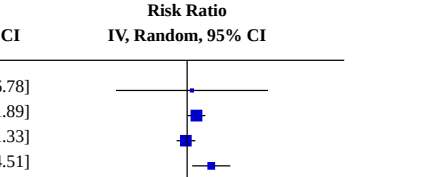
Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.90)
Test for subgroup differences: Not applicable



Analysis 13.29. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Betamimetics Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Francioli 1988	1	11	1	13	1.9%	1.18 [0.08 , 16.78]
Gamissans 1982	54	104	39	104	39.8%	1.38 [1.02 , 1.89]
Hatjis 1987	23	35	24	35	38.5%	0.96 [0.69 , 1.33]
Meyer 1990	23	34	7	24	19.8%	2.32 [1.19 , 4.51]
Total (95% CI)		**184**		**176**	**100.0%**	**1.33 [0.92 , 1.92]**
Total events:	101		71			

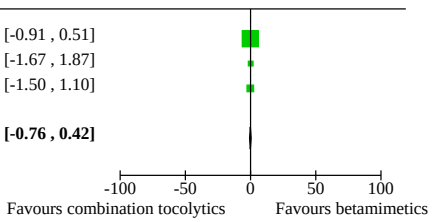
Heterogeneity: Tau² = 0.06; Chi² = 6.26, df = 3 (P = 0.10); I² = 52%
Test for overall effect: Z = 1.50 (P = 0.13)
Test for subgroup differences: Not applicable



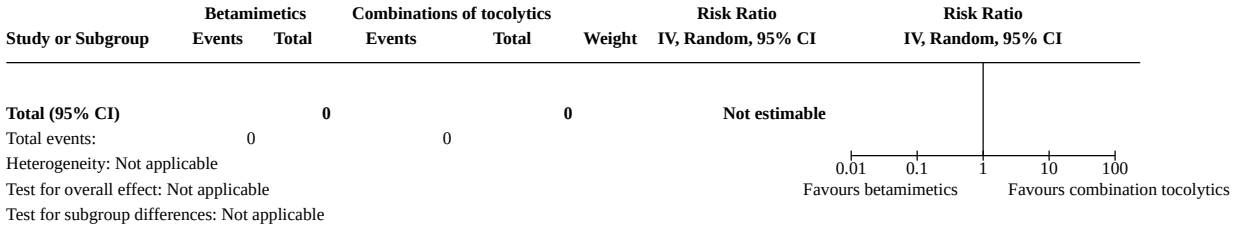
Analysis 13.30. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 30: Gestational age at birth

Study or Subgroup	Betamimetics Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ally 1992	37.2	1.4	51	37.4	2.3	56	68.3%	-0.20 [-0.91 , 0.51]
Hollander 1987	35.3	3	30	35.2	4	31	11.1%	0.10 [-1.67 , 1.87]
Surichamorn 2001	36	2.8	35	36.2	2.8	36	20.6%	-0.20 [-1.50 , 1.10]
Total (95% CI)			**116**			**123**	**100.0%**	**-0.17 [-0.76 , 0.42]**

Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 2 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.55 (P = 0.58)
Test for subgroup differences: Not applicable



Analysis 13.31. Comparison 13: Betamimetics vs combinations of tocolytics, Outcome 31: Neonatal infection



Comparison 14. Calcium channel blockers vs COX inhibitors

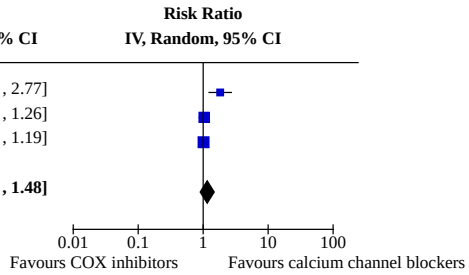
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Delay in birth by 48 hours	3	342	Risk Ratio (IV, Random, 95% CI)	1.15 [0.90, 1.48]
14.2 Delay in birth by 7 days	3	342	Risk Ratio (IV, Random, 95% CI)	1.13 [0.87, 1.48]
14.3 Neonatal death before 28 days	1	222	Risk Ratio (IV, Random, 95% CI)	0.49 [0.15, 1.64]
14.4 Pregnancy prolongation (time from trial entry to birth in days)	1	191	Mean Difference (IV, Random, 95% CI)	-1.00 [-7.09, 5.09]
14.5 Serious adverse effects of drugs	2	270	Risk Ratio (IV, Random, 95% CI)	3.57 [0.40, 31.81]
14.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.7 Cessation of treatment due to adverse effects	2	270	Risk Ratio (IV, Random, 95% CI)	1.13 [0.31, 4.18]
14.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.10 Birth before 34 weeks' gestation	1	191	Risk Ratio (IV, Random, 95% CI)	1.09 [0.88, 1.35]
14.11 Birth before 37 weeks' gestation	2	263	Risk Ratio (IV, Random, 95% CI)	0.94 [0.84, 1.04]
14.12 Maternal death	1	191	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.13 Pulmonary oedema	1	191	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.15 Palpitations	1	79	Risk Ratio (IV, Random, 95% CI)	6.83 [0.36, 128.02]
14.16 Headaches	1	79	Risk Ratio (IV, Random, 95% CI)	6.83 [0.36, 128.02]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.17 Nausea or vomiting	1	191	Risk Ratio (IV, Random, 95% CI)	2.51 [0.10, 60.95]
14.18 Tachycardia	1	191	Risk Ratio (IV, Random, 95% CI)	7.53 [0.97, 58.27]
14.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.20 Maternal hypotension	3	342	Risk Ratio (IV, Random, 95% CI)	10.85 [2.05, 57.34]
14.21 Perinatal death	2	301	Risk Ratio (IV, Random, 95% CI)	0.44 [0.14, 1.33]
14.22 Stillbirth	1	222	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.24 Neurodevelopmental morbidity	1	222	Risk Ratio (IV, Random, 95% CI)	0.62 [0.29, 1.33]
14.25 Gastrointestinal morbidity	1	222	Risk Ratio (IV, Random, 95% CI)	0.69 [0.19, 2.51]
14.26 Respiratory morbidity	1	222	Risk Ratio (IV, Random, 95% CI)	0.70 [0.49, 1.01]
14.27 Mean birthweight	2	294	Mean Difference (IV, Random, 95% CI)	101.46 [-80.34, 283.27]
14.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
14.30 Gestational age at birth	3	342	Mean Difference (IV, Random, 95% CI)	-0.24 [-1.26, 0.78]
14.31 Neonatal infection	1	222	Risk Ratio (IV, Random, 95% CI)	0.67 [0.30, 1.45]

Analysis 14.1. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	30	40	16	39	20.7%	1.83 [1.21 , 2.77]
Kashanian 2020	31	36	30	36	37.9%	1.03 [0.85 , 1.26]
Klauser 2014	80	104	66	87	41.3%	1.01 [0.87 , 1.19]
Total (95% CI)		**180**		**162**	**100.0%**	**1.15 [0.90 , 1.48]**
Total events:	141		112			

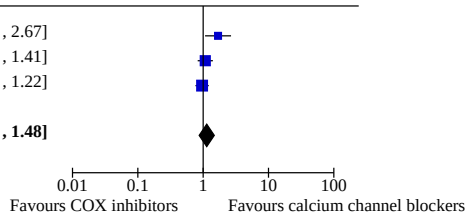
Heterogeneity: Tau² = 0.03; Chi² = 6.91, df = 2 (P = 0.03); I² = 71%
Test for overall effect: Z = 1.13 (P = 0.26)
Test for subgroup differences: Not applicable



Analysis 14.2. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	26	40	15	39	21.6%	1.69 [1.07 , 2.67]
Kashanian 2020	28	36	26	36	37.3%	1.08 [0.82 , 1.41]
Klauser 2014	61	104	53	87	41.1%	0.96 [0.76 , 1.22]
Total (95% CI)		**180**		**162**	**100.0%**	**1.13 [0.87 , 1.48]**
Total events:	115		94			

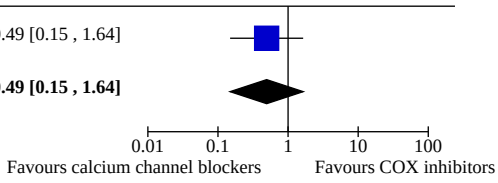
Heterogeneity: Tau² = 0.03; Chi² = 4.61, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 0.93 (P = 0.35)
Test for subgroup differences: Not applicable



Analysis 14.3. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	4	119	7	103	100.0%	0.49 [0.15 , 1.64]
Total (95% CI)		**119**		**103**	**100.0%**	**0.49 [0.15 , 1.64]**
Total events:	4		7			

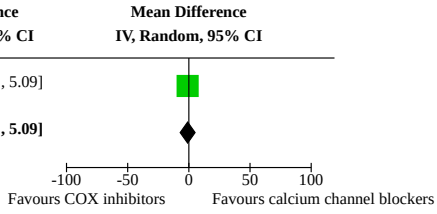
Heterogeneity: Not applicable
Test for overall effect: Z = 1.15 (P = 0.25)
Test for subgroup differences: Not applicable



Analysis 14.4. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	COX inhibitors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Klauser 2014	21.7	21.7	104	22.7	21.1	87	100.0%	-1.00 [-7.09 , 5.09]
Total (95% CI)			**104**			**87**	**100.0%**	**-1.00 [-7.09 , 5.09]**

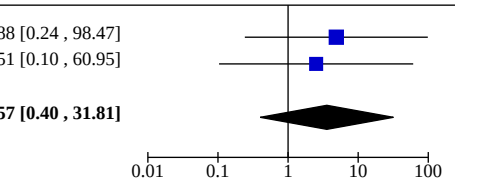
Heterogeneity: Not applicable
Test for overall effect: Z = 0.32 (P = 0.75)
Test for subgroup differences: Not applicable



Analysis 14.5. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	2	40	0	39	53.0%	4.88 [0.24 , 98.47]
Klauser 2014	1	104	0	87	47.0%	2.51 [0.10 , 60.95]
Total (95% CI)		**144**		**126**	**100.0%**	**3.57 [0.40 , 31.81]**
Total events:	3		0			

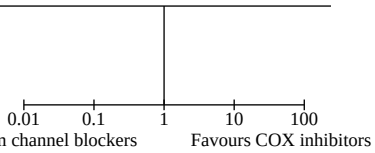
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 1.14 (P = 0.25)
Test for subgroup differences: Not applicable



Analysis 14.6. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 6: Maternal infection

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

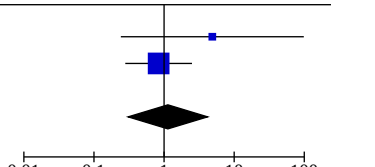
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.7. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	2	40	0	39	17.2%	4.88 [0.24 , 98.47]
Klauser 2014	6	104	6	87	82.8%	0.84 [0.28 , 2.50]
Total (95% CI)		**144**		**126**	**100.0%**	**1.13 [0.31 , 4.18]**
Total events:	8		6			

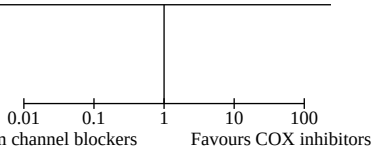
Heterogeneity: Tau² = 0.22; Chi² = 1.17, df = 1 (P = 0.28); I² = 14%
Test for overall effect: Z = 0.19 (P = 0.85)
Test for subgroup differences: Not applicable



Analysis 14.8. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

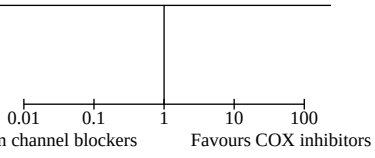
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.9. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

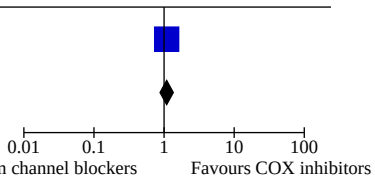
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.10. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	69	104	53	87	100.0%	1.09 [0.88 , 1.35]
Total (95% CI)		**104**		**87**	**100.0%**	**1.09 [0.88 , 1.35]**
Total events:	69		53			

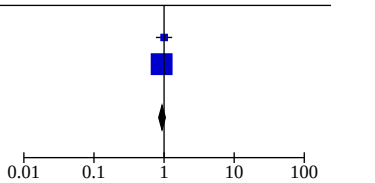
Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)
Test for subgroup differences: Not applicable



Analysis 14.11. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2020	27	36	27	36	16.4%	1.00 [0.77 , 1.31]
Klauser 2014	85	104	77	87	83.6%	0.92 [0.82 , 1.04]
Total (95% CI)		**140**		**123**	**100.0%**	**0.94 [0.84 , 1.04]**
Total events:	112		104			

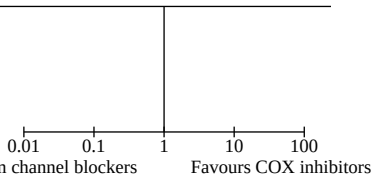
Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 1 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.21 (P = 0.23)
Test for subgroup differences: Not applicable



Analysis 14.12. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 12: Maternal death

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	104	0	87		Not estimable
Total (95% CI)		**104**		**87**		**Not estimable**
Total events:	0		0			

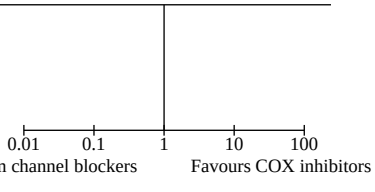
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.13. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 13: Pulmonary oedema

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	104	0	87		Not estimable
Total (95% CI)		**104**		**87**		**Not estimable**
Total events:	0		0			

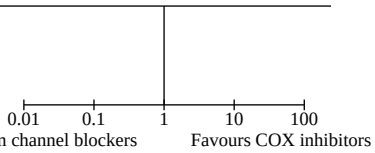
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.14. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 14: Dyspnoea

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

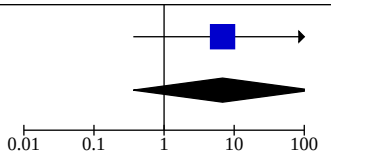
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.15. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 15: Palpitations

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	3	40	0	39	100.0%	6.83 [0.36 , 128.02]
Total (95% CI)		**40**		**39**	**100.0%**	**6.83 [0.36 , 128.02]**
Total events:	3		0			

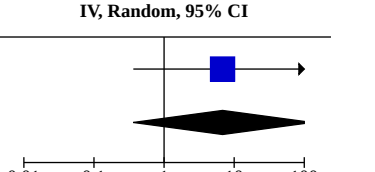
Heterogeneity: Not applicable
Test for overall effect: Z = 1.28 (P = 0.20)
Test for subgroup differences: Not applicable



Analysis 14.16. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 16: Headaches

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	3	40	0	39	100.0%	6.83 [0.36 , 128.02]
Total (95% CI)		**40**		**39**	**100.0%**	**6.83 [0.36 , 128.02]**
Total events:	3		0			

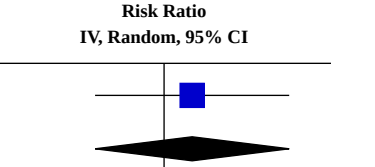
Heterogeneity: Not applicable
Test for overall effect: Z = 1.28 (P = 0.20)
Test for subgroup differences: Not applicable



Analysis 14.17. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 17: Nausea or vomiting

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	1	104	0	87	100.0%	2.51 [0.10 , 60.95]
Total (95% CI)		**104**		**87**	**100.0%**	**2.51 [0.10 , 60.95]**
Total events:	1		0			

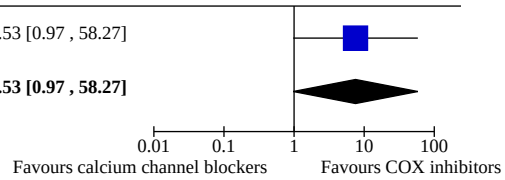
Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)
Test for subgroup differences: Not applicable



Analysis 14.18. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 18: Tachycardia

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	9	104	1	87	100.0%	7.53 [0.97 , 58.27]
Total (95% CI)		**104**		**87**	**100.0%**	**7.53 [0.97 , 58.27]**
Total events:	9		1			

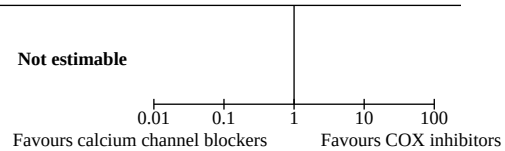
Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)
Test for subgroup differences: Not applicable



Analysis 14.19. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

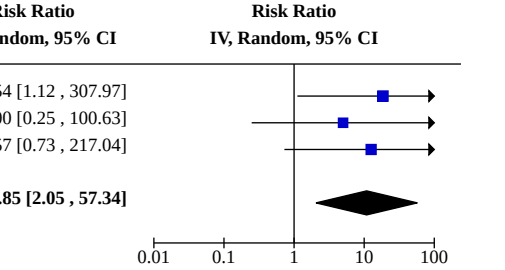
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.20. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 20: Maternal hypotension

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	9	40	0	39	35.1%	18.54 [1.12 , 307.97]
Kashanian 2020	2	36	0	36	30.8%	5.00 [0.25 , 100.63]
Klauser 2014	7	104	0	87	34.2%	12.57 [0.73 , 217.04]
Total (95% CI)		**180**		**162**	**100.0%**	**10.85 [2.05 , 57.34]**
Total events:	18		0			

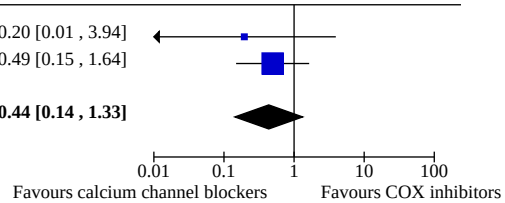
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 2 (P = 0.82); I² = 0%
Test for overall effect: Z = 2.81 (P = 0.005)
Test for subgroup differences: Not applicable



Analysis 14.21. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 21: Perinatal death

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2011	0	40	2	39	13.8%	0.20 [0.01 , 3.94]
Klauser 2014	4	119	7	103	86.2%	0.49 [0.15 , 1.64]
Total (95% CI)		**159**		**142**	**100.0%**	**0.44 [0.14 , 1.33]**
Total events:	4		9			

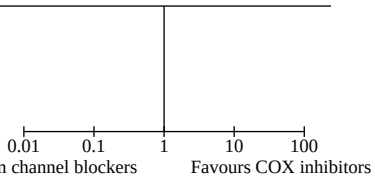
Heterogeneity: Tau² = 0.00; Chi² = 0.32, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 1.46 (P = 0.14)
Test for subgroup differences: Not applicable



Analysis 14.22. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 22: Stillbirth

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	119	0	103		Not estimable
Total (95% CI)		**119**		**103**		**Not estimable**
Total events:	0		0			

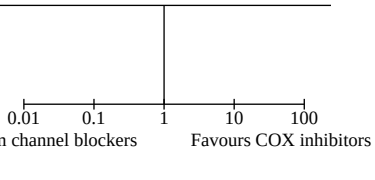
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.23. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

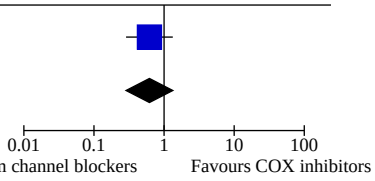
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.24. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	10	119	14	103	100.0%	0.62 [0.29 , 1.33]
Total (95% CI)		**119**		**103**	**100.0%**	**0.62 [0.29 , 1.33]**
Total events:	10		14			

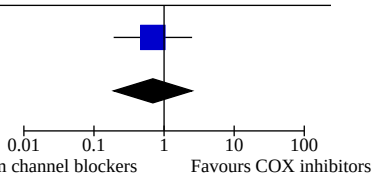
Heterogeneity: Not applicable
Test for overall effect: Z = 1.23 (P = 0.22)
Test for subgroup differences: Not applicable



Analysis 14.25. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	4	119	5	103	100.0%	0.69 [0.19 , 2.51]
Total (95% CI)		**119**		**103**	**100.0%**	**0.69 [0.19 , 2.51]**
Total events:	4		5			

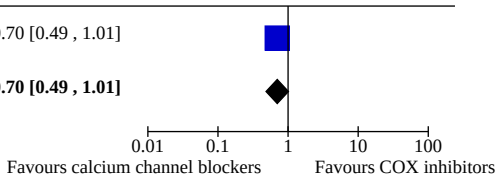
Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)
Test for subgroup differences: Not applicable



Analysis 14.26. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 26: Respiratory morbidity

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	34	119	42	103	100.0%	0.70 [0.49 , 1.01]
Total (95% CI)		**119**		**103**	**100.0%**	**0.70 [0.49 , 1.01]**
Total events:	34		42			

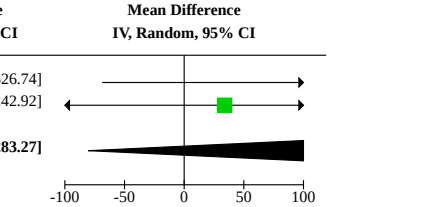
Heterogeneity: Not applicable
Test for overall effect: Z = 1.90 (P = 0.06)
Test for subgroup differences: Not applicable



Analysis 14.27. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 27: Mean birthweight

Study or Subgroup	Calcium channel blockers Mean	SD	Total	COX inhibitors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kashanian 2020	2578	564	36	2349	716	36	34.6%	229.00 [-68.74 , 526.74]
Klauser 2014	1780	772	119	1746	809	103	65.4%	34.00 [-174.92 , 242.92]
Total (95% CI)			**155**			**139**	**100.0%**	**101.46 [-80.34 , 283.27]**

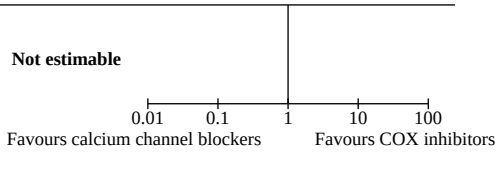
Heterogeneity: Tau² = 1793.05; Chi² = 1.10, df = 1 (P = 0.29); I² = 9%
Test for overall effect: Z = 1.09 (P = 0.27)
Test for subgroup differences: Not applicable



Analysis 14.28. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

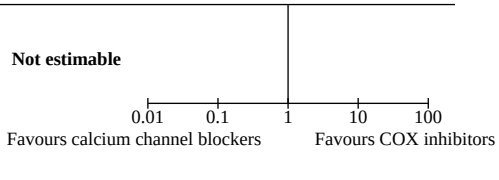
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.29. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

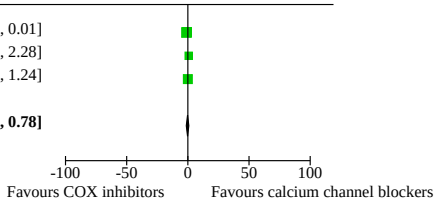
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 14.30. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 30: Gestational age at birth

Study or Subgroup	Calcium channel blockers Mean	SD	Total	COX inhibitors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kashanian 2011	34.1	2.8	40	35.2	2.2	39	38.7%	-1.10 [-2.21 , 0.01]
Kashanian 2020	33.9	3.1	36	33.2	3.7	36	26.4%	0.70 [-0.88 , 2.28]
Klauser 2014	31.8	4.5	104	31.8	4.2	87	34.9%	0.00 [-1.24 , 1.24]
Total (95% CI)			**180**			**162**	**100.0%**	**-0.24 [-1.26 , 0.78]**

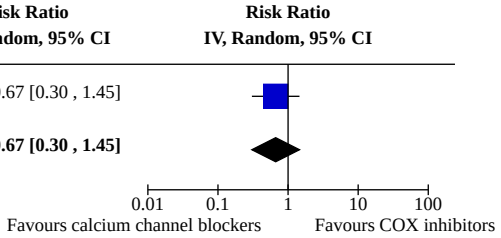
Heterogeneity: Tau² = 0.38; Chi² = 3.77, df = 2 (P = 0.15); I² = 47%
Test for overall effect: Z = 0.46 (P = 0.64)
Test for subgroup differences: Not applicable



Analysis 14.31. Comparison 14: Calcium channel blockers vs COX inhibitors, Outcome 31: Neonatal infection

Study or Subgroup	Calcium channel blockers Events	Total	COX inhibitors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	10	119	13	103	100.0%	0.67 [0.30 , 1.45]
Total (95% CI)		**119**		**103**	**100.0%**	**0.67 [0.30 , 1.45]**
Total events:	10		13			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)
Test for subgroup differences: Not applicable



Comparison 15. Calcium channel blockers vs magnesium sulphate

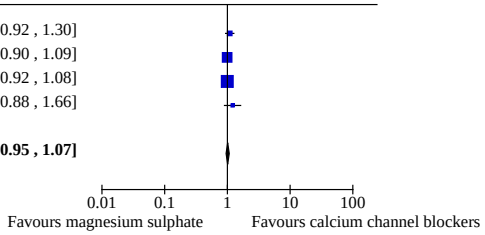
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.1 Delay in birth by 48 hours	4	623	Risk Ratio (IV, Random, 95% CI)	1.01 [0.95, 1.07]
15.2 Delay in birth by 7 days	1	189	Risk Ratio (IV, Random, 95% CI)	1.08 [0.84, 1.40]
15.3 Neonatal death before 28 days	4	642	Risk Ratio (IV, Random, 95% CI)	0.58 [0.18, 1.91]
15.4 Pregnancy prolongation (time from trial entry to birth in days)	3	401	Mean Difference (IV, Random, 95% CI)	-1.33 [-7.20, 4.53]
15.5 Serious adverse effects of drugs	3	471	Risk Ratio (IV, Random, 95% CI)	0.35 [0.05, 2.61]
15.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.7 Cessation of treatment due to adverse effects	3	401	Risk Ratio (IV, Random, 95% CI)	1.95 [0.29, 13.02]
15.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.9 Birth before 32 weeks' gestation	2	312	Risk Ratio (IV, Random, 95% CI)	0.76 [0.52, 1.11]
15.10 Birth before 34 weeks' gestation	2	279	Risk Ratio (IV, Random, 95% CI)	0.93 [0.77, 1.12]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.11 Birth before 37 weeks' gestation	4	591	Risk Ratio (IV, Random, 95% CI)	0.91 [0.84, 0.99]
15.12 Maternal death	1	189	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.13 Pulmonary oedema	2	381	Risk Ratio (IV, Random, 95% CI)	0.18 [0.02, 1.61]
15.14 Dyspnoea	2	381	Risk Ratio (IV, Random, 95% CI)	0.35 [0.13, 0.95]
15.15 Palpitations	1	192	Risk Ratio (IV, Random, 95% CI)	0.31 [0.01, 7.44]
15.16 Headaches	3	434	Risk Ratio (IV, Random, 95% CI)	1.69 [0.92, 3.11]
15.17 Nausea or vomiting	4	623	Risk Ratio (IV, Random, 95% CI)	0.19 [0.09, 0.38]
15.18 Tachycardia	1	189	Risk Ratio (IV, Random, 95% CI)	7.36 [0.95, 56.91]
15.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.20 Maternal hypotension	5	713	Risk Ratio (IV, Random, 95% CI)	2.11 [0.56, 7.88]
15.21 Perinatal death	4	647	Risk Ratio (IV, Random, 95% CI)	0.69 [0.23, 2.11]
15.22 Stillbirth	4	642	Risk Ratio (IV, Random, 95% CI)	2.41 [0.10, 57.65]
15.23 Neonatal death before 7 days	3	428	Risk Ratio (IV, Random, 95% CI)	0.32 [0.01, 7.80]
15.24 Neurodevelopmental morbidity	2	430	Risk Ratio (IV, Random, 95% CI)	0.71 [0.34, 1.49]
15.25 Gastrointestinal morbidity	2	430	Risk Ratio (IV, Random, 95% CI)	0.64 [0.18, 2.31]
15.26 Respiratory morbidity	3	520	Risk Ratio (IV, Random, 95% CI)	0.77 [0.57, 1.04]
15.27 Mean birthweight	4	672	Mean Difference (IV, Random, 95% CI)	-0.97 [-61.12, 59.18]
15.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
15.29 Birthweight < 2500 g	2	306	Risk Ratio (IV, Random, 95% CI)	0.77 [0.55, 1.06]
15.30 Gestational age at birth	4	770	Mean Difference (IV, Random, 95% CI)	0.22 [-0.11, 0.55]
15.31 Neonatal infection	2	430	Risk Ratio (IV, Random, 95% CI)	0.73 [0.36, 1.50]

Analysis 15.1. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	80	104	60	85	11.1%	1.09 [0.92 , 1.30]
Larmon 1999	53	57	61	65	36.9%	0.99 [0.90 , 1.09]
Lyell 2007a	92	100	85	92	48.8%	1.00 [0.92 , 1.08]
Taherian 2006	35	57	32	63	3.3%	1.21 [0.88 , 1.66]
Total (95% CI)		**318**		**305**	**100.0%**	**1.01 [0.95 , 1.07]**
Total events:	260		238			

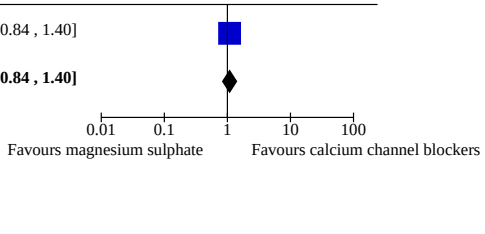
Heterogeneity: Tau² = 0.00; Chi² = 2.24, df = 3 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.35 (P = 0.73)
Test for subgroup differences: Not applicable



Analysis 15.2. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	61	104	46	85	100.0%	1.08 [0.84 , 1.40]
Total (95% CI)		**104**		**85**	**100.0%**	**1.08 [0.84 , 1.40]**
Total events:	61		46			

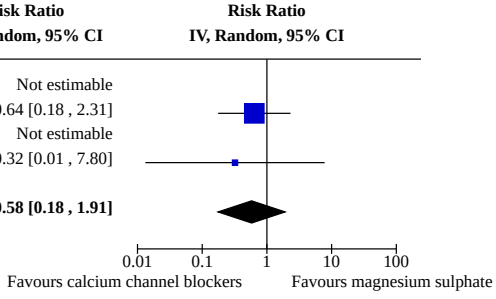
Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.53)
Test for subgroup differences: Not applicable



Analysis 15.3. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	0	50	0	40		Not estimable
Klauser 2014	4	119	5	95	86.0%	0.64 [0.18 , 2.31]
Larmon 1999	0	57	0	65		Not estimable
Lyell 2007a	0	110	1	106	14.0%	0.32 [0.01 , 7.80]
Total (95% CI)		**336**		**306**	**100.0%**	**0.58 [0.18 , 1.91]**
Total events:	4		6			

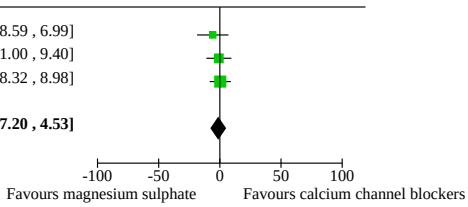
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 0.89 (P = 0.37)
Test for subgroup differences: Not applicable



Analysis 15.4. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Magnesium sulphate Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Floyd 1992	37.5	26	50	43.3	34.1	40	21.0%	-5.80 [-18.59 , 6.99]
Klauser 2014	21.7	21.7	104	22.5	43.8	85	33.0%	-0.80 [-11.00 , 9.40]
Larmon 1999	34.93	25.9	57	34.6	22.4	65	45.9%	0.33 [-8.32 , 8.98]
Total (95% CI)			**211**			**190**	**100.0%**	**-1.33 [-7.20 , 4.53]**

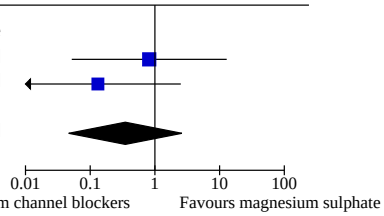
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 2 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.45 (P = 0.66)
Test for subgroup differences: Not applicable



Analysis 15.5. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	0	50	0	40		Not estimable
Klauser 2014	1	104	1	85	53.4%	0.82 [0.05 , 12.87]
Lyell 2007a	0	100	3	92	46.6%	0.13 [0.01 , 2.51]
Total (95% CI)		**254**		**217**	**100.0%**	**0.35 [0.05 , 2.61]**
Total events:	1		4			

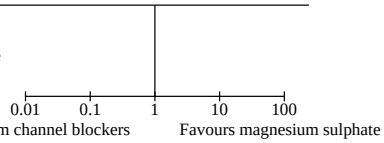
Heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 1 (P = 0.38); I² = 0%
Test for overall effect: Z = 1.03 (P = 0.31)
Test for subgroup differences: Not applicable



Analysis 15.6. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 6: Maternal infection

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

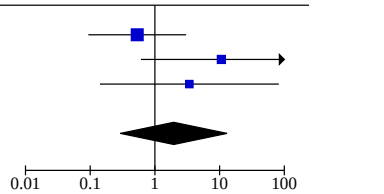
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 15.7. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	2	50	3	40	47.3%	0.53 [0.09 , 3.04]
Klauser 2014	6	104	0	85	28.2%	10.65 [0.61 , 186.35]
Larmon 1999	1	57	0	65	24.5%	3.41 [0.14 , 82.18]
Total (95% CI)		**211**		**190**	**100.0%**	**1.95 [0.29 , 13.02]**
Total events:	9		3			

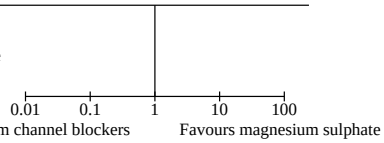
Heterogeneity: Tau² = 1.19; Chi² = 3.41, df = 2 (P = 0.18); I² = 41%
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 15.8. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

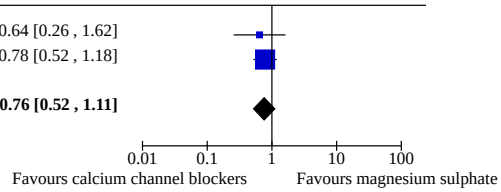
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 15.9. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lyell 2007a	7	100	10	92	16.6%	0.64 [0.26 , 1.62]
Taherian 2006	22	57	31	63	83.4%	0.78 [0.52 , 1.18]
Total (95% CI)		**157**		**155**	**100.0%**	**0.76 [0.52 , 1.11]**
Total events:	29		41			

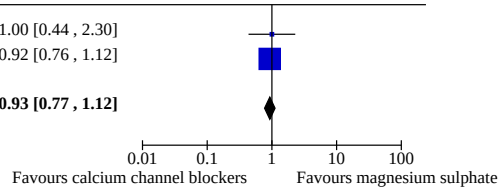
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.43 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 15.10. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	10	50	8	40	5.0%	1.00 [0.44 , 2.30]
Klauser 2014	69	104	61	85	95.0%	0.92 [0.76 , 1.12]
Total (95% CI)		**154**		**125**	**100.0%**	**0.93 [0.77 , 1.12]**
Total events:	79		69			

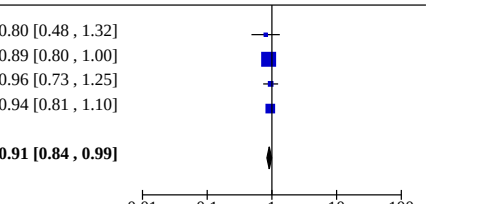
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%
Test for overall effect: Z = 0.78 (P = 0.43)
Test for subgroup differences: Not applicable



Analysis 15.11. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	18	50	18	40	2.8%	0.80 [0.48 , 1.32]
Klauser 2014	85	104	78	85	57.0%	0.89 [0.80 , 1.00]
Lyell 2007a	52	100	50	92	10.0%	0.96 [0.73 , 1.25]
Taherian 2006	47	57	55	63	30.3%	0.94 [0.81 , 1.10]
Total (95% CI)		**311**		**280**	**100.0%**	**0.91 [0.84 , 0.99]**
Total events:	202		201			

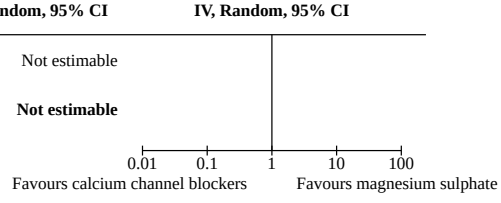
Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 3 (P = 0.86); I² = 0%
Test for overall effect: Z = 2.20 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 15.12. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 12: Maternal death

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	104	0	85		Not estimable
Total (95% CI)		**104**		**85**		**Not estimable**
Total events:	0		0			

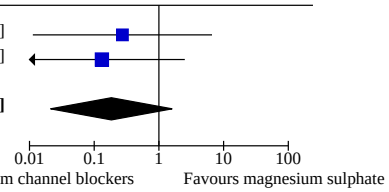
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 15.13. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 13: Pulmonary oedema

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	104	1	85	46.1%	0.27 [0.01 , 6.62]
Lyell 2007a	0	100	3	92	53.9%	0.13 [0.01 , 2.51]
Total (95% CI)		**204**		**177**	**100.0%**	**0.18 [0.02 , 1.61]**
Total events:	0		4			

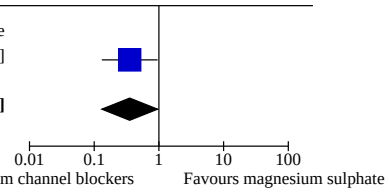
Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 1.53 (P = 0.13)
Test for subgroup differences: Not applicable



Analysis 15.14. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 14: Dyspnoea

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	104	0	85		Not estimable
Lyell 2007a	5	100	13	92	100.0%	0.35 [0.13 , 0.95]
Total (95% CI)		**204**		**177**	**100.0%**	**0.35 [0.13 , 0.95]**
Total events:	5		13			

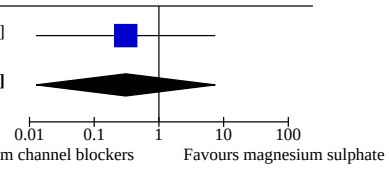
Heterogeneity: Not applicable
Test for overall effect: Z = 2.05 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 15.15. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 15: Palpitations

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Lyell 2007a	0	100	1	92	100.0%	0.31 [0.01 , 7.44]
Total (95% CI)		**100**		**92**	**100.0%**	**0.31 [0.01 , 7.44]**
Total events:	0		1			

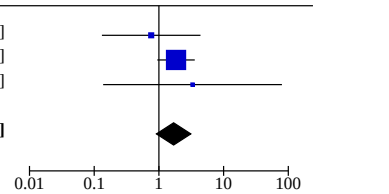
Heterogeneity: Not applicable
Test for overall effect: Z = 0.73 (P = 0.47)
Test for subgroup differences: Not applicable



Analysis 15.16. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 16: Headaches

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Larmon 1999	2	57	3	65	12.1%	0.76 [0.13 , 4.39]
Lyell 2007a	22	100	11	92	84.2%	1.84 [0.95 , 3.58]
Taherian 2006	1	57	0	63	3.7%	3.31 [0.14 , 79.67]
Total (95% CI)		**214**		**220**	**100.0%**	**1.69 [0.92 , 3.11]**
Total events:	25		14			

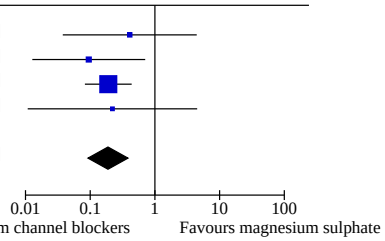
Heterogeneity: Tau² = 0.00; Chi² = 1.03, df = 2 (P = 0.60); I² = 0%
Test for overall effect: Z = 1.68 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 15.17. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 17: Nausea or vomiting

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	1	104	2	85	8.9%	0.41 [0.04 , 4.43]
Larmon 1999	1	57	12	65	12.5%	0.10 [0.01 , 0.71]
Lyell 2007a	6	100	29	92	73.0%	0.19 [0.08 , 0.44]
Taherian 2006	0	57	2	63	5.6%	0.22 [0.01 , 4.50]
Total (95% CI)		**318**		**305**	**100.0%**	**0.19 [0.09 , 0.38]**
Total events:	8		45			

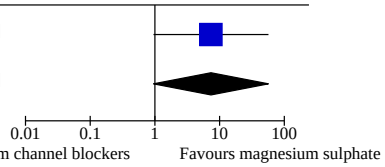
Heterogeneity: Tau² = 0.00; Chi² = 0.86, df = 3 (P = 0.83); I² = 0%
Test for overall effect: Z = 4.60 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 15.18. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 18: Tachycardia

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	9	104	1	85	100.0%	7.36 [0.95 , 56.91]
Total (95% CI)		**104**		**85**	**100.0%**	**7.36 [0.95 , 56.91]**
Total events:	9		1			

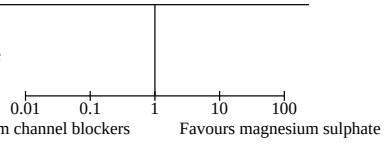
Heterogeneity: Not applicable
Test for overall effect: Z = 1.91 (P = 0.06)
Test for subgroup differences: Not applicable



Analysis 15.19. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

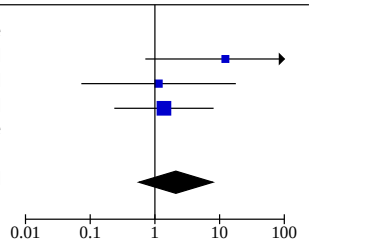
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 15.20. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 20: Maternal hypotension

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	0	50	0	40		Not estimable
Klauser 2014	7	104	0	85	21.4%	12.29 [0.71 , 212.07]
Larmon 1999	1	57	1	65	23.0%	1.14 [0.07 , 17.82]
Lyell 2007a	3	100	2	92	55.6%	1.38 [0.24 , 8.07]
Taherian 2006	0	57	0	63		Not estimable
Total (95% CI)		**368**		**345**	**100.0%**	**2.11 [0.56 , 7.88]**
Total events:	11		3			

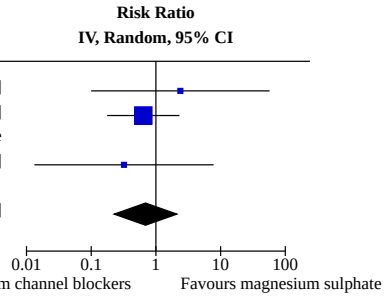
Heterogeneity: Tau² = 0.00; Chi² = 1.88, df = 2 (P = 0.39); I² = 0%
Test for overall effect: Z = 1.11 (P = 0.27)
Test for subgroup differences: Not applicable



Analysis 15.21. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 21: Perinatal death

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	1	53	0	42	12.4%	2.39 [0.10 , 57.18]
Klauser 2014	4	119	5	95	75.4%	0.64 [0.18 , 2.31]
Larmon 1999	0	57	0	65		Not estimable
Lyell 2007a	0	110	1	106	12.3%	0.32 [0.01 , 7.80]
Total (95% CI)		**339**		**308**	**100.0%**	**0.69 [0.23 , 2.11]**
Total events:	5		6			

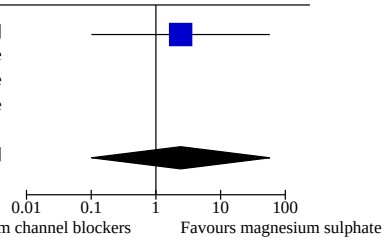
Heterogeneity: Tau² = 0.00; Chi² = 0.82, df = 2 (P = 0.66); I² = 0%
Test for overall effect: Z = 0.65 (P = 0.52)
Test for subgroup differences: Not applicable



Analysis 15.22. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 22: Stillbirth

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	1	50	0	40	100.0%	2.41 [0.10 , 57.65]
Klauser 2014	0	119	0	95		Not estimable
Larmon 1999	0	57	0	65		Not estimable
Lyell 2007a	0	110	0	106		Not estimable
Total (95% CI)		**336**		**306**	**100.0%**	**2.41 [0.10 , 57.65]**
Total events:	1		0			

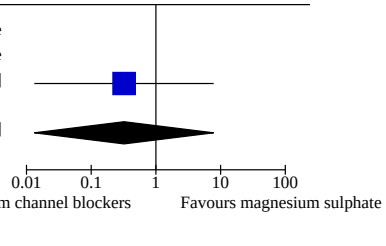
Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)
Test for subgroup differences: Not applicable



Analysis 15.23. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	0	50	0	40		Not estimable
Larmon 1999	0	57	0	65		Not estimable
Lyell 2007a	0	110	1	106	100.0%	0.32 [0.01 , 7.80]
Total (95% CI)		**217**		**211**	**100.0%**	**0.32 [0.01 , 7.80]**
Total events:	0		1			

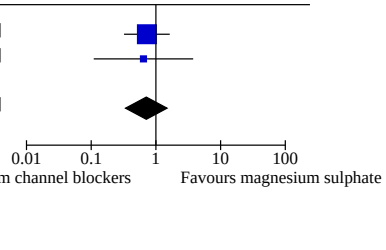
Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 15.24. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	10	119	11	95	82.6%	0.73 [0.32 , 1.64]
Lyell 2007a	2	110	3	106	17.4%	0.64 [0.11 , 3.77]
Total (95% CI)		**229**		**201**	**100.0%**	**0.71 [0.34 , 1.49]**
Total events:	12		14			

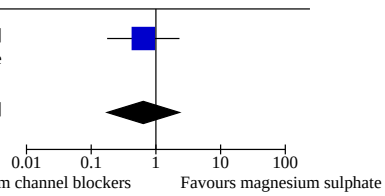
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.91 (P = 0.36)
Test for subgroup differences: Not applicable



Analysis 15.25. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	4	119	5	95	100.0%	0.64 [0.18 , 2.31]
Lyell 2007a	0	110	0	106		Not estimable
Total (95% CI)		**229**		**201**	**100.0%**	**0.64 [0.18 , 2.31]**
Total events:	4		5			

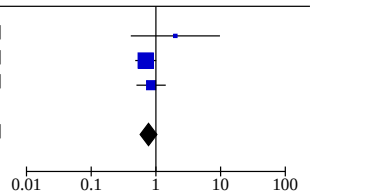
Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 15.26. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 26: Respiratory morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	5	50	2	40	3.5%	2.00 [0.41 , 9.77]
Klauser 2014	34	119	39	95	63.9%	0.70 [0.48 , 1.01]
Lyell 2007a	21	110	24	106	32.6%	0.84 [0.50 , 1.42]
Total (95% CI)		**279**		**241**	**100.0%**	**0.77 [0.57 , 1.04]**
Total events:	60		65			

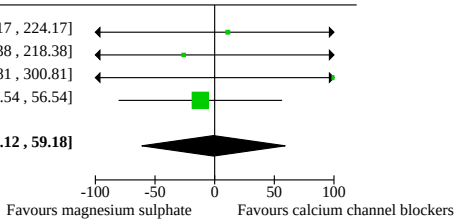
Heterogeneity: Tau² = 0.00; Chi² = 1.79, df = 2 (P = 0.41); I² = 0%
Test for overall effect: Z = 1.73 (P = 0.08)
Test for subgroup differences: Not applicable



Analysis 15.27. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 27: Mean birthweight

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Magnesium sulphate Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Klauser 2014	1780	772	119	1769	805	95	8.0%	11.00 [-202.17 , 224.17]
Larmon 1999	2449	729	57	2475	636	65	6.1%	-26.00 [-270.38 , 218.38]
Lyell 2007a	2650	698	110	2550	802	106	9.0%	100.00 [-100.81 , 300.81]
Taherian 2006	2002	213	57	2014	164	63	77.0%	-12.00 [-80.54 , 56.54]
Total (95% CI)			**343**			**329**	**100.0%**	**-0.97 [-61.12 , 59.18]**

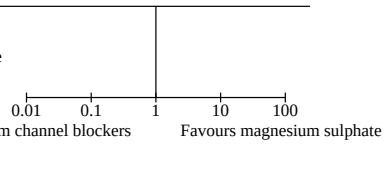
Heterogeneity: Tau² = 0.00; Chi² = 1.12, df = 3 (P = 0.77); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.97)
Test for subgroup differences: Not applicable



Analysis 15.28. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

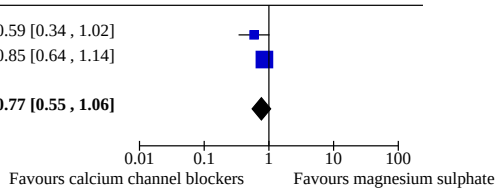
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 15.29. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Floyd 1992	14	50	19	40	29.2%	0.59 [0.34 , 1.02]
Lyell 2007a	46	110	52	106	70.8%	0.85 [0.64 , 1.14]
Total (95% CI)		**160**		**146**	**100.0%**	**0.77 [0.55 , 1.06]**
Total events:	60		71			

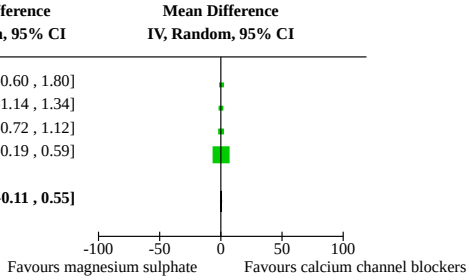
Heterogeneity: Tau² = 0.02; Chi² = 1.34, df = 1 (P = 0.25); I² = 25%
Test for overall effect: Z = 1.59 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 15.30. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 30: Gestational age at birth

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Magnesium sulphate Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Klauser 2014	31.8	4.5	104	31.2	3.9	85	7.6%	0.60 [-0.60 , 1.80]
Larmon 1999	35.6	3.7	57	35.5	3.2	65	7.1%	0.10 [-1.14 , 1.34]
Lyell 2007a	36	3.1	100	35.8	3.4	92	12.8%	0.20 [-0.72 , 1.12]
Taherian 2006	30.2	1.3	57	30	1.4	210	72.6%	0.20 [-0.19 , 0.59]
Total (95% CI)			**318**			**452**	**100.0%**	**0.22 [-0.11 , 0.55]**

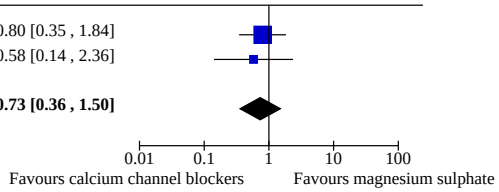
Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 3 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.33 (P = 0.18)
Test for subgroup differences: Not applicable



Analysis 15.31. Comparison 15: Calcium channel blockers vs magnesium sulphate, Outcome 31: Neonatal infection

Study or Subgroup	Calcium channel blockers Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	10	119	10	95	74.0%	0.80 [0.35 , 1.84]
Lyell 2007a	3	110	5	106	26.0%	0.58 [0.14 , 2.36]
Total (95% CI)		**229**		**201**	**100.0%**	**0.73 [0.36 , 1.50]**
Total events:	13		15			

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 0.84 (P = 0.40)
Test for subgroup differences: Not applicable



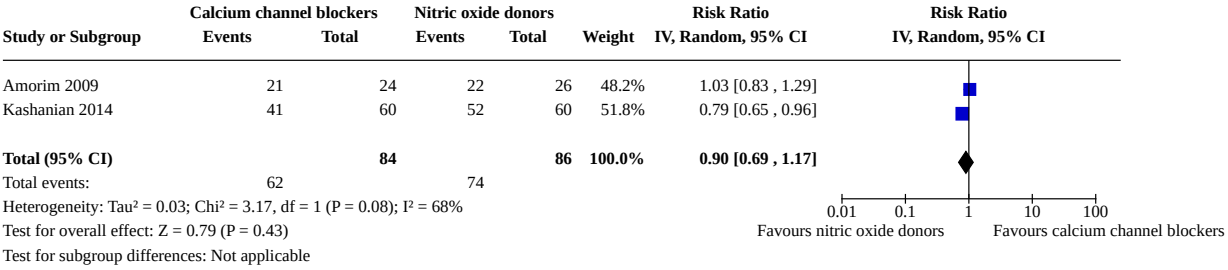
Comparison 16. Calcium channel blockers vs nitric oxide donors

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16.1 Delay in birth by 48 hours	2	170	Risk Ratio (IV, Random, 95% CI)	0.90 [0.69, 1.17]
16.2 Delay in birth by 7 days	1	120	Risk Ratio (IV, Random, 95% CI)	0.79 [0.62, 1.00]
16.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable

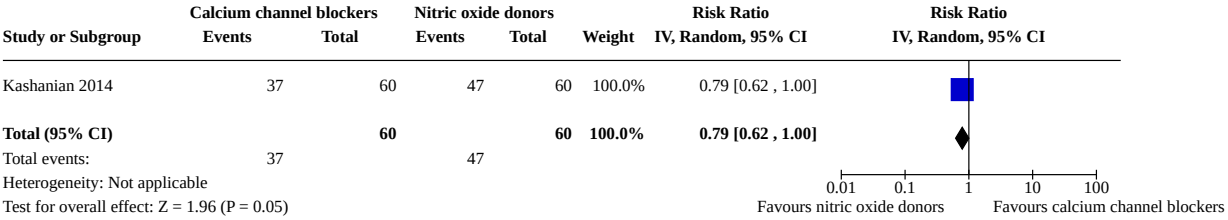
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.7 Cessation of treatment due to adverse effects	1	120	Risk Ratio (IV, Random, 95% CI)	5.00 [0.25, 102.00]
16.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.16 Headaches	2	170	Risk Ratio (IV, Random, 95% CI)	0.60 [0.13, 2.86]
16.17 Nausea or vomiting	1	50	Risk Ratio (IV, Random, 95% CI)	1.63 [0.30, 8.90]
16.18 Tachycardia	2	170	Risk Ratio (IV, Random, 95% CI)	3.24 [0.14, 75.91]
16.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.20 Maternal hypotension	2	170	Risk Ratio (IV, Random, 95% CI)	1.68 [0.82, 3.44]
16.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.27 Mean birthweight	1	120	Mean Difference (IV, Random, 95% CI)	-277.00 [-539.41, -14.59]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
16.30 Gestational age at birth	2	220	Mean Difference (IV, Random, 95% CI)	-1.21 [-1.81, -0.61]
16.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

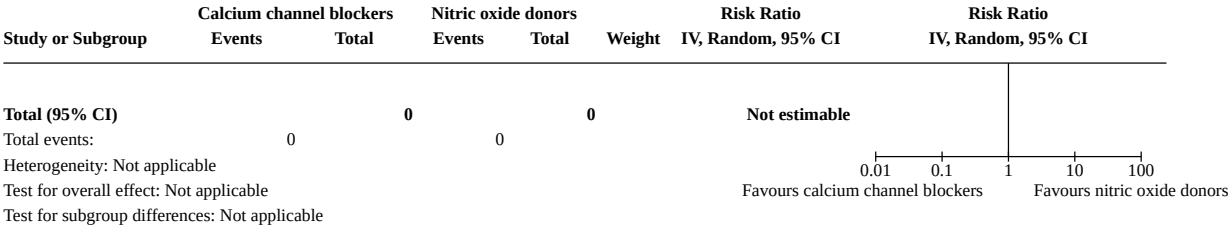
Analysis 16.1. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 1: Delay in birth by 48 hours



Analysis 16.2. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 2: Delay in birth by 7 days



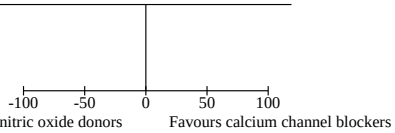
Analysis 16.3. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 3: Neonatal death before 28 days



Analysis 16.4. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**

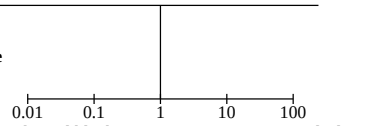
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.5. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

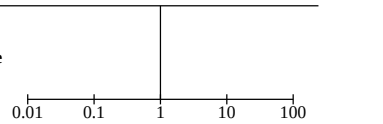
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.6. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 6: Maternal infection

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

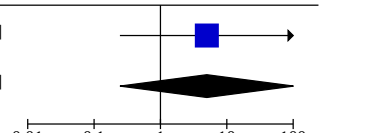
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.7. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2014	2	60	0	60	100.0%	5.00 [0.25 , 102.00]
Total (95% CI)		**60**		**60**	**100.0%**	**5.00 [0.25 , 102.00]**
Total events:	2		0			

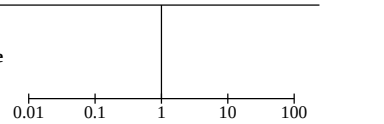
Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.30)
Test for subgroup differences: Not applicable



Analysis 16.8. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

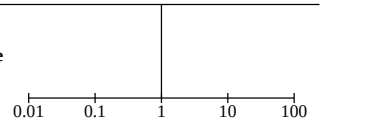
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.9. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

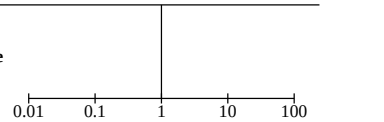
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.10. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

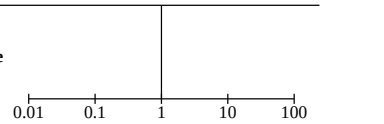
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.11. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

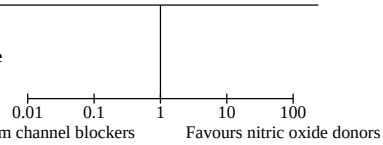
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.12. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 12: Maternal death

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

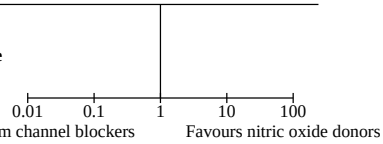
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.13. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 13: Pulmonary oedema

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

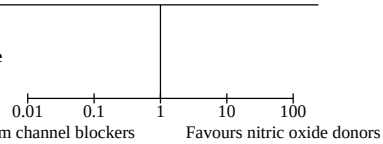
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.14. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 14: Dyspnoea

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

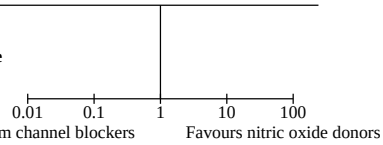
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.15. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 15: Palpitations

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

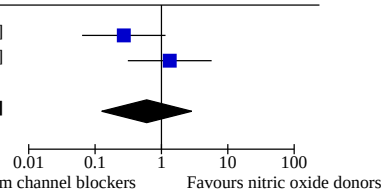
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.16. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 16: Headaches

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Amorim 2009	2	24	8	26	50.1%	0.27 [0.06 , 1.15]
Kashanian 2014	4	60	3	60	49.9%	1.33 [0.31 , 5.70]
Total (95% CI)		**84**		**86**	**100.0%**	**0.60 [0.13 , 2.86]**
Total events:	6		11			

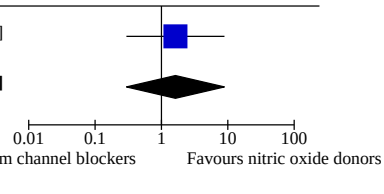
Heterogeneity: Tau² = 0.72; Chi² = 2.32, df = 1 (P = 0.13); I² = 57%
Test for overall effect: Z = 0.64 (P = 0.52)
Test for subgroup differences: Not applicable



Analysis 16.17. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 17: Nausea or vomiting

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Amorim 2009	3	24	2	26	100.0%	1.63 [0.30 , 8.90]
Total (95% CI)		**24**		**26**	**100.0%**	**1.63 [0.30 , 8.90]**
Total events:	3		2			

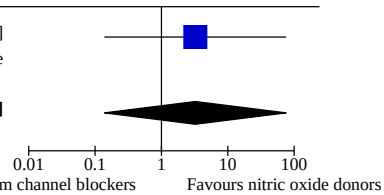
Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)
Test for subgroup differences: Not applicable



Analysis 16.18. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 18: Tachycardia

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Amorim 2009	1	24	0	26	100.0%	3.24 [0.14 , 75.91]
Kashanian 2014	0	60	0	60		Not estimable
Total (95% CI)		**84**		**86**	**100.0%**	**3.24 [0.14 , 75.91]**
Total events:	1		0			

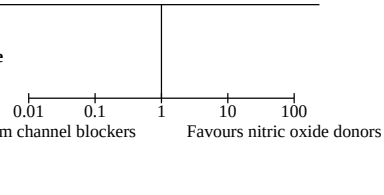
Heterogeneity: Not applicable
Test for overall effect: Z = 0.73 (P = 0.47)
Test for subgroup differences: Not applicable



Analysis 16.19. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

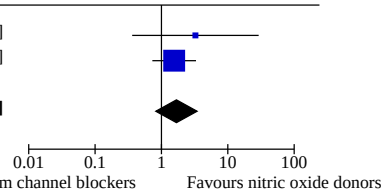
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.20. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 20: Maternal hypotension

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Amorim 2009	3	24	1	26	10.6%	3.25 [0.36 , 29.16]
Kashanian 2014	14	60	9	60	89.4%	1.56 [0.73 , 3.32]
Total (95% CI)		**84**		**86**	**100.0%**	**1.68 [0.82 , 3.44]**
Total events:	17		10			

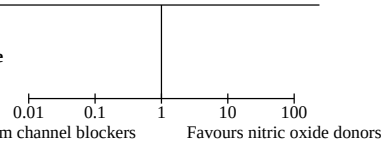
Heterogeneity: Tau² = 0.00; Chi² = 0.39, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 1.42 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 16.21. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 21: Perinatal death

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

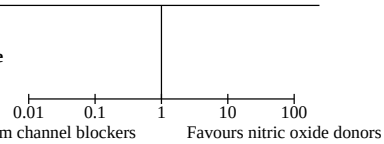
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.22. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 22: Stillbirth

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

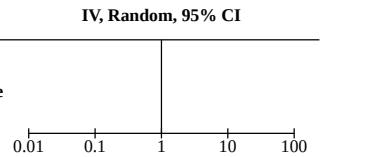
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.23. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

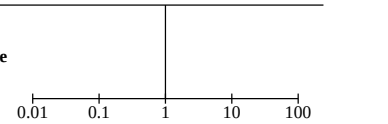
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.24. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

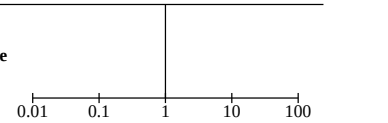
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.25. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

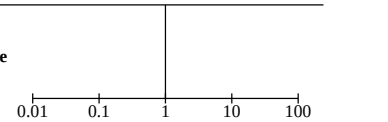
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.26. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 26: Respiratory morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

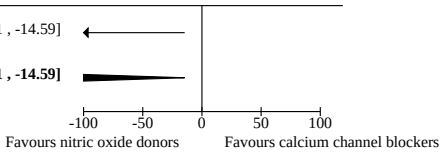
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.27. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 27: Mean birthweight

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Kashanian 2014	2357	857	60	2634	584	60	100.0%	-277.00 [-539.41 , -14.59]	
Total (95% CI)			**60**			**60**	**100.0%**	**-277.00 [-539.41 , -14.59]**	

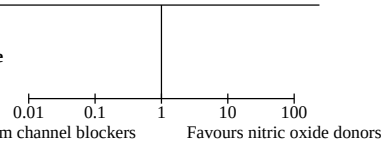
Heterogeneity: Not applicable
Test for overall effect: Z = 2.07 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 16.28. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

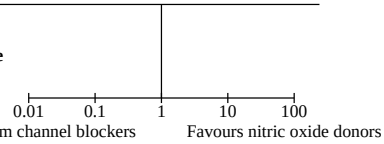
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.29. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

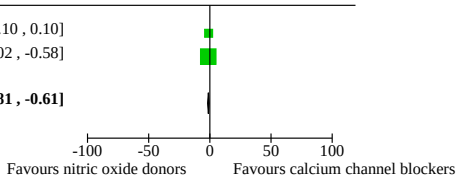
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 16.30. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 30: Gestational age at birth

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Janky 1990	34.6	2.8	50	35.6	2.8	50	29.9%	-1.00 [-2.10 , 0.10]
Kashanian 2014	34.3	2.1	60	35.6	1.9	60	70.1%	-1.30 [-2.02 , -0.58]
Total (95% CI)			**110**			**110**	**100.0%**	**-1.21 [-1.81 , -0.61]**

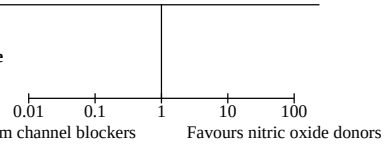
Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 3.95 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 16.31. Comparison 16: Calcium channel blockers vs nitric oxide donors, Outcome 31: Neonatal infection

Study or Subgroup	Calcium channel blockers Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Comparison 17. Calcium channel blockers vs oxytocin receptor antagonists

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.1 Delay in birth by 48 hours	3	728	Risk Ratio (IV, Random, 95% CI)	1.04 [0.96, 1.12]
17.2 Delay in birth by 7 days	3	728	Risk Ratio (IV, Random, 95% CI)	1.08 [0.95, 1.23]

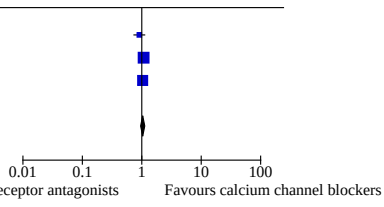
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.3 Neonatal death before 28 days	1	189	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.4 Pregnancy prolongation (time from trial entry to birth in days)	3	728	Mean Difference (IV, Random, 95% CI)	3.14 [-1.22, 7.49]
17.5 Serious adverse effects of drugs	1	503	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.6 Maternal infection	1	503	Risk Ratio (IV, Random, 95% CI)	6.17 [0.75, 50.87]
17.7 Cessation of treatment due to adverse effects	2	646	Risk Ratio (IV, Random, 95% CI)	2.22 [0.95, 5.20]
17.8 Birth before 28 weeks' gestation	1	145	Risk Ratio (IV, Random, 95% CI)	0.47 [0.04, 5.03]
17.9 Birth before 32 weeks' gestation	1	172	Risk Ratio (IV, Random, 95% CI)	0.90 [0.70, 1.16]
17.10 Birth before 34 weeks' gestation	1	145	Risk Ratio (IV, Random, 95% CI)	0.59 [0.31, 1.12]
17.11 Birth before 37 weeks' gestation	1	145	Risk Ratio (IV, Random, 95% CI)	0.64 [0.47, 0.89]
17.12 Maternal death	1	499	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.13 Pulmonary oedema	1	503	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.15 Palpitations	2	225	Risk Ratio (IV, Random, 95% CI)	4.60 [0.53, 39.75]
17.16 Headaches	2	225	Risk Ratio (IV, Random, 95% CI)	1.33 [0.43, 4.13]
17.17 Nausea or vomiting	1	145	Risk Ratio (IV, Random, 95% CI)	2.80 [0.12, 67.68]
17.18 Tachycardia	2	225	Risk Ratio (IV, Random, 95% CI)	4.66 [0.82, 26.63]
17.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.20 Maternal hypotension	3	728	Risk Ratio (IV, Random, 95% CI)	3.53 [0.52, 23.91]
17.21 Perinatal death	2	780	Risk Ratio (IV, Random, 95% CI)	2.26 [0.94, 5.42]
17.22 Stillbirth	1	189	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.24 Neurodevelopmental morbidity	2	780	Risk Ratio (IV, Random, 95% CI)	1.08 [0.21, 5.58]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.25 Gastrointestinal morbidity	2	780	Risk Ratio (IV, Random, 95% CI)	0.58 [0.04, 8.60]
17.26 Respiratory morbidity	2	780	Risk Ratio (IV, Random, 95% CI)	0.58 [0.33, 1.03]
17.27 Mean birthweight	2	306	Mean Difference (IV, Random, 95% CI)	57.75 [-40.38, 155.88]
17.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
17.29 Birthweight < 2500 g	1	189	Risk Ratio (IV, Random, 95% CI)	0.84 [0.66, 1.05]
17.30 Gestational age at birth	2	648	Mean Difference (IV, Random, 95% CI)	0.91 [0.30, 1.51]
17.31 Neonatal infection	2	780	Risk Ratio (IV, Random, 95% CI)	1.02 [0.61, 1.69]

Analysis 17.1. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 1: Delay in birth by 48 hours

	Calcium channel blockers		Oxytocin receptor antagonists			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Kashanian 2005	30	40	33	40	12.0%	0.91 [0.72 , 1.14]	
Salim 2012	69	75	60	70	46.2%	1.07 [0.96 , 1.21]	
Van Vliet 2016	169	248	168	255	41.8%	1.03 [0.91 , 1.17]	
Total (95% CI)		**363**		**365**	**100.0%**	**1.04 [0.96 , 1.12]**	
Total events:	268		261				

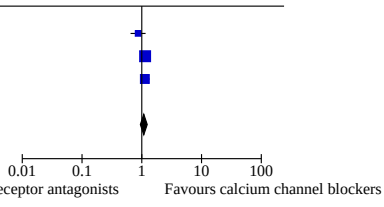
Heterogeneity: Tau² = 0.00; Chi² = 1.61, df = 2 (P = 0.45); I² = 0%
Test for overall effect: Z = 0.87 (P = 0.38)
Test for subgroup differences: Not applicable



Analysis 17.2. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 2: Delay in birth by 7 days

	Calcium channel blockers		Oxytocin receptor antagonists			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Kashanian 2005	26	40	30	40	17.5%	0.87 [0.65 , 1.16]	
Salim 2012	67	75	55	70	46.9%	1.14 [0.98 , 1.31]	
Van Vliet 2016	127	248	116	255	35.6%	1.13 [0.94 , 1.35]	
Total (95% CI)		**363**		**365**	**100.0%**	**1.08 [0.95 , 1.23]**	
Total events:	220		201				

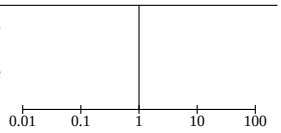
Heterogeneity: Tau² = 0.00; Chi² = 2.86, df = 2 (P = 0.24); I² = 30%
Test for overall effect: Z = 1.15 (P = 0.25)
Test for subgroup differences: Not applicable



Analysis 17.3. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	0	98	0	91		Not estimable
Total (95% CI)		**98**		**91**		**Not estimable**
Total events:	0		0			

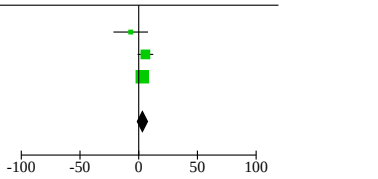
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 17.4. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kashanian 2005	19.3	27.4	40	26.1	38.8	40	8.4%	-6.80 [-21.52 , 7.92]
Salim 2012	37.4	20.3	75	31.7	20.6	70	35.6%	5.70 [-0.96 , 12.36]
Van Vliet 2016	7	28.9	248	4	28.2	255	56.0%	3.00 [-1.99 , 7.99]
Total (95% CI)			**363**			**365**	**100.0%**	**3.14 [-1.22 , 7.49]**

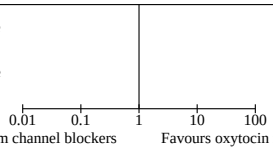
Heterogeneity: $Tau^2 = 2.35$; $Chi^2 = 2.32$, df = 2 (P = 0.31); $I^2 = 14\%$
Test for overall effect: Z = 1.41 (P = 0.16)
Test for subgroup differences: Not applicable



Analysis 17.5. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Van Vliet 2016	0	248	0	255		Not estimable
Total (95% CI)		**248**		**255**		**Not estimable**
Total events:	0		0			

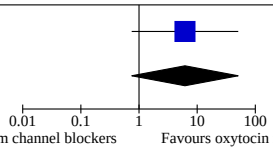
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 17.6. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 6: Maternal infection

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Van Vliet 2016	6	248	1	255	100.0%	6.17 [0.75 , 50.87]
Total (95% CI)		**248**		**255**	**100.0%**	**6.17 [0.75 , 50.87]**
Total events:	6		1			

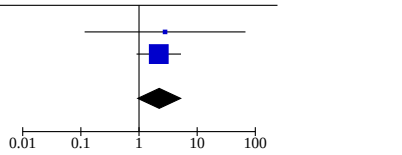
Heterogeneity: Not applicable
Test for overall effect: Z = 1.69 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 17.7. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	1	75	0	70	7.1%	2.80 [0.12 , 67.68]
Van Vliet 2016	15	248	7	253	92.9%	2.19 [0.91 , 5.27]
Total (95% CI)		**323**		**323**	**100.0%**	**2.22 [0.95 , 5.20]**
Total events:	16		7			

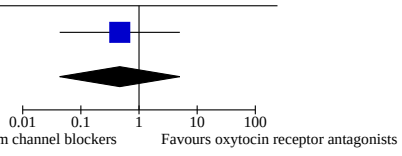
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.88); I² = 0%
Test for overall effect: Z = 1.85 (P = 0.06)
Test for subgroup differences: Not applicable



Analysis 17.8. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	1	75	2	70	100.0%	0.47 [0.04 , 5.03]
Total (95% CI)		**75**		**70**	**100.0%**	**0.47 [0.04 , 5.03]**
Total events:	1		2			

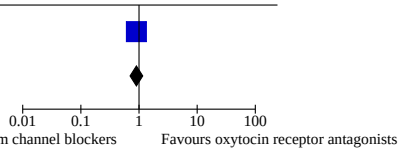
Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)
Test for subgroup differences: Not applicable



Analysis 17.9. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Van Vliet 2016	46	82	56	90	100.0%	0.90 [0.70 , 1.16]
Total (95% CI)		**82**		**90**	**100.0%**	**0.90 [0.70 , 1.16]**
Total events:	46		56			

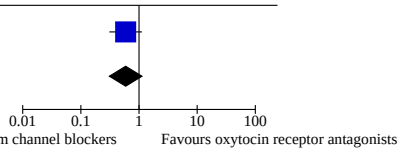
Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)
Test for subgroup differences: Not applicable



Analysis 17.10. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	12	75	19	70	100.0%	0.59 [0.31 , 1.12]
Total (95% CI)		**75**		**70**	**100.0%**	**0.59 [0.31 , 1.12]**
Total events:	12		19			

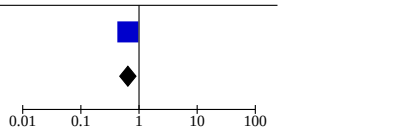
Heterogeneity: Not applicable
Test for overall effect: Z = 1.61 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 17.11. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	31	75	45	70	100.0%	0.64 [0.47 , 0.89]
Total (95% CI)		**75**		**70**	**100.0%**	**0.64 [0.47 , 0.89]**
Total events:	31		45			

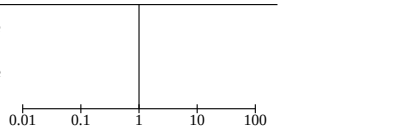
Heterogeneity: Not applicable
Test for overall effect: Z = 2.69 (P = 0.007)
Test for subgroup differences: Not applicable



Analysis 17.12. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 12: Maternal death

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Van Vliet 2016	0	244	0	255		Not estimable
Total (95% CI)		**244**		**255**		**Not estimable**
Total events:	0		0			

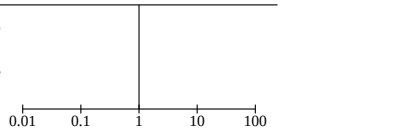
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 17.13. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 13: Pulmonary oedema

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Van Vliet 2016	0	248	0	255		Not estimable
Total (95% CI)		**248**		**255**		**Not estimable**
Total events:	0		0			

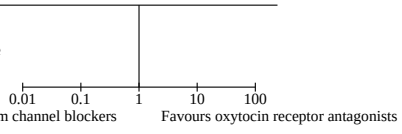
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 17.14. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 14: Dyspnoea

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

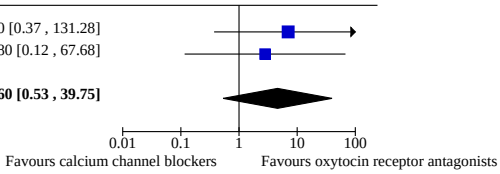
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 17.15. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 15: Palpitations

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2005	3	40	0	40	54.1%	7.00 [0.37 , 131.28]
Salim 2012	1	75	0	70	45.9%	2.80 [0.12 , 67.68]
Total (95% CI)		**115**		**110**	**100.0%**	**4.60 [0.53 , 39.75]**
Total events:	4		0			

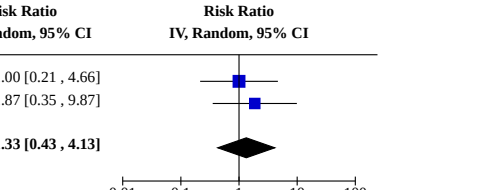
Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 1 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.39 (P = 0.17)
Test for subgroup differences: Not applicable



Analysis 17.16. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 16: Headaches

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2005	3	40	3	40	53.9%	1.00 [0.21 , 4.66]
Salim 2012	4	75	2	70	46.1%	1.87 [0.35 , 9.87]
Total (95% CI)		**115**		**110**	**100.0%**	**1.33 [0.43 , 4.13]**
Total events:	7		5			

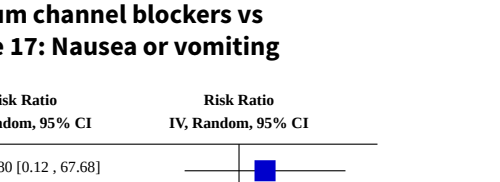
Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 1 (P = 0.59); I² = 0%
Test for overall effect: Z = 0.50 (P = 0.62)
Test for subgroup differences: Not applicable



Analysis 17.17. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 17: Nausea or vomiting

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	1	75	0	70	100.0%	2.80 [0.12 , 67.68]
Total (95% CI)		**75**		**70**	**100.0%**	**2.80 [0.12 , 67.68]**
Total events:	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)
Test for subgroup differences: Not applicable



Analysis 17.18. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 18: Tachycardia

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2005	3	40	0	40	35.3%	7.00 [0.37 , 131.28]
Salim 2012	4	75	1	70	64.7%	3.73 [0.43 , 32.60]
Total (95% CI)		**115**		**110**	**100.0%**	**4.66 [0.82 , 26.63]**
Total events:	7		1			

Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 1.73 (P = 0.08)
Test for subgroup differences: Not applicable

Analysis 17.19. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 19: Maternal cardiac arrhythmias

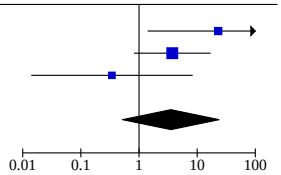
Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 17.20. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 20: Maternal hypotension

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2005	11	40	0	40	28.0%	23.00 [1.40 , 377.52]
Salim 2012	8	75	2	70	48.4%	3.73 [0.82 , 16.98]
Van Vliet 2016	0	248	1	255	23.7%	0.34 [0.01 , 8.37]
Total (95% CI)		**363**		**365**	**100.0%**	**3.53 [0.52 , 23.91]**
Total events:	19		3			

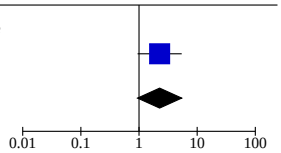
Heterogeneity: Tau² = 1.37; Chi² = 3.77, df = 2 (P = 0.15); I² = 47%
Test for overall effect: Z = 1.29 (P = 0.20)
Test for subgroup differences: Not applicable



Analysis 17.21. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 21: Perinatal death

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	0	98	0	91		Not estimable
Van Vliet 2016	16	297	7	294	100.0%	2.26 [0.94 , 5.42]
Total (95% CI)		**395**		**385**	**100.0%**	**2.26 [0.94 , 5.42]**
Total events:	16		7			

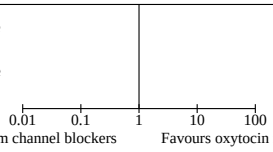
Heterogeneity: Not applicable
Test for overall effect: Z = 1.83 (P = 0.07)
Test for subgroup differences: Not applicable



Analysis 17.22. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 22: Stillbirth

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	0	98	0	91		Not estimable
Total (95% CI)		**98**		**91**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 17.23. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 23: Neonatal death before 7 days

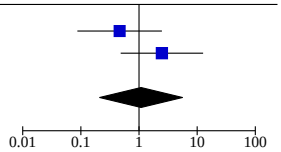
Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 17.24. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	2	98	4	91	49.4%	0.46 [0.09 , 2.47]
Van Vliet 2016	5	297	2	294	50.6%	2.47 [0.48 , 12.65]
Total (95% CI)		**395**		**385**	**100.0%**	**1.08 [0.21 , 5.58]**
Total events:	7		6			

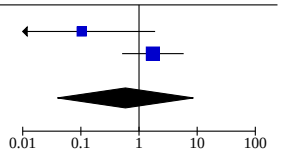
Heterogeneity: Tau² = 0.69; Chi² = 1.97, df = 1 (P = 0.16); I² = 49%
Test for overall effect: Z = 0.10 (P = 0.92)
Test for subgroup differences: Not applicable



Analysis 17.25. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	0	98	4	91	38.6%	0.10 [0.01 , 1.89]
Van Vliet 2016	7	297	4	294	61.4%	1.73 [0.51 , 5.86]
Total (95% CI)		**395**		**385**	**100.0%**	**0.58 [0.04 , 8.60]**
Total events:	7		8			

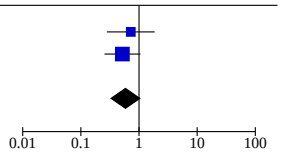
Heterogeneity: Tau² = 2.68; Chi² = 3.07, df = 1 (P = 0.08); I² = 67%
Test for overall effect: Z = 0.39 (P = 0.69)
Test for subgroup differences: Not applicable



Analysis 17.26. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 26: Respiratory morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	7	98	9	91	36.1%	0.72 [0.28 , 1.86]
Van Vliet 2016	11	297	21	294	63.9%	0.52 [0.25 , 1.06]
Total (95% CI)		**395**		**385**	**100.0%**	**0.58 [0.33 , 1.03]**
Total events:	18		30			

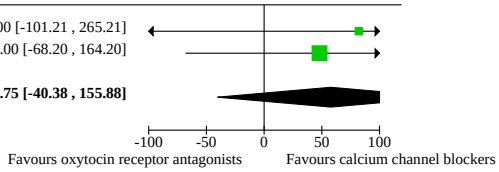
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 1.85 (P = 0.06)
Test for subgroup differences: Not applicable



Analysis 17.27. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 27: Mean birthweight

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Salim 2012	2408	658	98	2326	627	91	28.7%	82.00 [-101.21 , 265.21]
Van Vliet 2016	1358	318	51	1310	318	66	71.3%	48.00 [-68.20 , 164.20]
Total (95% CI)			**149**			**157**	**100.0%**	**57.75 [-40.38 , 155.88]**

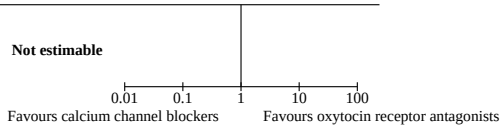
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.15 (P = 0.25)
Test for subgroup differences: Not applicable



Analysis 17.28. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

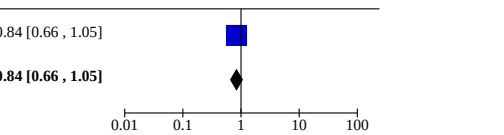
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 17.29. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Calcium channel blockers Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Salim 2012	54	98	60	91	100.0%	0.84 [0.66 , 1.05]
Total (95% CI)		**98**		**91**	**100.0%**	**0.84 [0.66 , 1.05]**
Total events:	54		60			

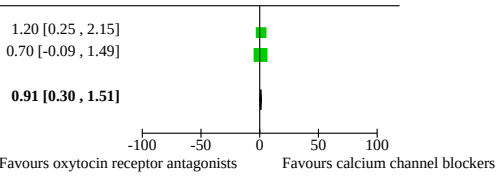
Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)
Test for subgroup differences: Not applicable



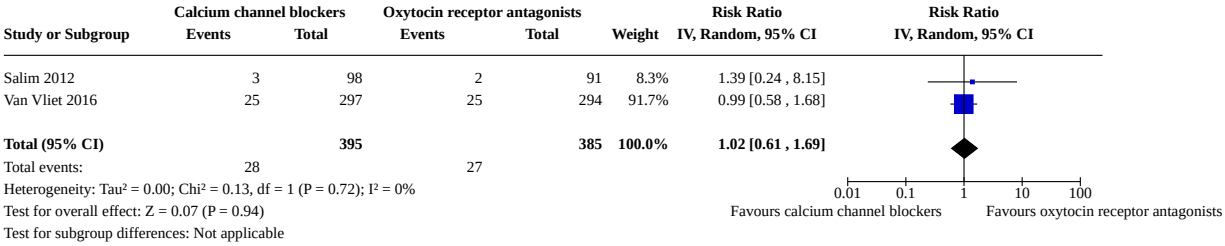
Analysis 17.30. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 30: Gestational age at birth

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Salim 2012	36.4	2.8	75	35.2	3	70	41.0%	1.20 [0.25 , 2.15]
Van Vliet 2016	33.1	4.8	248	32.4	4.2	255	59.0%	0.70 [-0.09 , 1.49]
Total (95% CI)			**323**			**325**	**100.0%**	**0.91 [0.30 , 1.51]**

Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 2.93 (P = 0.003)
Test for subgroup differences: Not applicable



Analysis 17.31. Comparison 17: Calcium channel blockers vs oxytocin receptor antagonists, Outcome 31: Neonatal infection

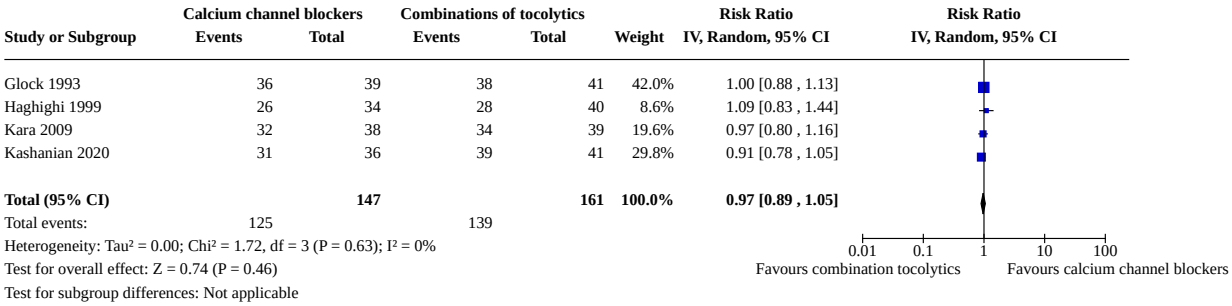


Comparison 18. Calcium channel blockers vs combinations of tocolytics

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
18.1 Delay in birth by 48 hours	4	308	Risk Ratio (IV, Random, 95% CI)	0.97 [0.89, 1.05]
18.2 Delay in birth by 7 days	2	154	Risk Ratio (IV, Random, 95% CI)	0.88 [0.77, 1.02]
18.3 Neonatal death before 28 days	1	80	Risk Ratio (IV, Random, 95% CI)	5.25 [0.26, 106.01]
18.4 Pregnancy prolongation (time from trial entry to birth in days)	1	77	Mean Difference (IV, Random, 95% CI)	-2.80 [-8.81, 3.21]
18.5 Serious adverse effects of drugs	1	80	Risk Ratio (IV, Random, 95% CI)	0.35 [0.01, 8.34]
18.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.7 Cessation of treatment due to adverse effects	2	154	Risk Ratio (IV, Random, 95% CI)	0.12 [0.01, 2.10]
18.8 Birth before 28 weeks' gestation	1	80	Risk Ratio (IV, Random, 95% CI)	5.25 [0.26, 106.01]
18.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.10 Birth before 34 weeks' gestation	1	80	Risk Ratio (IV, Random, 95% CI)	1.21 [0.67, 2.21]
18.11 Birth before 37 weeks' gestation	3	234	Risk Ratio (IV, Random, 95% CI)	1.17 [0.78, 1.75]
18.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.13 Pulmonary oedema	1	80	Risk Ratio (IV, Random, 95% CI)	0.35 [0.01, 8.34]
18.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
18.16 Headaches	2	157	Risk Ratio (IV, Random, 95% CI)	4.45 [0.25, 77.71]
18.17 Nausea or vomiting	3	234	Risk Ratio (IV, Random, 95% CI)	1.05 [0.46, 2.37]
18.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.20 Maternal hypotension	2	157	Risk Ratio (IV, Random, 95% CI)	5.98 [1.79, 19.96]
18.21 Perinatal death	1	80	Risk Ratio (IV, Random, 95% CI)	5.25 [0.26, 106.01]
18.22 Stillbirth	1	80	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.27 Mean birthweight	4	308	Mean Difference (IV, Random, 95% CI)	-112.94 [-267.34, 41.45]
18.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
18.30 Gestational age at birth	3	234	Mean Difference (IV, Random, 95% CI)	-0.78 [-1.90, 0.34]
18.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

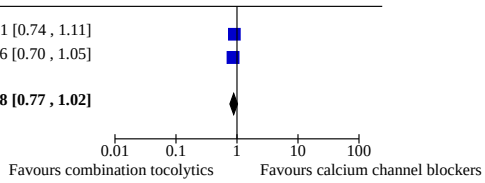
Analysis 18.1. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 1: Delay in birth by 48 hours



Analysis 18.2. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kara 2009	30	38	34	39	49.5%	0.91 [0.74 , 1.11]
Kashanian 2020	28	36	37	41	50.5%	0.86 [0.70 , 1.05]
Total (95% CI)		**74**		**80**	**100.0%**	**0.88 [0.77 , 1.02]**
Total events:	58		71			

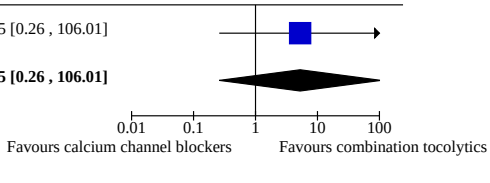
Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.73); I² = 0%
Test for overall effect: Z = 1.70 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 18.3. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	2	39	0	41	100.0%	5.25 [0.26 , 106.01]
Total (95% CI)		**39**		**41**	**100.0%**	**5.25 [0.26 , 106.01]**
Total events:	2		0			

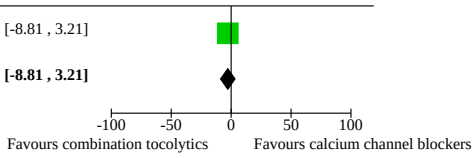
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 18.4. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kara 2009	21.4	14.4	38	24.2	12.4	39	100.0%	-2.80 [-8.81 , 3.21]
Total (95% CI)			**38**			**39**	**100.0%**	**-2.80 [-8.81 , 3.21]**

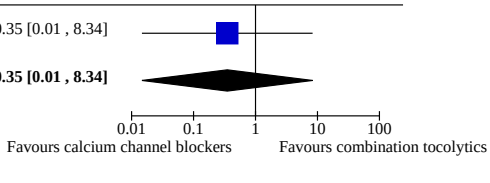
Heterogeneity: Not applicable
Test for overall effect: Z = 0.91 (P = 0.36)
Test for subgroup differences: Not applicable



Analysis 18.5. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	0	39	1	41	100.0%	0.35 [0.01 , 8.34]
Total (95% CI)		**39**		**41**	**100.0%**	**0.35 [0.01 , 8.34]**
Total events:	0		1			

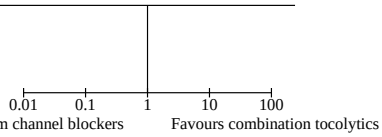
Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.52)
Test for subgroup differences: Not applicable



Analysis 18.6. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 6: Maternal infection

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

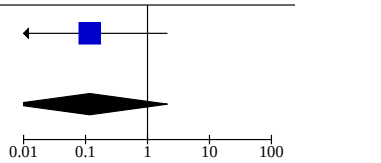
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.7. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	0	39	4	41	100.0%	0.12 [0.01 , 2.10]
Haghighi 1999	0	34	0	40		Not estimable
Total (95% CI)		**73**		**81**	**100.0%**	**0.12 [0.01 , 2.10]**
Total events:	0		4			

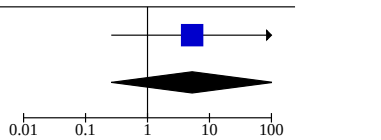
Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 18.8. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	2	39	0	41	100.0%	5.25 [0.26 , 106.01]
Total (95% CI)		**39**		**41**	**100.0%**	**5.25 [0.26 , 106.01]**
Total events:	2		0			

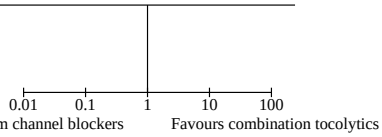
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 18.9. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

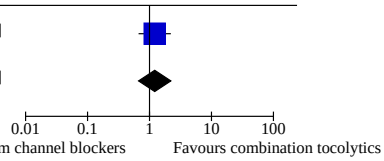
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.10. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	15	39	13	41	100.0%	1.21 [0.67 , 2.21]
Total (95% CI)		**39**		**41**	**100.0%**	**1.21 [0.67 , 2.21]**
Total events:	15		13			

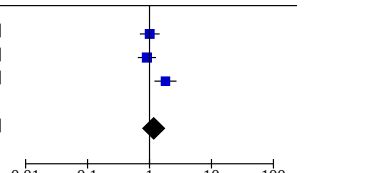
Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)
Test for subgroup differences: Not applicable



Analysis 18.11. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	23	39	24	41	33.6%	1.01 [0.70 , 1.45]
Kara 2009	23	38	26	39	35.0%	0.91 [0.65 , 1.27]
Kashanian 2020	27	36	17	41	31.4%	1.81 [1.20 , 2.72]
Total (95% CI)		**113**		**121**	**100.0%**	**1.17 [0.78 , 1.75]**
Total events:	73		67			

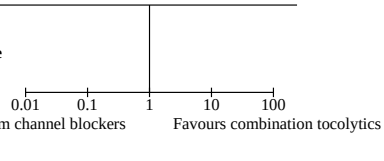
Heterogeneity: Tau² = 0.09; Chi² = 7.04, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 0.76 (P = 0.45)
Test for subgroup differences: Not applicable



Analysis 18.12. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 12: Maternal death

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

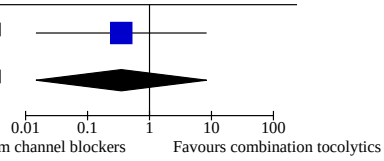
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.13. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 13: Pulmonary oedema

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	0	39	1	41	100.0%	0.35 [0.01 , 8.34]
Total (95% CI)		**39**		**41**	**100.0%**	**0.35 [0.01 , 8.34]**
Total events:	0		1			

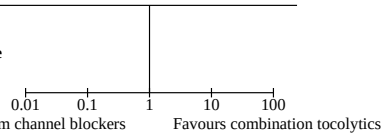
Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.52)
Test for subgroup differences: Not applicable



Analysis 18.14. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 14: Dyspnoea

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

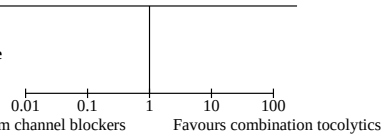
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.15. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 15: Palpitations

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

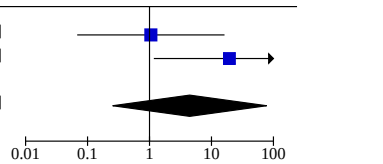
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.16. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 16: Headaches

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	1	39	1	41	50.6%	1.05 [0.07 , 16.23]
Kara 2009	9	38	0	39	49.4%	19.49 [1.17 , 323.49]
Total (95% CI)		**77**		**80**	**100.0%**	**4.45 [0.25 , 77.71]**
Total events:	10		1			

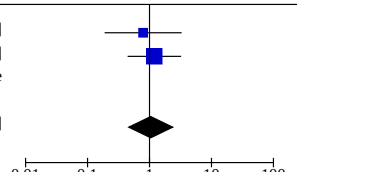
Heterogeneity: Tau² = 2.26; Chi² = 2.13, df = 1 (P = 0.14); I² = 53%
Test for overall effect: Z = 1.02 (P = 0.31)
Test for subgroup differences: Not applicable



Analysis 18.17. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 17: Nausea or vomiting

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	3	39	4	41	32.6%	0.79 [0.19 , 3.30]
Kara 2009	7	38	6	39	67.4%	1.20 [0.44 , 3.24]
Kashanian 2020	0	36	0	41		Not estimable
Total (95% CI)		**113**		**121**	**100.0%**	**1.05 [0.46 , 2.37]**
Total events:	10		10			

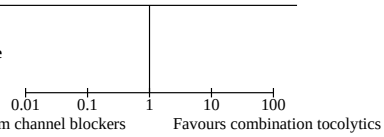
Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.11 (P = 0.92)
Test for subgroup differences: Not applicable



Analysis 18.18. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 18: Tachycardia

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

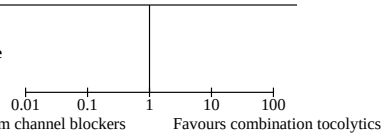
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.19. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

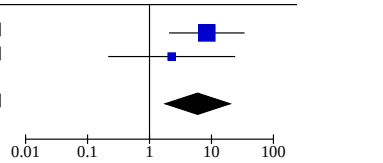
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.20. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 20: Maternal hypotension

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	16	39	2	41	73.9%	8.41 [2.07 , 34.21]
Kashanian 2020	2	36	1	41	26.1%	2.28 [0.22 , 24.08]
Total (95% CI)		**75**		**82**	**100.0%**	**5.98 [1.79 , 19.96]**
Total events:	18		3			

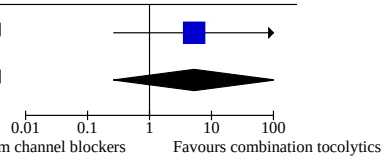
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.87$, df = 1 (P = 0.35); $I^2 = 0\%$
Test for overall effect: Z = 2.91 (P = 0.004)
Test for subgroup differences: Not applicable



Analysis 18.21. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 21: Perinatal death

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Glock 1993	2	39	0	41	100.0%	5.25 [0.26 , 106.01]
Total (95% CI)		**39**		**41**	**100.0%**	**5.25 [0.26 , 106.01]**
Total events:	2		0			

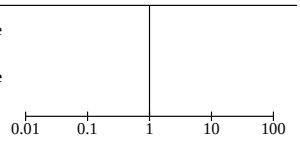
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 18.22. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 22: Stillbirth

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Glock 1993	0	39	0	41		Not estimable	
Total (95% CI)		**39**		**41**		**Not estimable**	
Total events:	0		0				

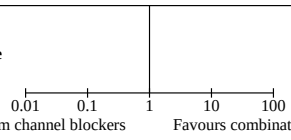
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.23. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

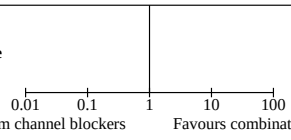
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.24. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

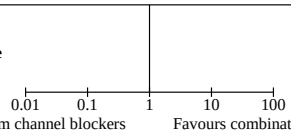
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.25. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

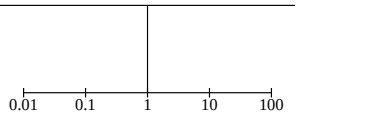
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.26. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 26: Respiratory morbidity

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

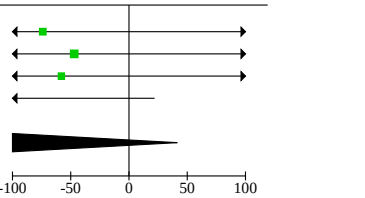
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.27. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 27: Mean birthweight

Study or Subgroup	Calcium channel blockers Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Glock 1993	2434	716	39	2508	693	41	25.0%	-74.00 [-383.02 , 235.02]
Haghighi 1999	2405	674	34	2452	532	40	30.4%	-47.00 [-327.19 , 233.19]
Kara 2009	2492	759	38	2550	669	39	23.3%	-58.00 [-377.88 , 261.88]
Kashanian 2020	2578	564	36	2890	910	41	21.4%	-312.00 [-645.96 , 21.96]
Total (95% CI)			**147**			**161**	**100.0%**	**-112.94 [-267.34 , 41.45]**

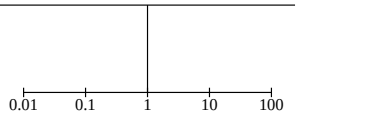
Heterogeneity: Tau² = 0.00; Chi² = 1.75, df = 3 (P = 0.63); I² = 0%
Test for overall effect: Z = 1.43 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 18.28. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

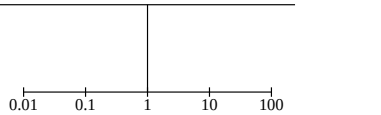
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



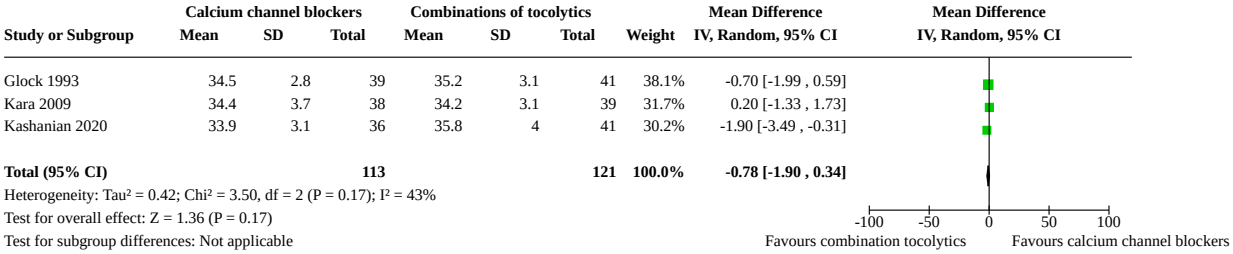
Analysis 18.29. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Calcium channel blockers Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

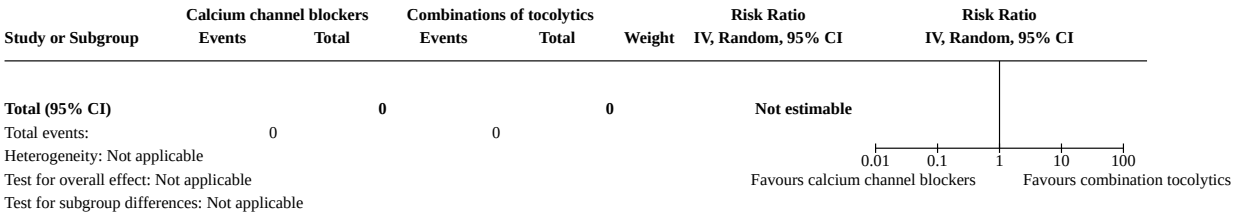
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 18.30. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 30: Gestational age at birth



Analysis 18.31. Comparison 18: Calcium channel blockers vs combinations of tocolytics, Outcome 31: Neonatal infection



Comparison 19. COX inhibitors vs magnesium sulphate

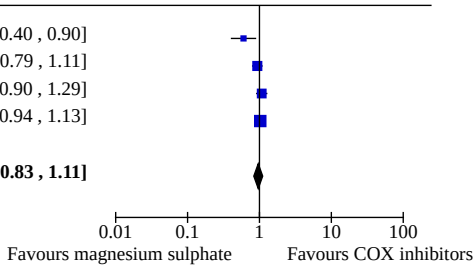
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
19.1 Delay in birth by 48 hours	4	610	Risk Ratio (IV, Random, 95% CI)	0.96 [0.83, 1.11]
19.2 Delay in birth by 7 days	1	172	Risk Ratio (IV, Random, 95% CI)	1.13 [0.87, 1.46]
19.3 Neonatal death before 28 days	3	424	Risk Ratio (IV, Random, 95% CI)	0.93 [0.30, 2.85]
19.4 Pregnancy prolongation (time from trial entry to birth in days)	1	172	Mean Difference (IV, Random, 95% CI)	0.20 [-10.11, 10.51]
19.5 Serious adverse effects of drugs	4	610	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.89]
19.6 Maternal infection	2	316	Risk Ratio (IV, Random, 95% CI)	0.38 [0.02, 9.13]
19.7 Cessation of treatment due to adverse effects	3	506	Risk Ratio (IV, Random, 95% CI)	1.01 [0.01, 144.87]
19.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.10 Birth before 34 weeks' gestation	1	172	Risk Ratio (IV, Random, 95% CI)	0.85 [0.68, 1.05]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
19.11 Birth before 37 weeks' gestation	1	172	Risk Ratio (IV, Random, 95% CI)	0.96 [0.87, 1.06]
19.12 Maternal death	2	292	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.13 Pulmonary oedema	3	396	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.89]
19.14 Dyspnoea	2	386	Risk Ratio (IV, Random, 95% CI)	5.19 [0.62, 43.69]
19.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.16 Headaches	1	214	Risk Ratio (IV, Random, 95% CI)	0.62 [0.15, 2.54]
19.17 Nausea or vomiting	2	386	Risk Ratio (IV, Random, 95% CI)	1.14 [0.07, 18.76]
19.18 Tachycardia	2	276	Risk Ratio (IV, Random, 95% CI)	0.98 [0.06, 15.37]
19.19 Maternal cardiac arrhythmias	1	214	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.20 Maternal hypotension	2	276	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.21 Perinatal death	3	424	Risk Ratio (IV, Random, 95% CI)	0.93 [0.30, 2.85]
19.22 Stillbirth	1	198	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.23 Neonatal death before 7 days	1	194	Risk Ratio (IV, Random, 95% CI)	0.22 [0.01, 4.55]
19.24 Neurodevelopmental morbidity	3	424	Risk Ratio (IV, Random, 95% CI)	1.03 [0.61, 1.74]
19.25 Gastrointestinal morbidity	4	544	Risk Ratio (IV, Random, 95% CI)	1.35 [0.47, 3.88]
19.26 Respiratory morbidity	3	424	Risk Ratio (IV, Random, 95% CI)	1.03 [0.78, 1.36]
19.27 Mean birthweight	4	528	Mean Difference (IV, Random, 95% CI)	-6.46 [-138.66, 125.73]
19.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
19.30 Gestational age at birth	4	502	Mean Difference (IV, Random, 95% CI)	0.25 [-0.35, 0.85]
19.31 Neonatal infection	2	392	Risk Ratio (IV, Random, 95% CI)	1.05 [0.55, 1.98]

Analysis 19.1. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Asgharnia 2002	21	60	35	60	9.6%	0.60 [0.40 , 0.90]
Borna 2007	42	52	45	52	27.1%	0.93 [0.79 , 1.11]
Klauser 2014	66	87	60	85	25.8%	1.07 [0.90 , 1.29]
McWhorter 2004	95	105	96	109	37.5%	1.03 [0.94 , 1.13]
Total (95% CI)		**304**		**306**	**100.0%**	**0.96 [0.83 , 1.11]**
Total events:	224		236			

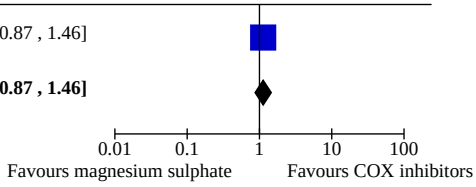
Heterogeneity: Tau² = 0.01; Chi² = 7.65, df = 3 (P = 0.05); I² = 61%
Test for overall effect: Z = 0.54 (P = 0.59)
Test for subgroup differences: Not applicable



Analysis 19.2. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 2: Delay in birth by 7 days

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	53	87	46	85	100.0%	1.13 [0.87 , 1.46]
Total (95% CI)		**87**		**85**	**100.0%**	**1.13 [0.87 , 1.46]**
Total events:	53		46			

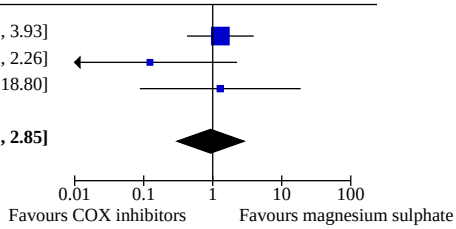
Heterogeneity: Not applicable
Test for overall effect: Z = 0.90 (P = 0.37)
Test for subgroup differences: Not applicable



Analysis 19.3. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 3: Neonatal death before 28 days

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	7	103	5	95	70.0%	1.29 [0.42 , 3.93]
McWhorter 2004	0	92	4	102	13.9%	0.12 [0.01 , 2.26]
Parilla 1997	1	14	1	18	16.1%	1.29 [0.09 , 18.80]
Total (95% CI)		**209**		**215**	**100.0%**	**0.93 [0.30 , 2.85]**
Total events:	8		10			

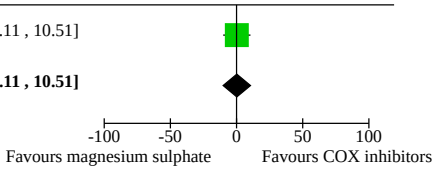
Heterogeneity: Tau² = 0.14; Chi² = 2.23, df = 2 (P = 0.33); I² = 10%
Test for overall effect: Z = 0.12 (P = 0.90)
Test for subgroup differences: Not applicable



Analysis 19.4. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	COX inhibitors Mean	SD	Total	Magnesium sulphate Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Klauser 2014	22.7	21.1	87	22.5	43.8	85	100.0%	0.20 [-10.11 , 10.51]
Total (95% CI)			**87**			**85**	**100.0%**	**0.20 [-10.11 , 10.51]**

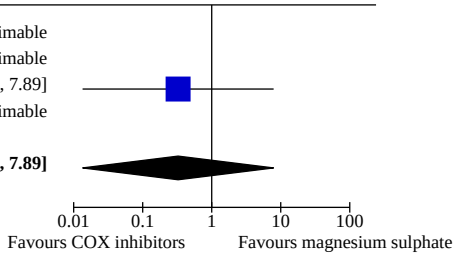
Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.97)
Test for subgroup differences: Not applicable



Analysis 19.5. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Asgharnia 2002	0	60	0	60		Not estimable
Borna 2007	0	52	0	52		Not estimable
Klauser 2014	0	87	1	85	100.0%	0.33 [0.01 , 7.89]
McWhorter 2004	0	105	0	109		Not estimable
Total (95% CI)		**304**		**306**	**100.0%**	**0.33 [0.01 , 7.89]**
Total events:	0		1			

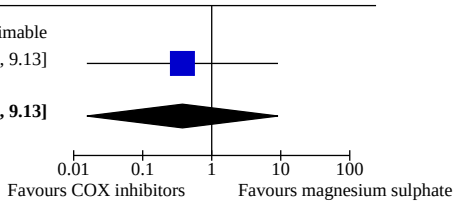
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 19.6. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Asgharnia 2002	0	60	0	60		Not estimable
McWhorter 2004	0	92	1	104	100.0%	0.38 [0.02 , 9.13]
Total (95% CI)		**152**		**164**	**100.0%**	**0.38 [0.02 , 9.13]**
Total events:	0		1			

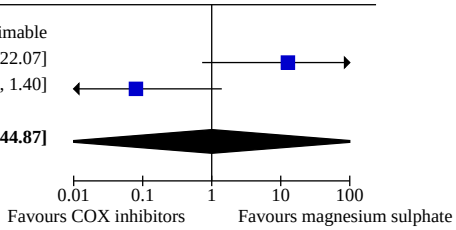
Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable



Analysis 19.7. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Asgharnia 2002	0	60	0	60		Not estimable
Klauser 2014	6	87	0	85	50.0%	12.70 [0.73 , 222.07]
McWhorter 2004	0	105	6	109	50.0%	0.08 [0.00 , 1.40]
Total (95% CI)		**252**		**254**	**100.0%**	**1.01 [0.01 , 144.87]**
Total events:	6		6			

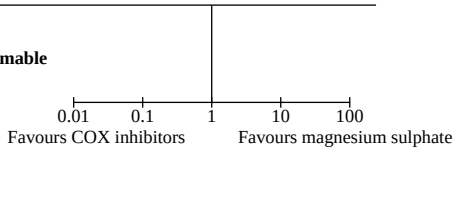
Heterogeneity: Tau² = 10.72; Chi² = 6.02, df = 1 (P = 0.01); I² = 83%
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



Analysis 19.8. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

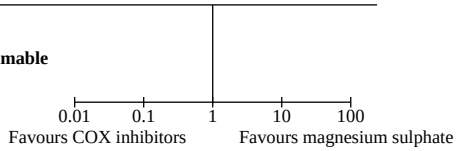
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 19.9. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

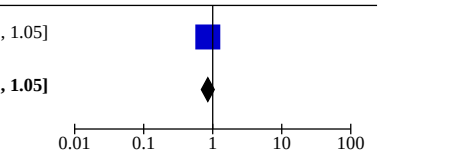
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 19.10. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	53	87	61	85	100.0%	0.85 [0.68 , 1.05]
Total (95% CI)		**87**		**85**	**100.0%**	**0.85 [0.68 , 1.05]**
Total events:	53		61			

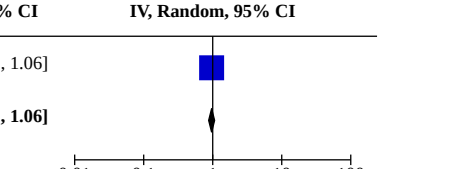
Heterogeneity: Not applicable
Test for overall effect: Z = 1.50 (P = 0.13)
Test for subgroup differences: Not applicable



Analysis 19.11. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	77	87	78	85	100.0%	0.96 [0.87 , 1.06]
Total (95% CI)		**87**		**85**	**100.0%**	**0.96 [0.87 , 1.06]**
Total events:	77		78			

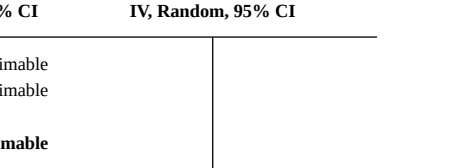
Heterogeneity: Not applicable
Test for overall effect: Z = 0.72 (P = 0.47)
Test for subgroup differences: Not applicable



Analysis 19.12. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Asgharnia 2002	0	60	0	60		Not estimable
Klauser 2014	0	87	0	85		Not estimable
Total (95% CI)		**147**		**145**		**Not estimable**
Total events:	0		0			

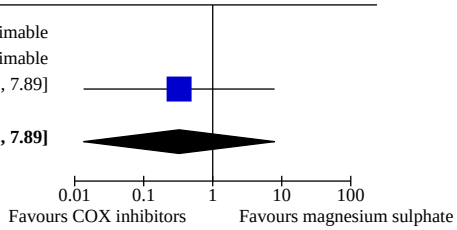
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 19.13. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 13: Pulmonary oedema

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Asgharnia 2002	0	60	0	60		Not estimable
Borna 2007	0	52	0	52		Not estimable
Klauser 2014	0	87	1	85	100.0%	0.33 [0.01 , 7.89]
Total (95% CI)		**199**		**197**	**100.0%**	**0.33 [0.01 , 7.89]**
Total events:	0		1			

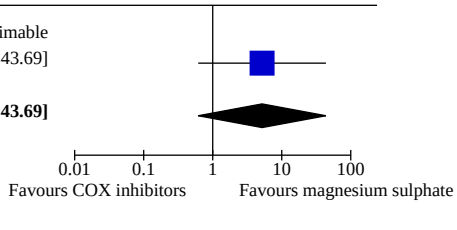
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 19.14. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	87	0	85		Not estimable
McWhorter 2004	5	105	1	109	100.0%	5.19 [0.62 , 43.69]
Total (95% CI)		**192**		**194**	**100.0%**	**5.19 [0.62 , 43.69]**
Total events:	5		1			

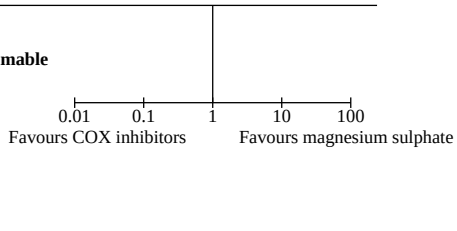
Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)
Test for subgroup differences: Not applicable



Analysis 19.15. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

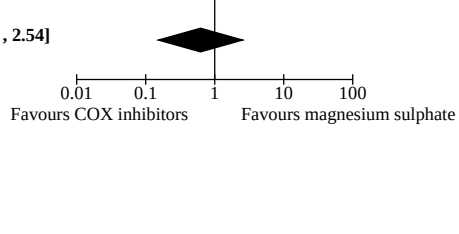
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 19.16. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 16: Headaches

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
McWhorter 2004	3	105	5	109	100.0%	0.62 [0.15 , 2.54]
Total (95% CI)		**105**		**109**	**100.0%**	**0.62 [0.15 , 2.54]**
Total events:	3		5			

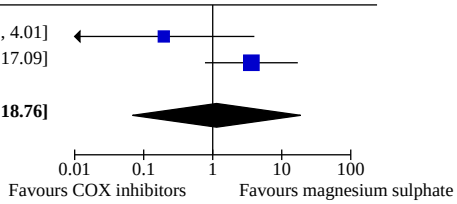
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)
Test for subgroup differences: Not applicable



Analysis 19.17. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 17: Nausea or vomiting

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	87	2	85	39.7%	0.20 [0.01 , 4.01]
McWhorter 2004	7	105	2	109	60.3%	3.63 [0.77 , 17.09]
Total (95% CI)		**192**		**194**	**100.0%**	**1.14 [0.07 , 18.76]**
Total events:	7		4			

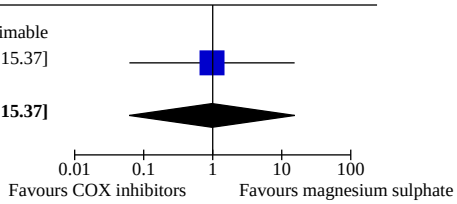
Heterogeneity: Tau² = 2.77; Chi² = 2.85, df = 1 (P = 0.09); I² = 65%
Test for overall effect: Z = 0.09 (P = 0.93)
Test for subgroup differences: Not applicable



Analysis 19.18. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 18: Tachycardia

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Borna 2007	0	52	0	52		Not estimable
Klauser 2014	1	87	1	85	100.0%	0.98 [0.06 , 15.37]
Total (95% CI)		**139**		**137**	**100.0%**	**0.98 [0.06 , 15.37]**
Total events:	1		1			

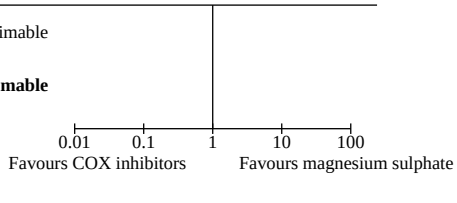
Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.99)
Test for subgroup differences: Not applicable



Analysis 19.19. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
McWhorter 2004	0	105	0	109		Not estimable
Total (95% CI)		**105**		**109**		**Not estimable**
Total events:	0		0			

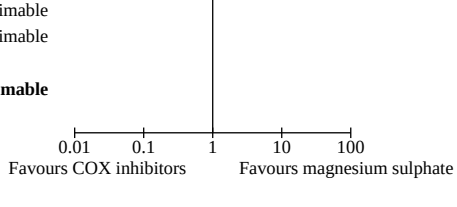
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 19.20. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 20: Maternal hypotension

Study or Subgroup	COX inhibitors Events	Total	Magnesium sulphate Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Borna 2007	0	52	0	52		Not estimable
Klauser 2014	0	87	0	85		Not estimable
Total (95% CI)		**139**		**137**		**Not estimable**
Total events:	0		0			

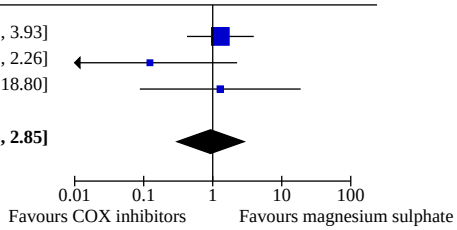
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 19.21. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 21: Perinatal death

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	7	103	5	95	70.0%	1.29 [0.42 , 3.93]
McWhorter 2004	0	92	4	102	13.9%	0.12 [0.01 , 2.26]
Parilla 1997	1	14	1	18	16.1%	1.29 [0.09 , 18.80]
Total (95% CI)		**209**		**215**	**100.0%**	**0.93 [0.30 , 2.85]**
Total events:	8		10			

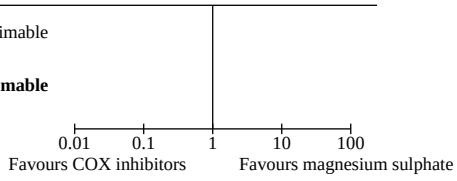
Heterogeneity: Tau² = 0.14; Chi² = 2.23, df = 2 (P = 0.33); I² = 10%
Test for overall effect: Z = 0.12 (P = 0.90)
Test for subgroup differences: Not applicable



Analysis 19.22. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 22: Stillbirth

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	0	103	0	95		Not estimable
Total (95% CI)		**103**		**95**		**Not estimable**
Total events:	0		0			

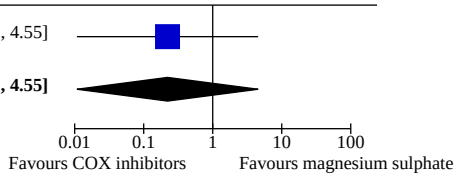
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 19.23. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 23: Neonatal death before 7 days

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
McWhorter 2004	0	92	2	102	100.0%	0.22 [0.01 , 4.55]
Total (95% CI)		**92**		**102**	**100.0%**	**0.22 [0.01 , 4.55]**
Total events:	0		2			

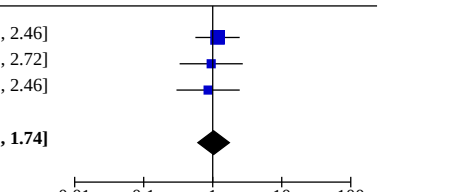
Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)
Test for subgroup differences: Not applicable



Analysis 19.24. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	14	103	11	95	50.4%	1.17 [0.56 , 2.46]
McWhorter 2004	6	92	7	102	24.8%	0.95 [0.33 , 2.72]
Parilla 1997	4	14	6	18	24.7%	0.86 [0.30 , 2.46]
Total (95% CI)		**209**		**215**	**100.0%**	**1.03 [0.61 , 1.74]**
Total events:	24		24			

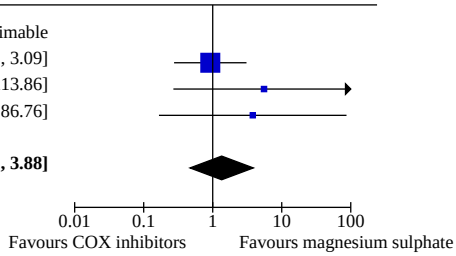
Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 2 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.11 (P = 0.91)
Test for subgroup differences: Not applicable



Analysis 19.25. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Asgharnia 2002	0	60	0	60		Not estimable
Klauser 2014	5	103	5	95	76.4%	0.92 [0.28 , 3.09]
McWhorter 2004	2	92	0	102	12.2%	5.54 [0.27 , 113.86]
Parilla 1997	1	14	0	18	11.4%	3.80 [0.17 , 86.76]
Total (95% CI)		**269**		**275**	**100.0%**	**1.35 [0.47 , 3.88]**
Total events:	8		5			

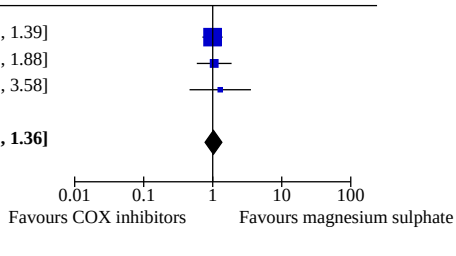
Heterogeneity: Tau² = 0.00; Chi² = 1.64, df = 2 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.56 (P = 0.58)
Test for subgroup differences: Not applicable



Analysis 19.26. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 26: Respiratory morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Klauser 2014	42	103	39	95	69.4%	0.99 [0.71 , 1.39]
McWhorter 2004	18	92	19	102	23.2%	1.05 [0.59 , 1.88]
Parilla 1997	5	14	5	18	7.4%	1.29 [0.46 , 3.58]
Total (95% CI)		**209**		**215**	**100.0%**	**1.03 [0.78 , 1.36]**
Total events:	65		63			

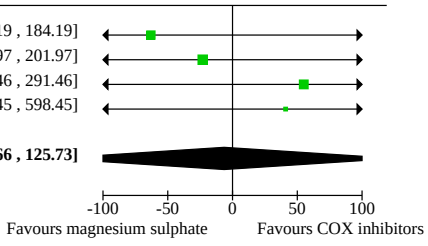
Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 2 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.18 (P = 0.86)
Test for subgroup differences: Not applicable



Analysis 19.27. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 27: Mean birthweight

Study or Subgroup	COX inhibitors Mean	COX inhibitors SD	COX inhibitors Total	Magnesium sulphate Mean	Magnesium sulphate SD	Magnesium sulphate Total	Weight	Mean Difference IV, Random, 95% CI
Borna 2007	2448	632	52	2511	654	52	28.6%	-63.00 [-310.19 , 184.19]
Klauser 2014	1746	809	103	1769	805	95	34.5%	-23.00 [-247.97 , 201.97]
McWhorter 2004	2585	778	92	2530	902	102	31.3%	55.00 [-181.46 , 291.46]
Parilla 1997	1622	589	14	1581	1005	18	5.6%	41.00 [-516.45 , 598.45]
Total (95% CI)			**261**			**267**	**100.0%**	**-6.46 [-138.66 , 125.73]**

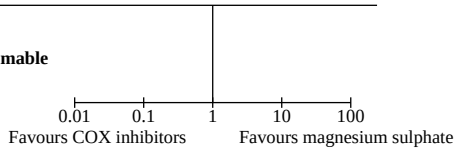
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 3 (P = 0.92); I² = 0%
Test for overall effect: Z = 0.10 (P = 0.92)
Test for subgroup differences: Not applicable



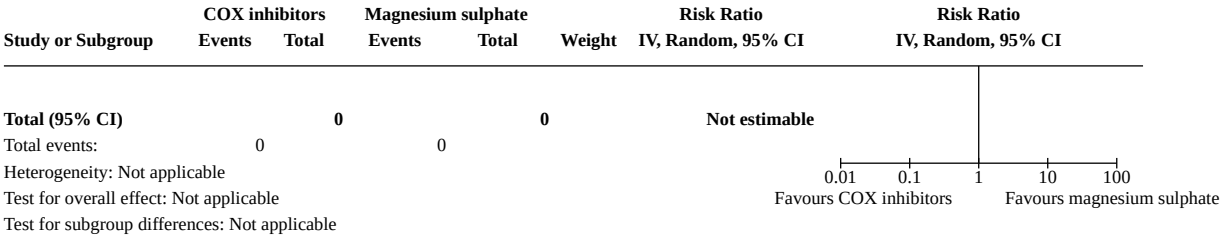
Analysis 19.28. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 28: Birthweight < 2000 g

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Magnesium sulphate Events	Magnesium sulphate Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

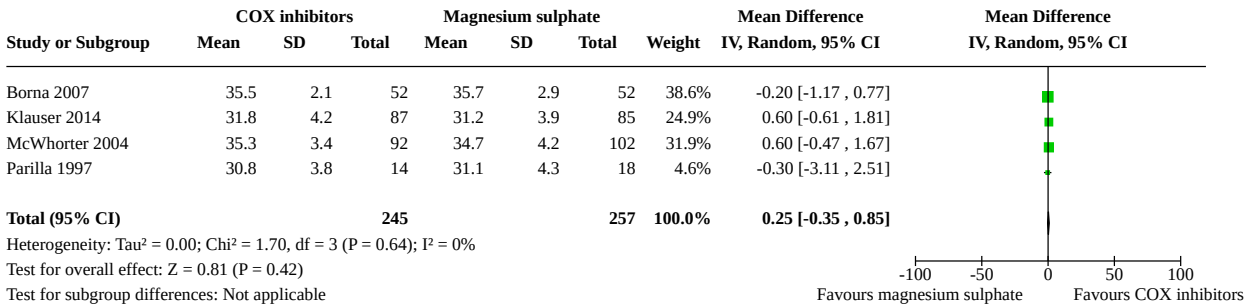
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



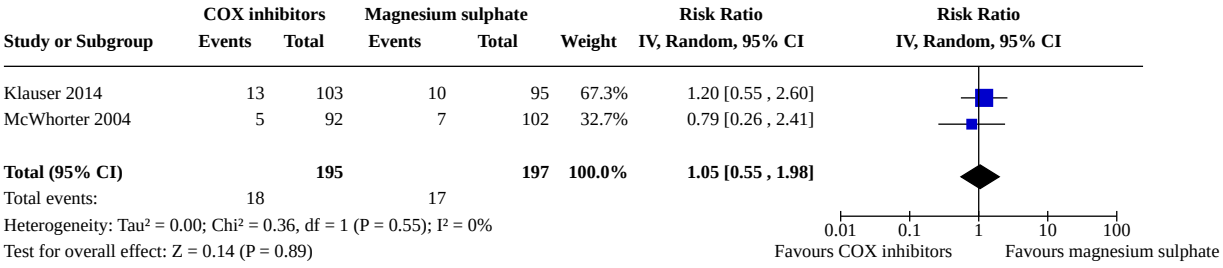
Analysis 19.29. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 29: Birthweight < 2500 g



Analysis 19.30. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 30: Gestational age at birth



Analysis 19.31. Comparison 19: COX inhibitors vs magnesium sulphate, Outcome 31: Neonatal infection



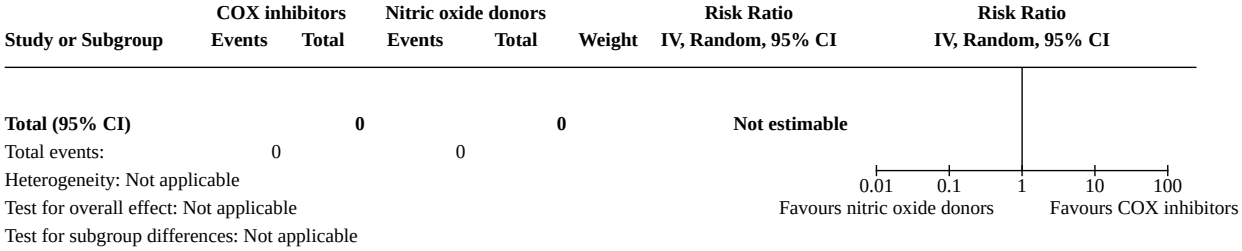
Comparison 20. COX inhibitors vs nitric oxide donors

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20.1 Delay in birth by 48 hours	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable

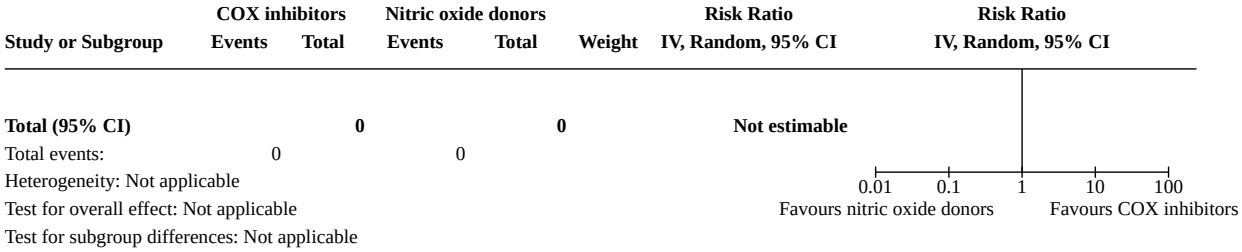
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.7 Cessation of treatment due to adverse effects	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.27 Mean birthweight	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
20.30 Gestational age at birth	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
20.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

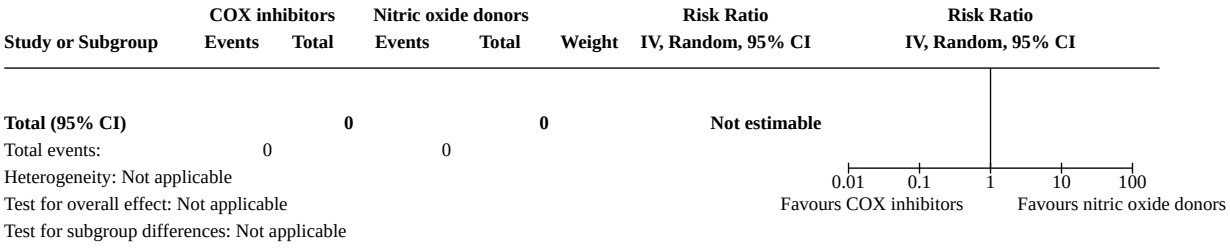
Analysis 20.1. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 1: Delay in birth by 48 hours



Analysis 20.2. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 2: Delay in birth by 7 days

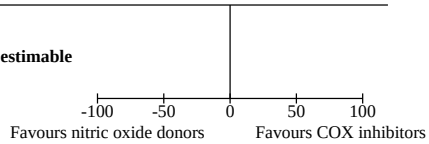


Analysis 20.3. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 3: Neonatal death before 28 days



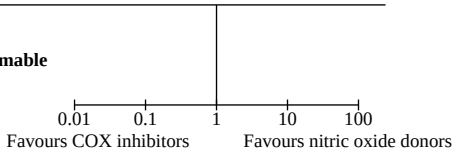
Analysis 20.4. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	COX inhibitors Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



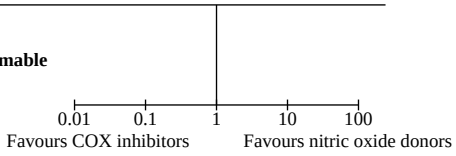
Analysis 20.5. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



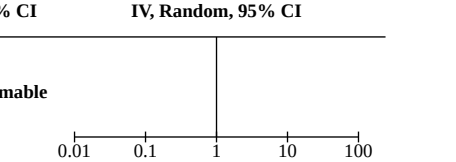
Analysis 20.6. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 20.7. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 7: Cessation of treatment due to adverse effects

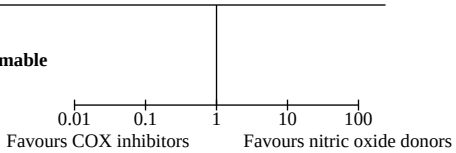
Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 20.8. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

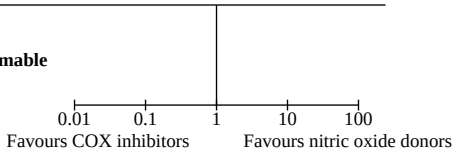
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.9. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

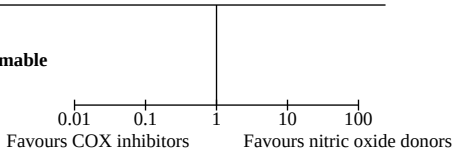
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.10. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

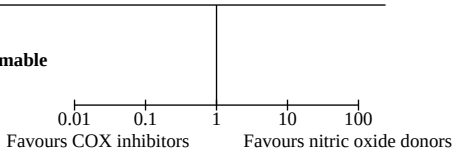
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.11. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

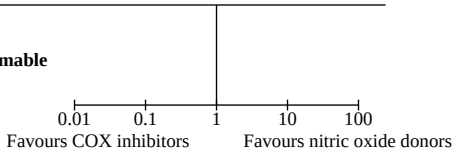
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.12. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

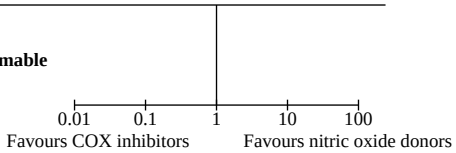
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.13. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 13: Pulmonary oedema

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

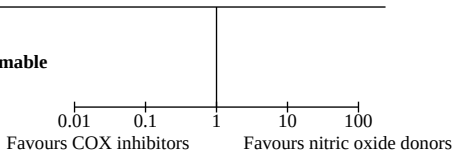
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.14. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

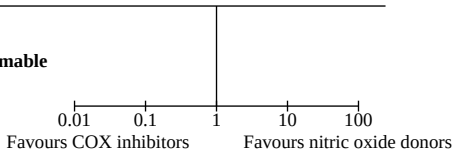
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.15. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

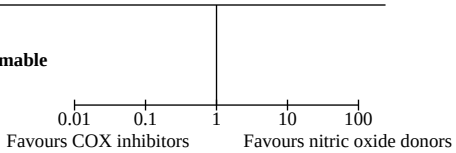
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.16. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 16: Headaches

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

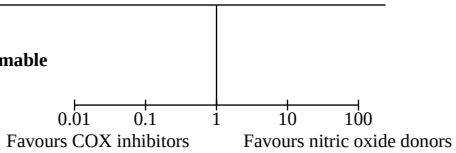
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.17. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 17: Nausea or vomiting

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

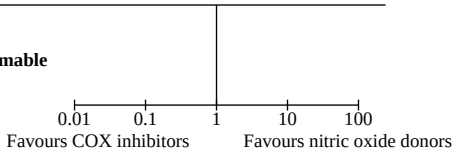
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.18. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 18: Tachycardia

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

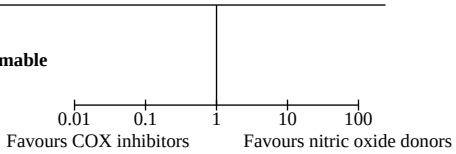
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.19. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 19: Maternal cardiac arrhythmias

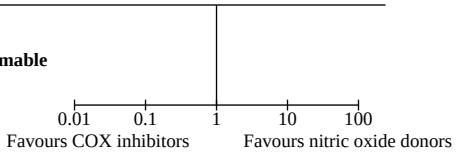
Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



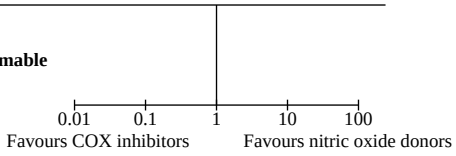
Analysis 20.20. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 20: Maternal hypotension

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



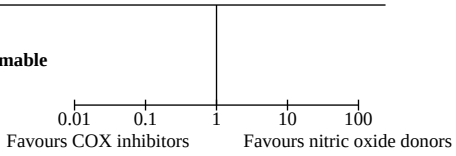
Analysis 20.21. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 21: Perinatal death

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



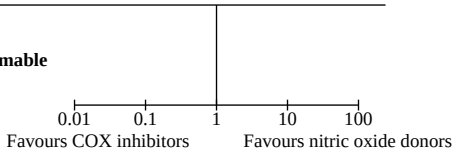
Analysis 20.22. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 22: Stillbirth

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 20.23. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 23: Neonatal death before 7 days

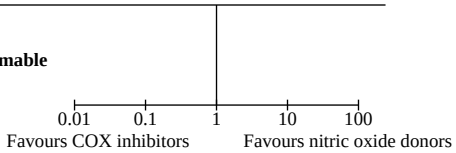
Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 20.24. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

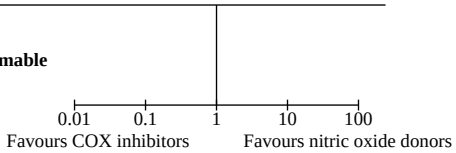
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.25. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

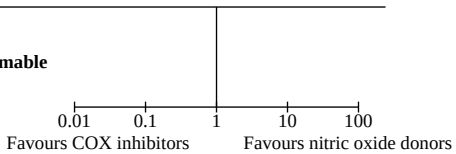
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.26. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 26: Respiratory morbidity

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

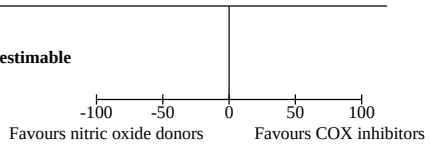
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 20.27. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 27: Mean birthweight

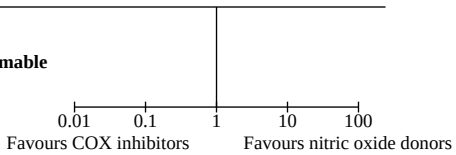
Study or Subgroup	COX inhibitors Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**	

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



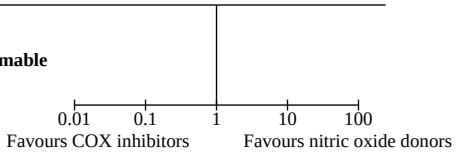
Analysis 20.28. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 28: Birthweight < 2000 g

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



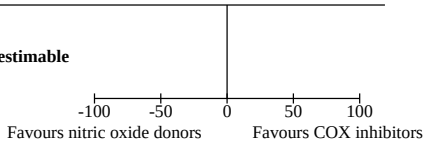
Analysis 20.29. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 29: Birthweight < 2500 g

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



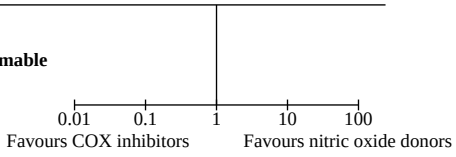
Analysis 20.30. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 30: Gestational age at birth

Study or Subgroup	COX inhibitors Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**	
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
Test for subgroup differences: Not applicable									



Analysis 20.31. Comparison 20: COX inhibitors vs nitric oxide donors, Outcome 31: Neonatal infection

Study or Subgroup	COX inhibitors Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Comparison 21. COX inhibitors vs oxytocin receptor antagonists

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21.1 Delay in birth by 48 hours	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

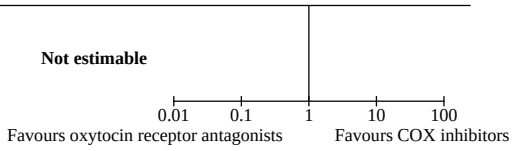
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
21.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.7 Cessation of treatment due to adverse effects	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.27 Mean birthweight	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
21.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
21.30 Gestational age at birth	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
21.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 21.1. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

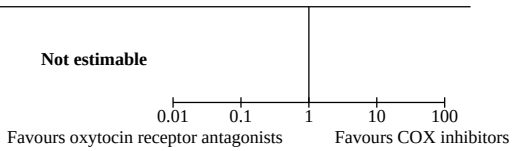
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.2. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 2: Delay in birth by 7 days

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

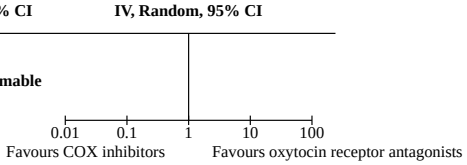
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.3. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 3: Neonatal death before 28 days

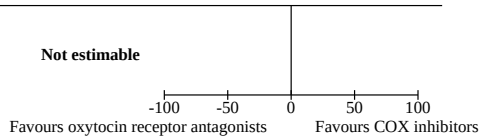
Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



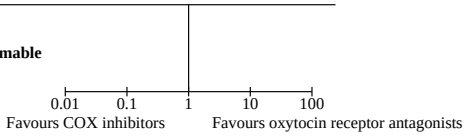
Analysis 21.4. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	COX inhibitors Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



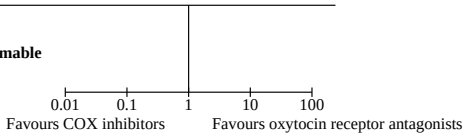
Analysis 21.5. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



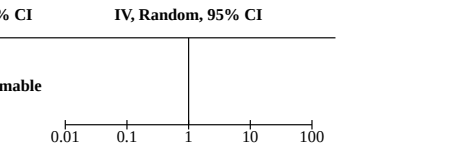
Analysis 21.6. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



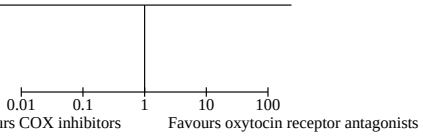
Analysis 21.7. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



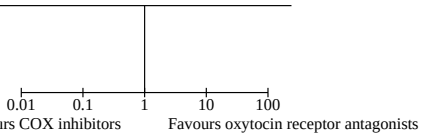
Analysis 21.8. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



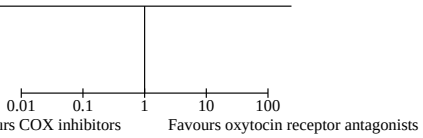
Analysis 21.9. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



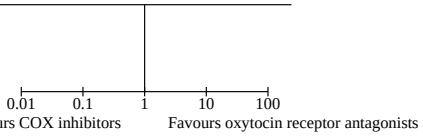
Analysis 21.10. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Analysis 21.11. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 11: Birth before 37 weeks' gestation

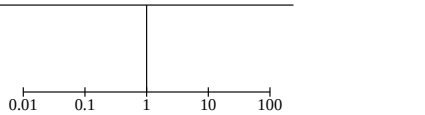
Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Analysis 21.12. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

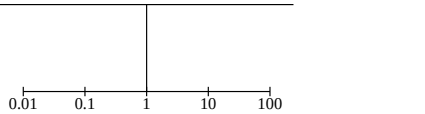
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.13. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 13: Pulmonary oedema

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

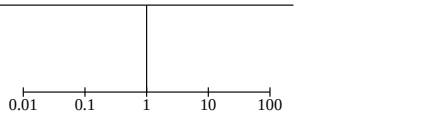
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.14. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

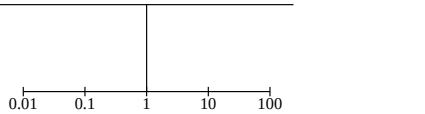
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.15. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

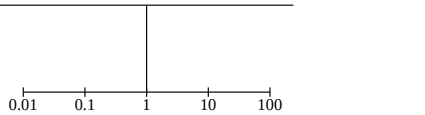
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.16. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 16: Headaches

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

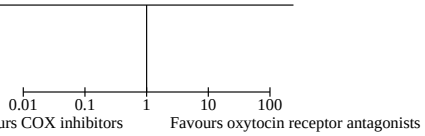
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.17. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 17: Nausea or vomiting

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

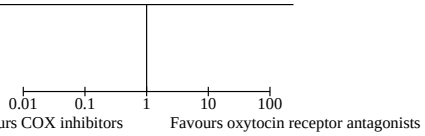
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.18. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 18: Tachycardia

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

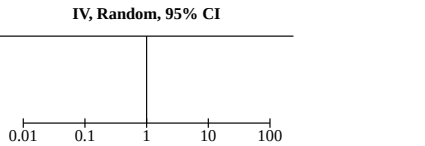
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.19. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

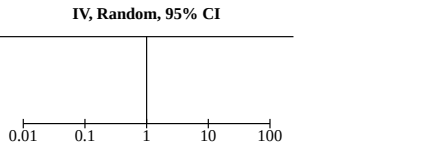
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.20. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 20: Maternal hypotension

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

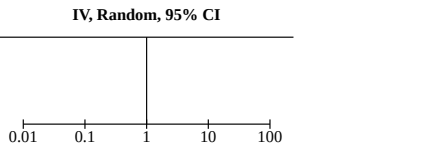
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.21. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 21: Perinatal death

Study or Subgroup	COX inhibitors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

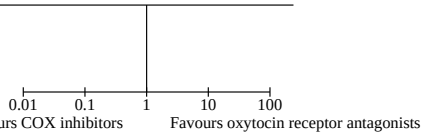
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.22. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 22: Stillbirth

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

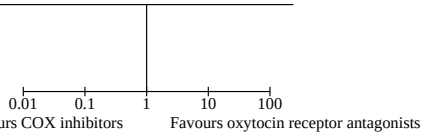
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.23. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 23: Neonatal death before 7 days

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

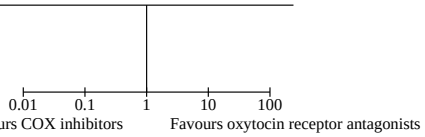
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.24. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

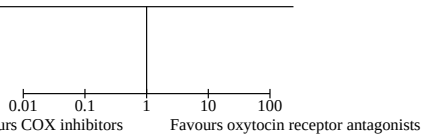
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.25. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

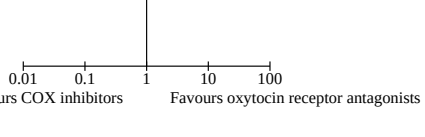
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 21.26. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 26: Respiratory morbidity

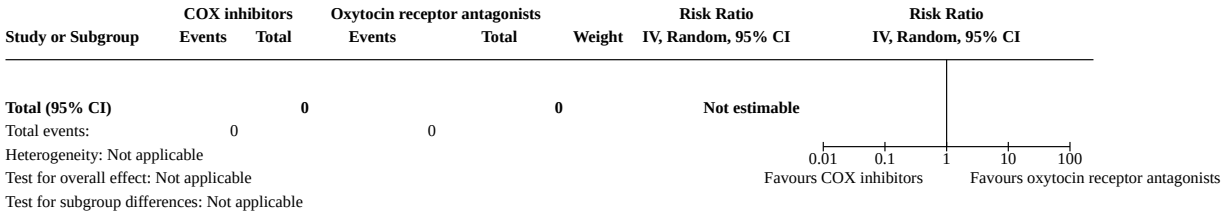
Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

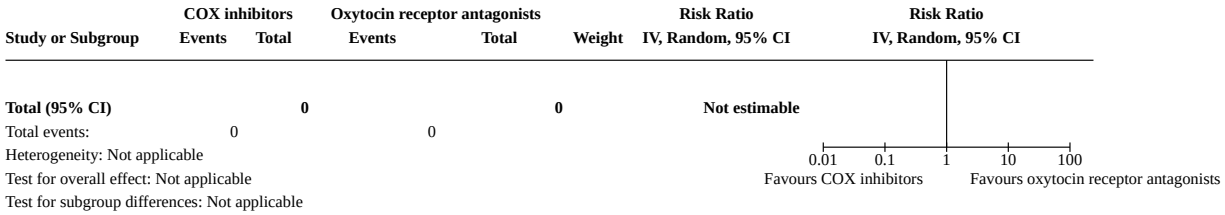


Analysis 21.27. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 27: Mean birthweight

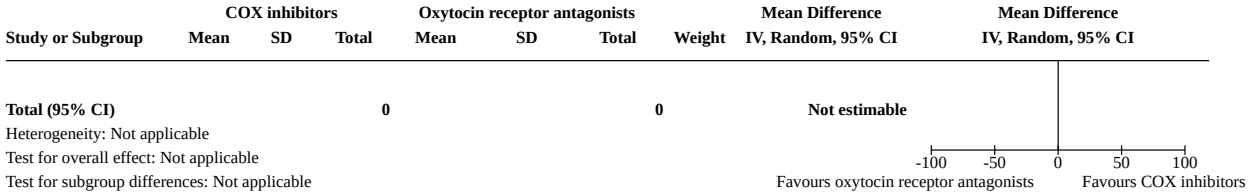
Analysis 21.28. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 28: Birthweight < 2000 g



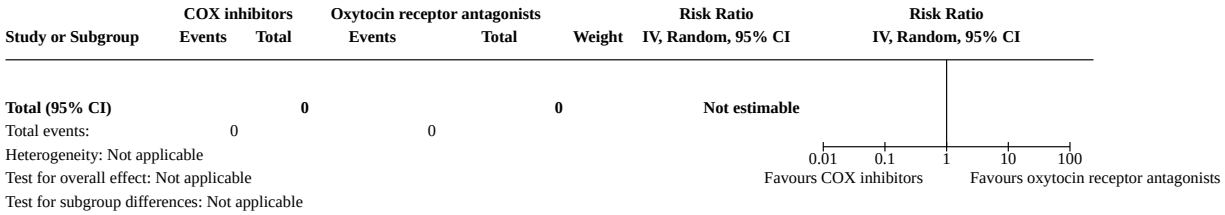
Analysis 21.29. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 29: Birthweight < 2500 g



Analysis 21.30. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 30: Gestational age at birth



Analysis 21.31. Comparison 21: COX inhibitors vs oxytocin receptor antagonists, Outcome 31: Neonatal infection



Comparison 22. COX inhibitors vs combinations of tocolytics

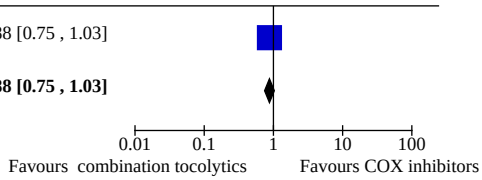
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
22.1 Delay in birth by 48 hours	1	77	Risk Ratio (IV, Random, 95% CI)	0.88 [0.75, 1.03]
22.2 Delay in birth by 7 days	1	77	Risk Ratio (IV, Random, 95% CI)	0.80 [0.64, 1.00]
22.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
22.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.7 Cessation of treatment due to adverse effects	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.11 Birth before 37 weeks' gestation	1	77	Risk Ratio (IV, Random, 95% CI)	1.81 [1.20, 2.72]
22.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.20 Maternal hypotension	1	77	Risk Ratio (IV, Random, 95% CI)	0.38 [0.02, 9.01]
22.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
22.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.27 Mean birthweight	1	77	Mean Difference (IV, Random, 95% CI)	-541.00 [-904.72, -177.28]
22.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
22.30 Gestational age at birth	1	77	Mean Difference (IV, Random, 95% CI)	-2.60 [-4.32, -0.88]
22.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 22.1. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2020	30	36	39	41	100.0%	0.88 [0.75 , 1.03]
Total (95% CI)		**36**		**41**	**100.0%**	**0.88 [0.75 , 1.03]**
Total events:	30		39			

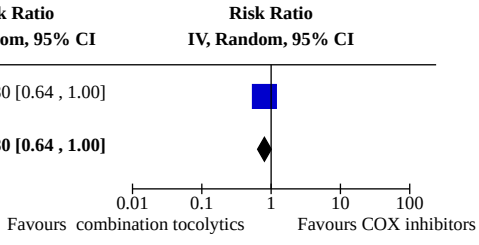
Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 22.2. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 2: Delay in birth by 7 days

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2020	26	36	37	41	100.0%	0.80 [0.64 , 1.00]
Total (95% CI)		**36**		**41**	**100.0%**	**0.80 [0.64 , 1.00]**
Total events:	26		37			

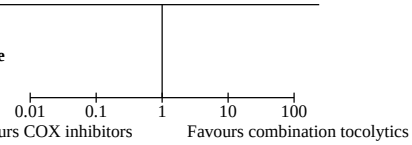
Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)
Test for subgroup differences: Not applicable



Analysis 22.3. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 3: Neonatal death before 28 days

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

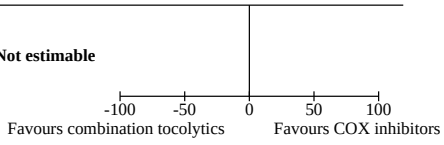
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.4. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	COX inhibitors Mean	COX inhibitors SD	COX inhibitors Total	Combinations of tocolytics Mean	Combinations of tocolytics SD	Combinations of tocolytics Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**	

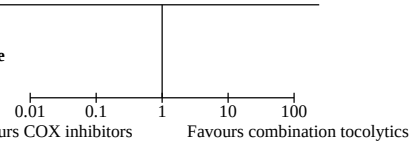
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.5. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

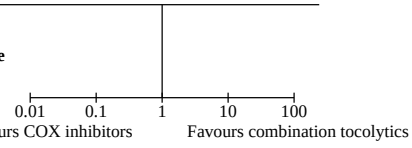
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.6. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 6: Maternal infection

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

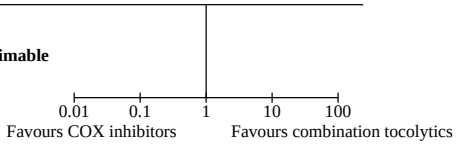
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.7. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

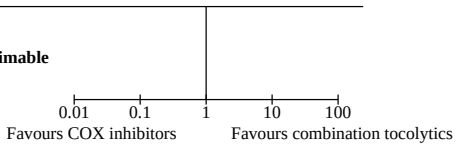
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.8. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

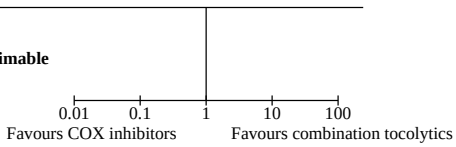
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.9. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

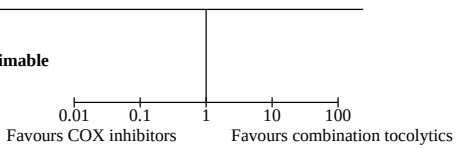
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.10. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

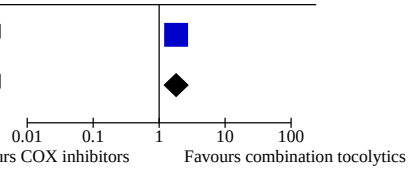
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.11. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2020	27	36	17	41	100.0%	1.81 [1.20 , 2.72]
Total (95% CI)		**36**		**41**	**100.0%**	**1.81 [1.20 , 2.72]**
Total events:	27		17			

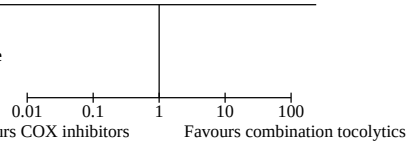
Heterogeneity: Not applicable
Test for overall effect: Z = 2.84 (P = 0.005)
Test for subgroup differences: Not applicable



Analysis 22.12. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 12: Maternal death

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

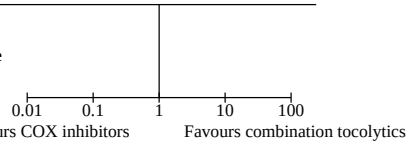
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.13. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 13: Pulmonary oedema

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

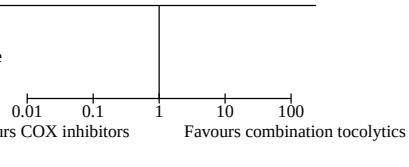
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.14. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 14: Dyspnoea

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

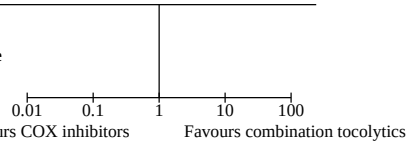
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.15. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 15: Palpitations

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

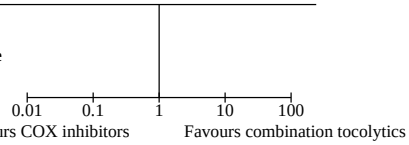
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.16. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 16: Headaches

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

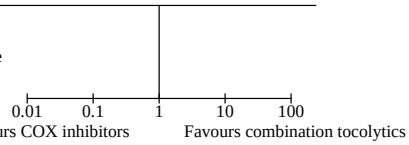
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.17. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 17: Nausea or vomiting

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

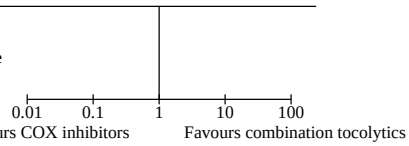
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.18. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 18: Tachycardia

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

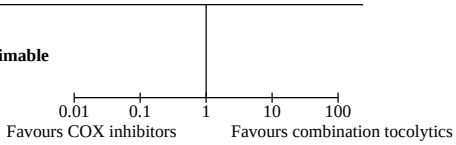
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.19. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

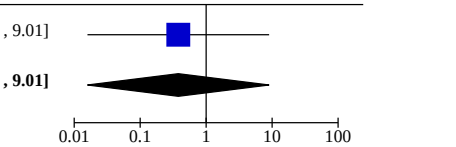
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.20. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 20: Maternal hypotension

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kashanian 2020	0	36	1	41	100.0%	0.38 [0.02 , 9.01]
Total (95% CI)		**36**		**41**	**100.0%**	**0.38 [0.02 , 9.01]**
Total events:	0		1			

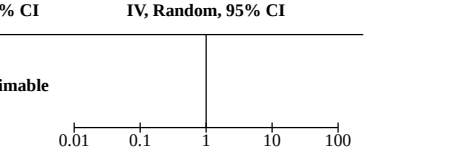
Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable



Analysis 22.21. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 21: Perinatal death

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

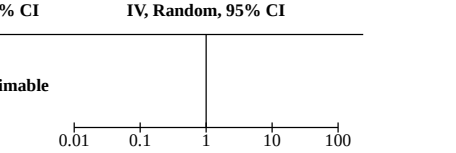
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.22. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 22: Stillbirth

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

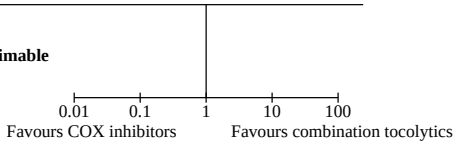
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.23. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 23: Neonatal death before 7 days

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

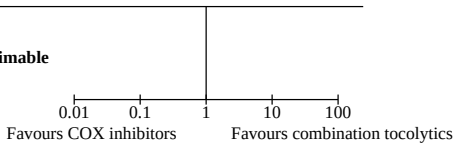
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.24. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

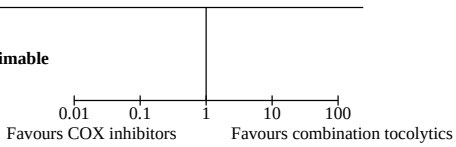
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.25. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

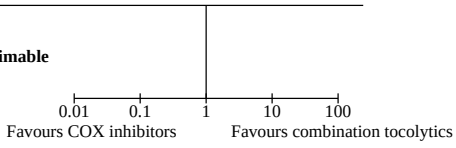
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.26. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 26: Respiratory morbidity

Study or Subgroup	COX inhibitors Events	COX inhibitors Total	Combinations of tocolytics Events	Combinations of tocolytics Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

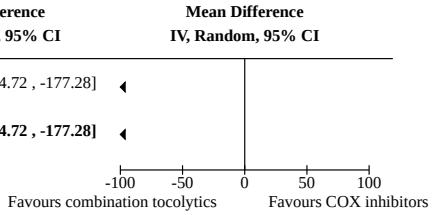
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.27. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 27: Mean birthweight

Study or Subgroup	COX inhibitors Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kashanian 2020	2349	716	36	2890	910	41	100.0%	-541.00 [-904.72 , -177.28]
Total (95% CI)			**36**			**41**	**100.0%**	**-541.00 [-904.72 , -177.28]**

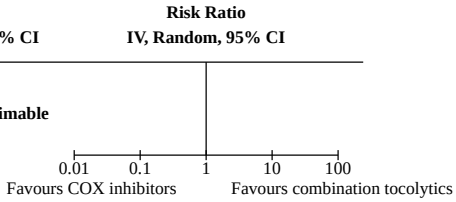
Heterogeneity: Not applicable
Test for overall effect: Z = 2.92 (P = 0.004)
Test for subgroup differences: Not applicable



Analysis 22.28. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 28: Birthweight < 2000 g

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

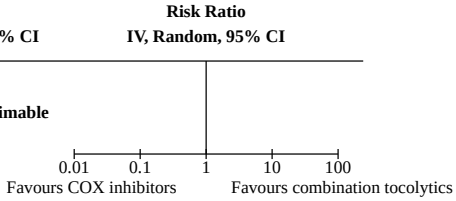
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.29. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 29: Birthweight < 2500 g

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

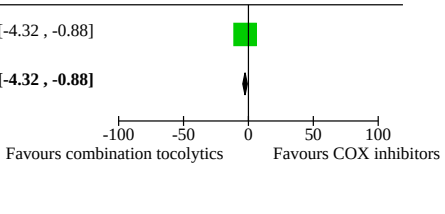
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 22.30. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 30: Gestational age at birth

Study or Subgroup	COX inhibitors Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kashanian 2020	33.2	3.7	36	35.8	4	41	100.0%	-2.60 [-4.32 , -0.88]
Total (95% CI)			**36**			**41**	**100.0%**	**-2.60 [-4.32 , -0.88]**

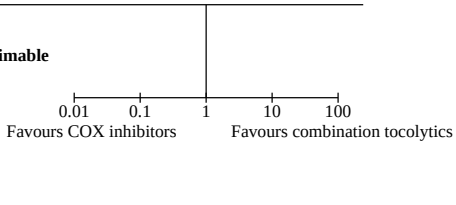
Heterogeneity: Not applicable
Test for overall effect: Z = 2.96 (P = 0.003)
Test for subgroup differences: Not applicable



Analysis 22.31. Comparison 22: COX inhibitors vs combinations of tocolytics, Outcome 31: Neonatal infection

Study or Subgroup	COX inhibitors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

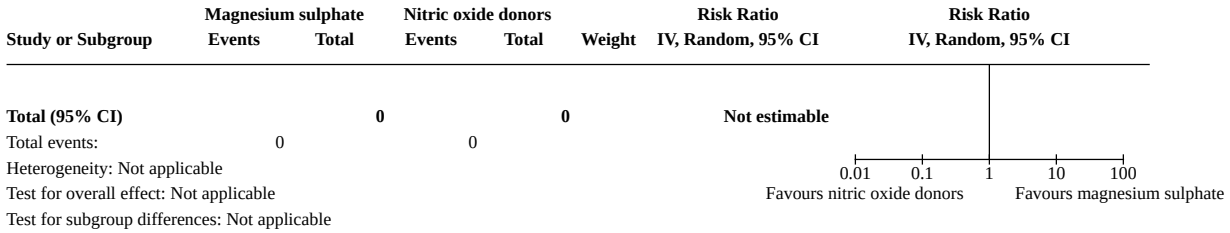


Comparison 23. Magnesium sulphate vs nitric oxide donors

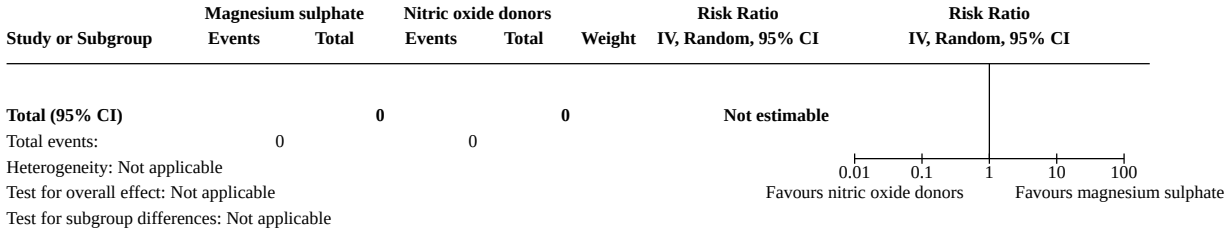
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
23.1 Delay in birth by 48 hours	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
23.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.7 Cessation of treatment due to adverse effects	1	30	Risk Ratio (IV, Random, 95% CI)	1.14 [0.08, 16.63]
23.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.14 Dyspnoea	1	30	Risk Ratio (IV, Random, 95% CI)	10.20 [0.60, 174.24]
23.15 Palpitations	1	30	Risk Ratio (IV, Random, 95% CI)	2.29 [0.23, 22.59]
23.16 Headaches	1	30	Risk Ratio (IV, Random, 95% CI)	0.42 [0.17, 1.01]
23.17 Nausea or vomiting	1	30	Risk Ratio (IV, Random, 95% CI)	1.47 [0.75, 2.90]
23.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.20 Maternal hypotension	1	30	Risk Ratio (IV, Random, 95% CI)	0.13 [0.01, 2.15]
23.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
23.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.27 Mean birthweight	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
23.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
23.30 Gestational age at birth	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
23.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 23.1. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 1: Delay in birth by 48 hours

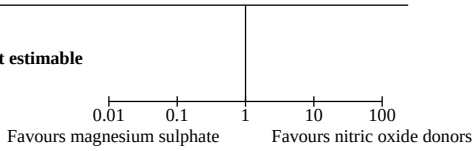


Analysis 23.2. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 2: Delay in birth by 7 days



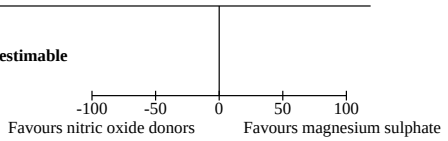
Analysis 23.3. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Magnesium sulphate Events	Magnesium sulphate Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



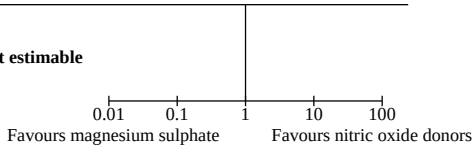
Analysis 23.4. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Magnesium sulphate Mean	Magnesium sulphate SD	Magnesium sulphate Total	Nitric oxide donors Mean	Nitric oxide donors SD	Nitric oxide donors Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**	
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
Test for subgroup differences: Not applicable									



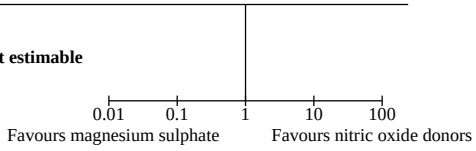
Analysis 23.5. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Magnesium sulphate Events	Magnesium sulphate Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Analysis 23.6. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 6: Maternal infection

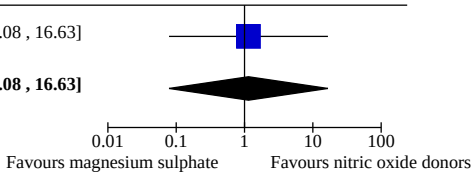
Study or Subgroup	Magnesium sulphate Events	Magnesium sulphate Total	Nitric oxide donors Events	Nitric oxide donors Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Analysis 23.7. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Sayed 1999	1	14	1	16	100.0%	1.14 [0.08 , 16.63]
Total (95% CI)		**14**		**16**	**100.0%**	**1.14 [0.08 , 16.63]**
Total events:	1		1			

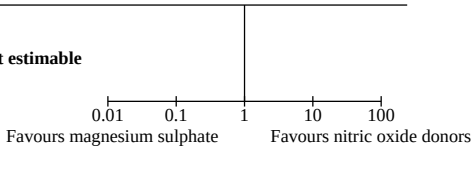
Heterogeneity: Not applicable
Test for overall effect: Z = 0.10 (P = 0.92)
Test for subgroup differences: Not applicable



Analysis 23.8. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

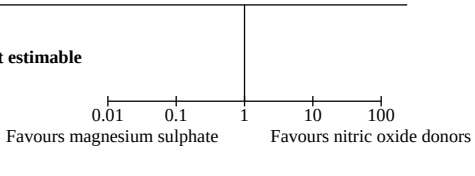
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.9. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

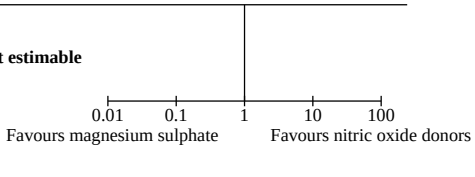
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.10. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

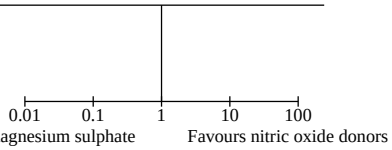
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.11. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

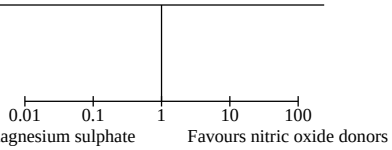
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.12. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 12: Maternal death

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

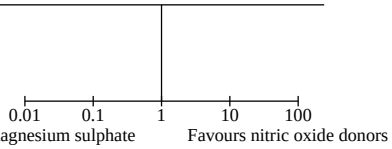
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.13. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 13: Pulmonary oedema

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

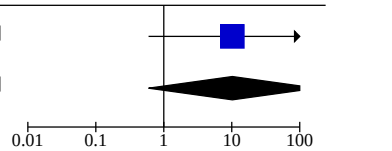
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.14. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 14: Dyspnoea

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Sayed 1999	4	14	0	16	100.0%	10.20 [0.60 , 174.24]
Total (95% CI)		**14**		**16**	**100.0%**	**10.20 [0.60 , 174.24]**
Total events:	4		0			

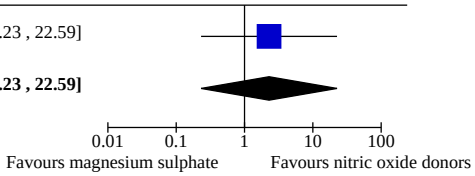
Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)
Test for subgroup differences: Not applicable



Analysis 23.15. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 15: Palpitations

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Sayed 1999	2	14	1	16	100.0%	2.29 [0.23 , 22.59]
Total (95% CI)		**14**		**16**	**100.0%**	**2.29 [0.23 , 22.59]**
Total events:	2		1			

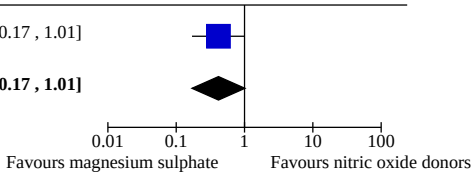
Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)
Test for subgroup differences: Not applicable



Analysis 23.16. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 16: Headaches

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Sayed 1999	4	14	11	16	100.0%	0.42 [0.17 , 1.01]
Total (95% CI)		**14**		**16**	**100.0%**	**0.42 [0.17 , 1.01]**
Total events:	4		11			

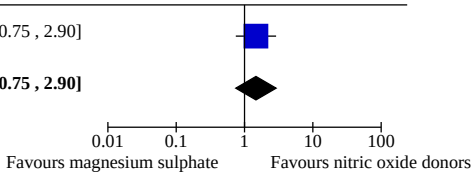
Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)
Test for subgroup differences: Not applicable



Analysis 23.17. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 17: Nausea or vomiting

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Sayed 1999	9	14	7	16	100.0%	1.47 [0.75 , 2.90]
Total (95% CI)		**14**		**16**	**100.0%**	**1.47 [0.75 , 2.90]**
Total events:	9		7			

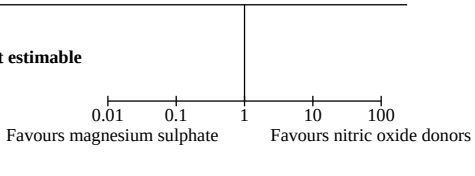
Heterogeneity: Not applicable
Test for overall effect: Z = 1.11 (P = 0.27)
Test for subgroup differences: Not applicable



Analysis 23.18. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 18: Tachycardia

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

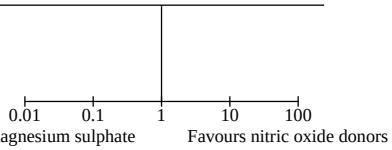
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.19. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

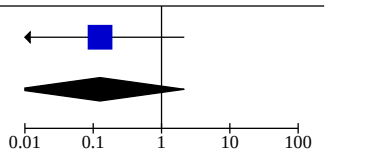
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.20. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 20: Maternal hypotension

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Sayed 1999	0	14	4	16	100.0%	0.13 [0.01 , 2.15]
Total (95% CI)		**14**		**16**	**100.0%**	**0.13 [0.01 , 2.15]**
Total events:	0		4			

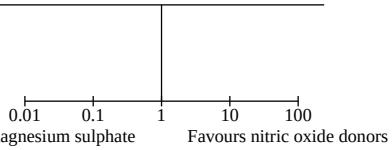
Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 23.21. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 21: Perinatal death

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

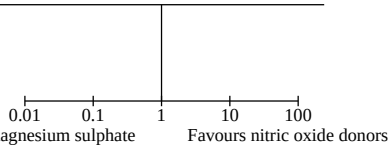
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.22. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 22: Stillbirth

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

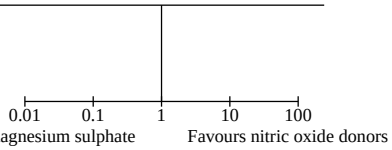
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.23. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

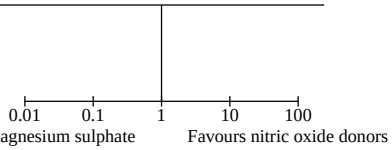
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.24. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

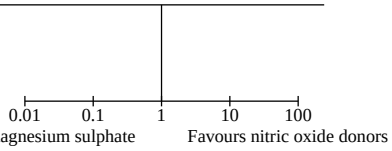
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.25. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

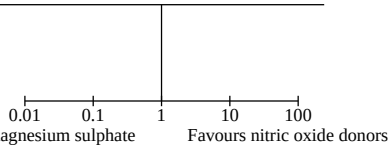
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 23.26. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 26: Respiratory morbidity

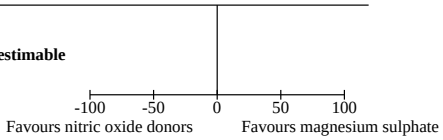
Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



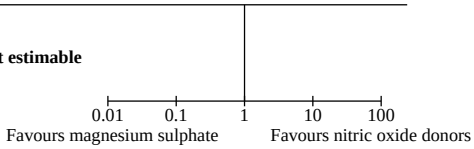
Analysis 23.27. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 27: Mean birthweight

Study or Subgroup	Magnesium sulphate Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**	
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
Test for subgroup differences: Not applicable									



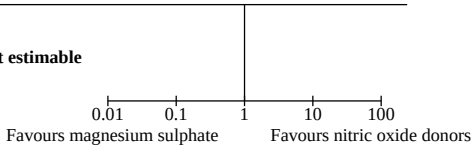
Analysis 23.28. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



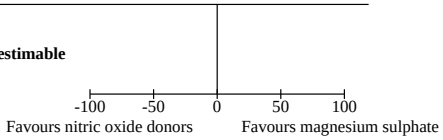
Analysis 23.29. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



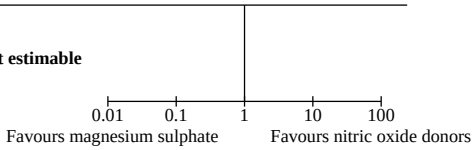
Analysis 23.30. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 30: Gestational age at birth

Study or Subgroup	Magnesium sulphate Mean	SD	Total	Nitric oxide donors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**	
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
Test for subgroup differences: Not applicable									



Analysis 23.31. Comparison 23: Magnesium sulphate vs nitric oxide donors, Outcome 31: Neonatal infection

Study or Subgroup	Magnesium sulphate Events	Total	Nitric oxide donors Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

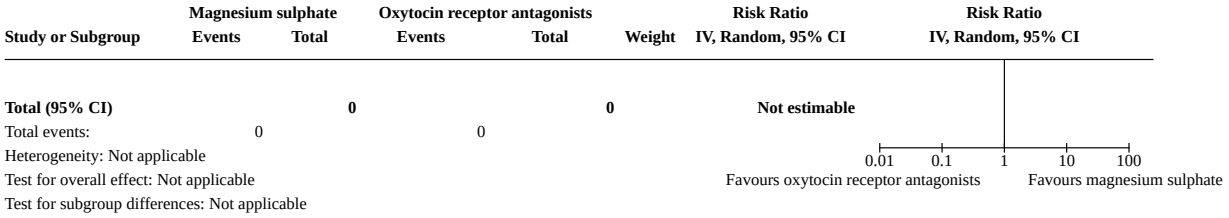


Comparison 24. Magnesium sulphate vs oxytocin receptor antagonists

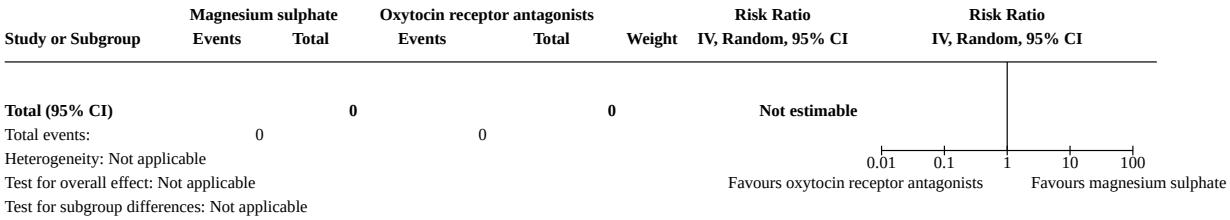
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
24.1 Delay in birth by 48 hours	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
24.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.7 Cessation of treatment due to adverse effects	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
24.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.27 Mean birthweight	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
24.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
24.30 Gestational age at birth	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
24.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

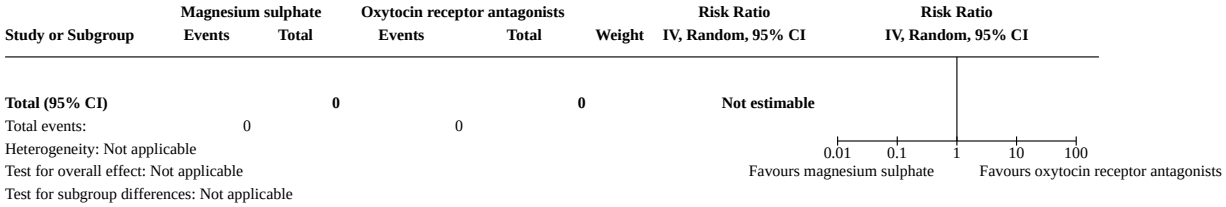
Analysis 24.1. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 1: Delay in birth by 48 hours



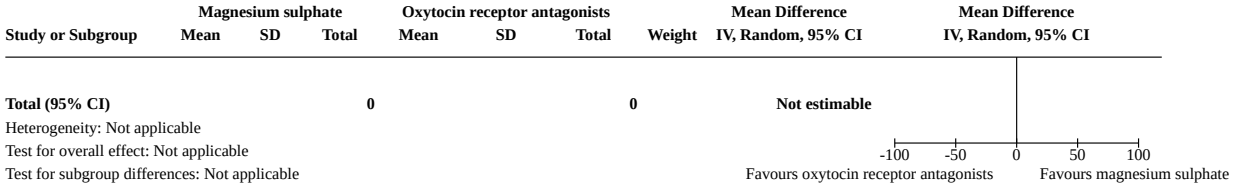
Analysis 24.2. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 2: Delay in birth by 7 days



Analysis 24.3. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 3: Neonatal death before 28 days

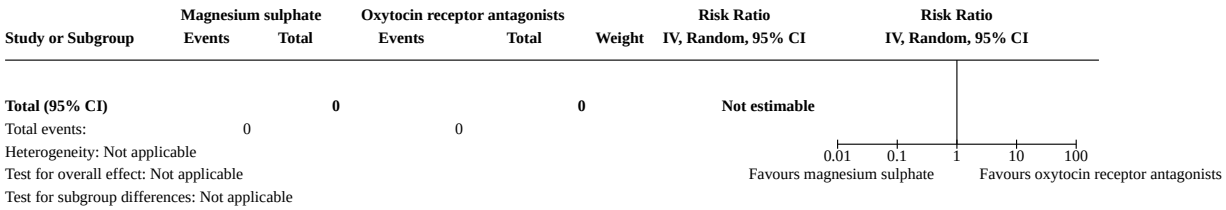


Analysis 24.4. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)



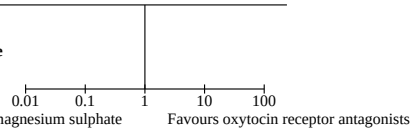
Analysis 24.5. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 5: Serious adverse effects of drugs

Analysis 24.6. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 6: Maternal infection



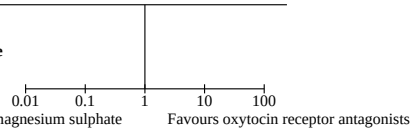
Analysis 24.7. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



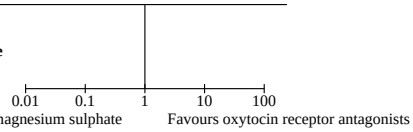
Analysis 24.8. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



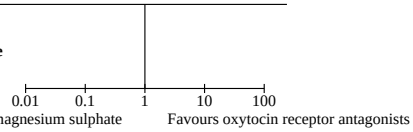
Analysis 24.9. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Analysis 24.10. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 10: Birth before 34 weeks' gestation

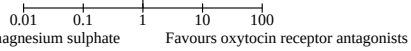
Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							



Analysis 24.11. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.12. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 12: Maternal death

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 24.13. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 13: Pulmonary oedema

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 24.14. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 14: Dyspnoea

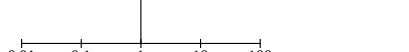
Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 24.15. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 15: Palpitations

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

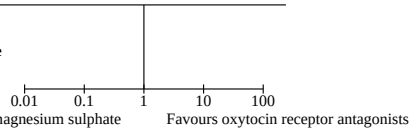
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.16. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 16: Headaches

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

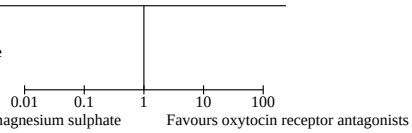
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.17. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 17: Nausea or vomiting

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

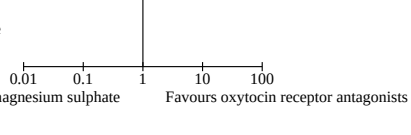
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.18. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 18: Tachycardia

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

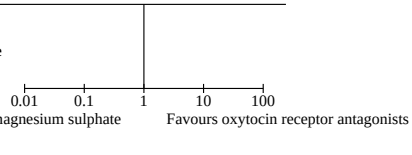
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.19. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

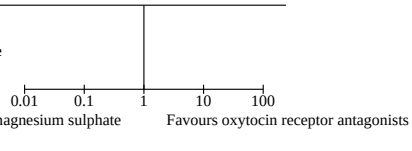
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.20. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 20: Maternal hypotension

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

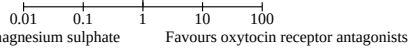
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.21. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 21: Perinatal death

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.22. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 22: Stillbirth

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 24.23. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 24.24. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 24.25. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 25: Gastrointestinal morbidity

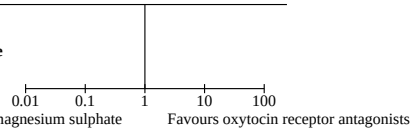
Study or Subgroup	Magnesium sulphate Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 24.26. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 26: Respiratory morbidity

Study or Subgroup	Magnesium sulphate Events	Magnesium sulphate Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

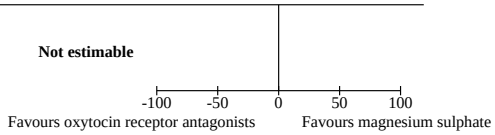
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.27. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 27: Mean birthweight

Study or Subgroup	Magnesium sulphate Mean	Magnesium sulphate SD	Magnesium sulphate Total	Oxytocin receptor antagonists Mean	Oxytocin receptor antagonists SD	Oxytocin receptor antagonists Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**

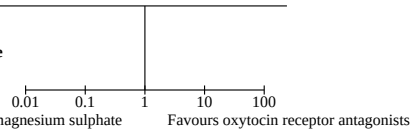
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.28. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Magnesium sulphate Events	Magnesium sulphate Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

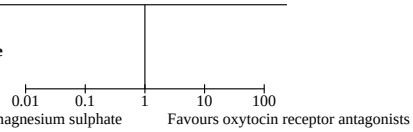
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



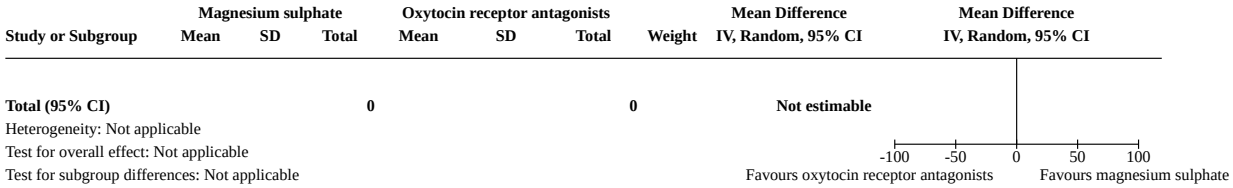
Analysis 24.29. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Magnesium sulphate Events	Magnesium sulphate Total	Oxytocin receptor antagonists Events	Oxytocin receptor antagonists Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

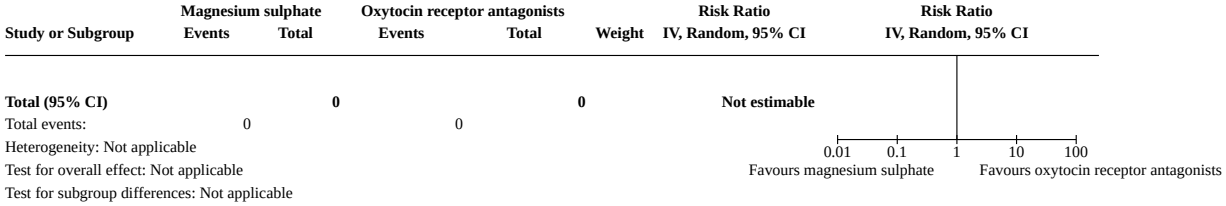
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 24.30. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 30: Gestational age at birth



Analysis 24.31. Comparison 24: Magnesium sulphate vs oxytocin receptor antagonists, Outcome 31: Neonatal infection



Comparison 25. Magnesium sulphate vs combinations of tocolytics

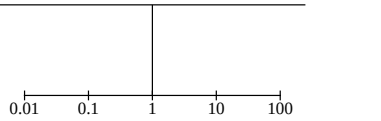
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
25.1 Delay in birth by 48 hours	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.3 Neonatal death before 28 days	1	88	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
25.5 Serious adverse effects of drugs	1	88	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.6 Maternal infection	1	88	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.7 Cessation of treatment due to adverse effects	1	88	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.9 Birth before 32 weeks' gestation	1	88	Risk Ratio (IV, Random, 95% CI)	1.05 [0.07, 16.21]
25.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
25.11 Birth before 37 weeks' gestation	1	86	Risk Ratio (IV, Random, 95% CI)	1.75 [0.55, 5.55]
25.12 Maternal death	1	88	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.13 Pulmonary oedema	1	88	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.24 Neurodevelopmental morbidity	1	88	Risk Ratio (IV, Random, 95% CI)	1.05 [0.07, 16.21]
25.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.26 Respiratory morbidity	1	88	Risk Ratio (IV, Random, 95% CI)	2.09 [0.40, 10.85]
25.27 Mean birthweight	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
25.28 Birthweight < 2000 g	1	88	Risk Ratio (IV, Random, 95% CI)	1.05 [0.07, 16.21]
25.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
25.30 Gestational age at birth	1	88	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.76, 1.56]
25.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 25.1. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

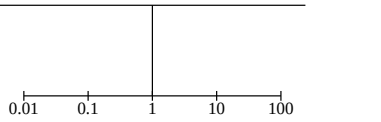
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.2. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

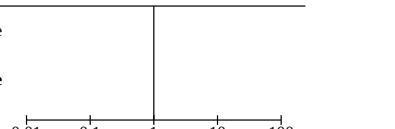
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.3. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	0	43	0	45		Not estimable
Total (95% CI)		**43**		**45**		**Not estimable**
Total events:	0		0			

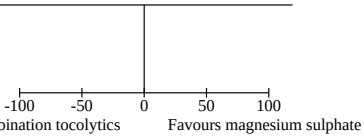
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.4. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Magnesium sulphate Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**

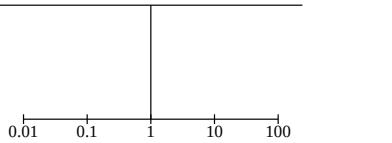
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.5. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	0	43	0	45		Not estimable
Total (95% CI)		**43**		**45**		**Not estimable**
Total events:	0		0			

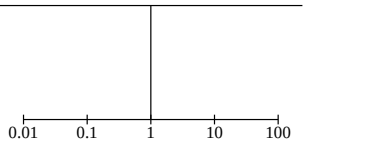
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.6. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 6: Maternal infection

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	0	43	0	45		Not estimable
Total (95% CI)		**43**		**45**		**Not estimable**
Total events:	0		0			

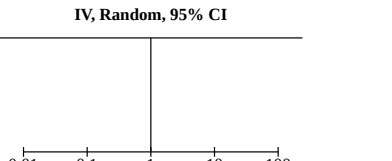
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.7. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	0	43	0	45		Not estimable
Total (95% CI)		**43**		**45**		**Not estimable**
Total events:	0		0			

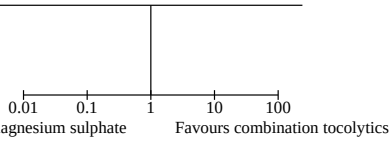
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.8. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

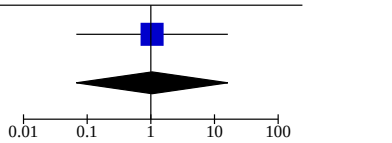
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.9. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	1	43	1	45	100.0%	1.05 [0.07 , 16.21]
Total (95% CI)		**43**		**45**	**100.0%**	**1.05 [0.07 , 16.21]**
Total events:	1		1			

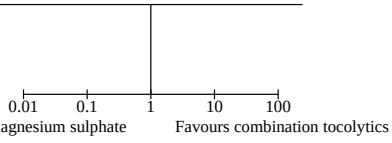
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.97)
Test for subgroup differences: Not applicable



Analysis 25.10. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

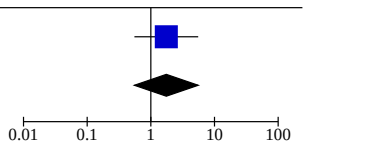
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.11. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	7	43	4	43	100.0%	1.75 [0.55 , 5.55]
Total (95% CI)		**43**		**43**	**100.0%**	**1.75 [0.55 , 5.55]**
Total events:	7		4			

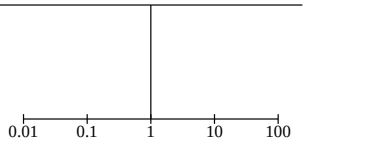
Heterogeneity: Not applicable
Test for overall effect: Z = 0.95 (P = 0.34)
Test for subgroup differences: Not applicable



Analysis 25.12. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 12: Maternal death

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	0	43	0	45		Not estimable
Total (95% CI)		**43**		**45**		**Not estimable**
Total events:	0		0			

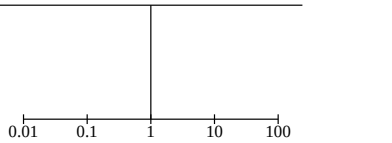
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.13. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 13: Pulmonary oedema

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	0	43	0	45		Not estimable
Total (95% CI)		**43**		**45**		**Not estimable**
Total events:	0		0			

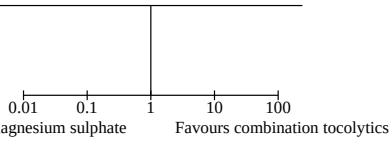
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.14. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 14: Dyspnoea

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

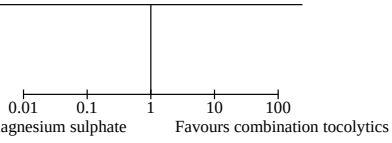
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.15. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 15: Palpitations

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

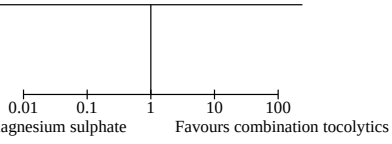
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.16. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 16: Headaches

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

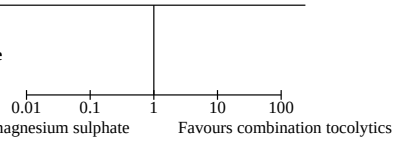
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.17. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 17: Nausea or vomiting

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

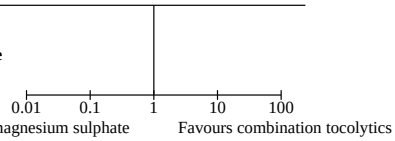
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.18. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 18: Tachycardia

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

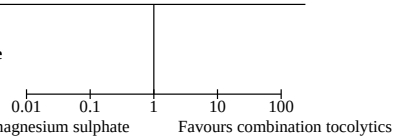
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.19. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

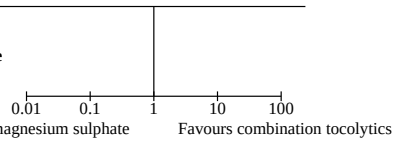
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.20. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 20: Maternal hypotension

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

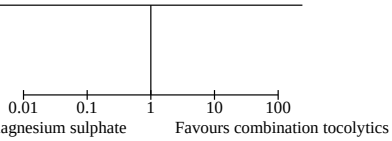
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.21. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 21: Perinatal death

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

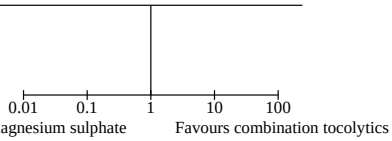
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.22. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 22: Stillbirth

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

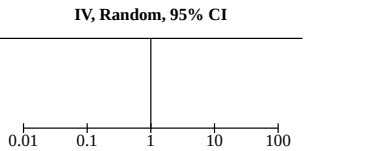
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.23. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

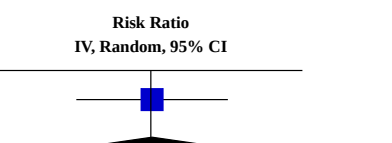
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.24. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	1	43	1	45	100.0%	1.05 [0.07 , 16.21]
Total (95% CI)		**43**		**45**	**100.0%**	**1.05 [0.07 , 16.21]**
Total events:	1		1			

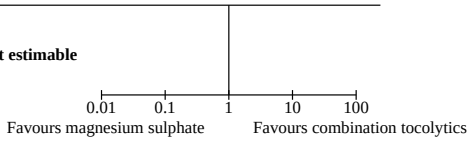
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.97)
Test for subgroup differences: Not applicable



Analysis 25.25. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

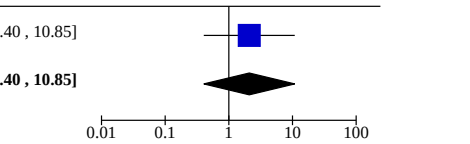
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 25.26. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 26: Respiratory morbidity

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	4	43	2	45	100.0%	2.09 [0.40 , 10.85]
Total (95% CI)		**43**		**45**	**100.0%**	**2.09 [0.40 , 10.85]**
Total events:	4		2			

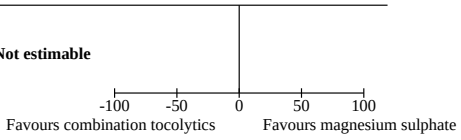
Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)
Test for subgroup differences: Not applicable



Analysis 25.27. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 27: Mean birthweight

Study or Subgroup	Magnesium sulphate Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**

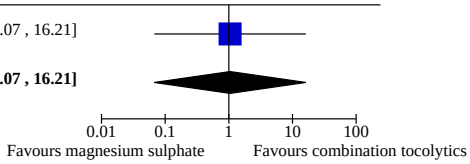
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



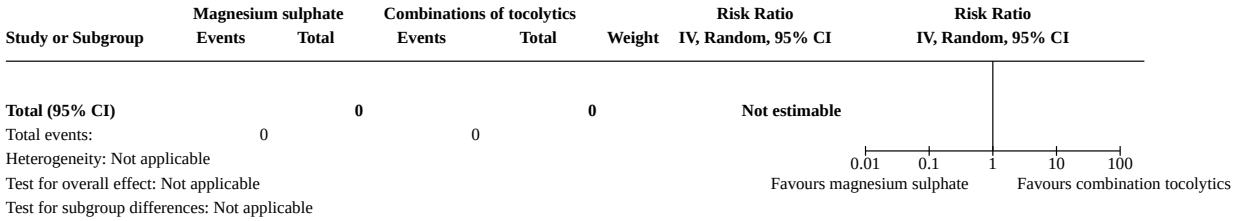
Analysis 25.28. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Magnesium sulphate Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schorr 1998	1	43	1	45	100.0%	1.05 [0.07 , 16.21]
Total (95% CI)		**43**		**45**	**100.0%**	**1.05 [0.07 , 16.21]**
Total events:	1		1			

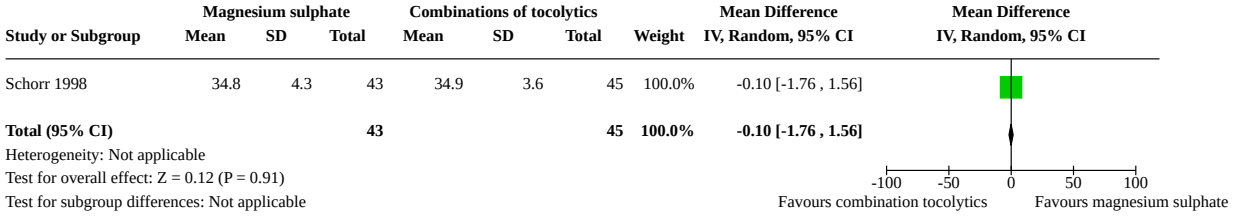
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.97)
Test for subgroup differences: Not applicable



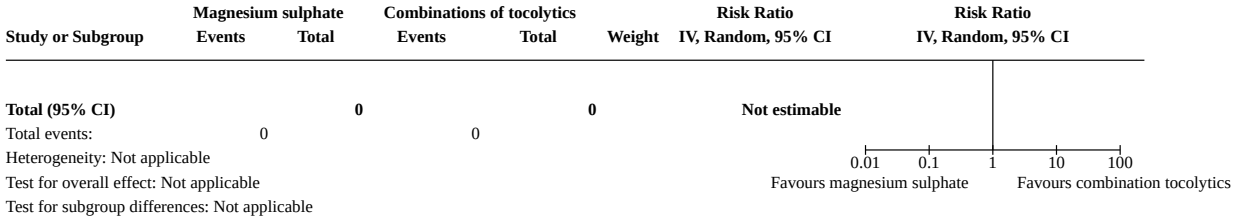
Analysis 25.29. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 29: Birthweight < 2500 g



Analysis 25.30. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 30: Gestational age at birth



Analysis 25.31. Comparison 25: Magnesium sulphate vs combinations of tocolytics, Outcome 31: Neonatal infection



Comparison 26. Nitric oxide donors vs oxytocin receptor antagonists

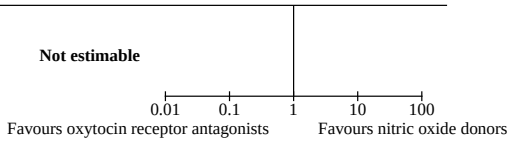
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
26.1 Delay in birth by 48 hours	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
26.5 Serious adverse effects of drugs	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
26.7 Cessation of treatment due to adverse effects	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.16 Headaches	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.17 Nausea or vomiting	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.18 Tachycardia	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.27 Mean birthweight	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
26.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
26.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
26.30 Gestational age at birth	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
26.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

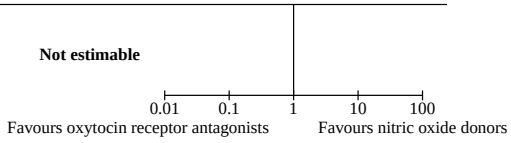
Analysis 26.1. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 1: Delay in birth by 48 hours

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



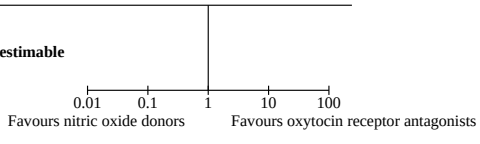
Analysis 26.2. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



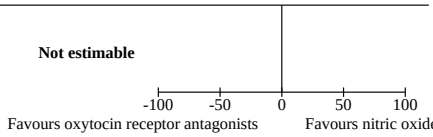
Analysis 26.3. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



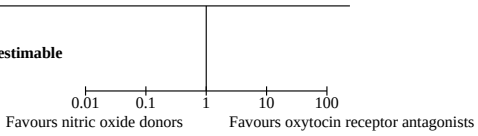
Analysis 26.4. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Nitric oxide donors Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



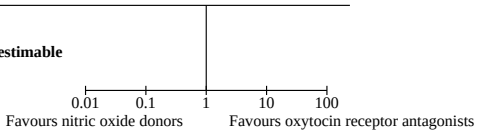
Analysis 26.5. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



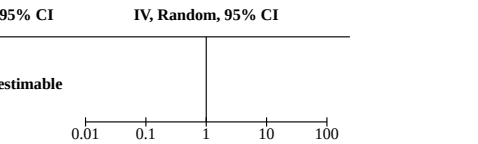
Analysis 26.6. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 6: Maternal infection

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



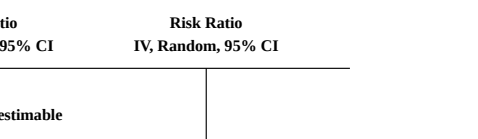
Analysis 26.7. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 26.8. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 8: Birth before 28 weeks' gestation

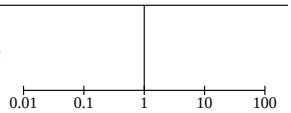
Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 26.9. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

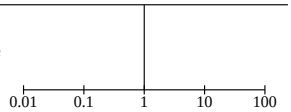
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.10. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.11. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 11: Birth before 37 weeks' gestation

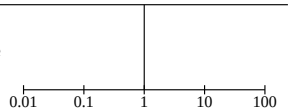
Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 26.12. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 12: Maternal death

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

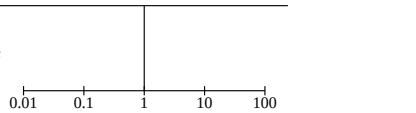
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.13. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 13: Pulmonary oedema

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

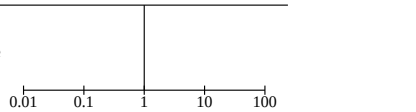
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.14. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 14: Dyspnoea

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

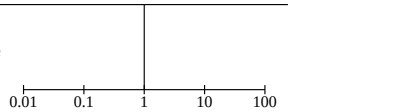
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.15. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 15: Palpitations

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

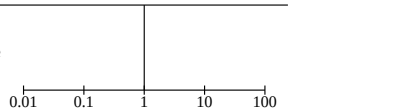
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.16. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 16: Headaches

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

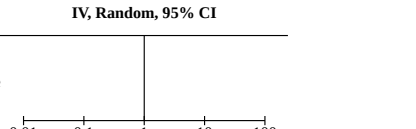
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.17. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 17: Nausea or vomiting

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

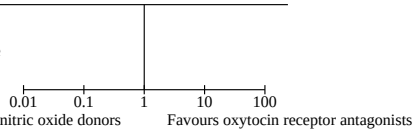
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.18. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 18: Tachycardia

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

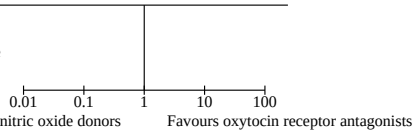
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.19. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

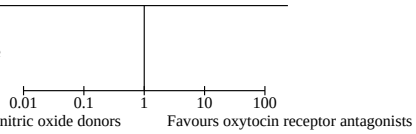
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.20. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 20: Maternal hypotension

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

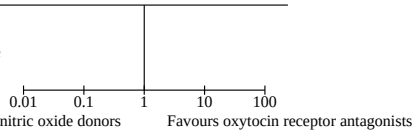
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.21. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 21: Perinatal death

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

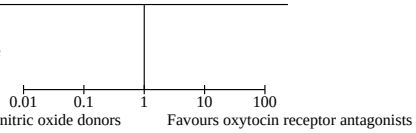
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.22. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 22: Stillbirth

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

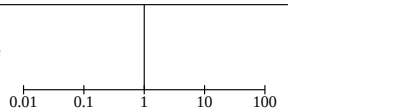
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.23. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

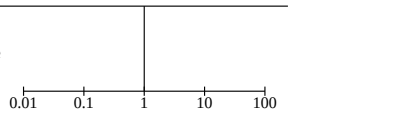
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.24. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

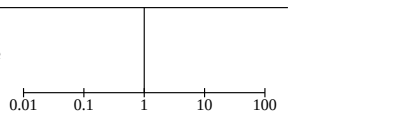
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.25. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

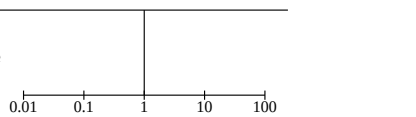
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 26.26. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 26: Respiratory morbidity

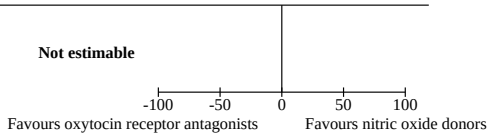
Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



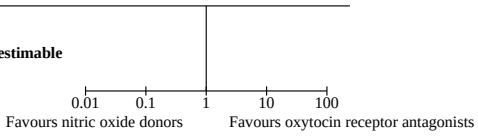
Analysis 26.27. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 27: Mean birthweight

Study or Subgroup	Nitric oxide donors Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



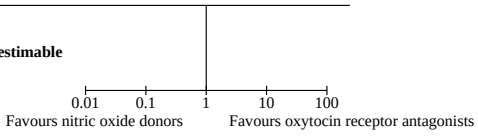
Analysis 26.28. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



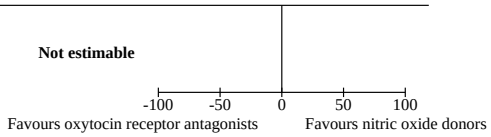
Analysis 26.29. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Nitric oxide donors Events	Total	Oxytocin receptor antagonists Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 26.30. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 30: Gestational age at birth

Study or Subgroup	Nitric oxide donors Mean	SD	Total	Oxytocin receptor antagonists Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



Analysis 26.31. Comparison 26: Nitric oxide donors vs oxytocin receptor antagonists, Outcome 31: Neonatal infection

Comparison 27. Nitric oxide donors vs combinations of tocolytics

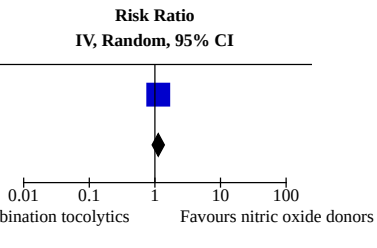
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
27.1 Delay in birth by 48 hours	1	60	Risk Ratio (IV, Random, 95% CI)	1.12 [0.91, 1.39]
27.2 Delay in birth by 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.3 Neonatal death before 28 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.4 Pregnancy prolongation (time from trial entry to birth in days)	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
27.5 Serious adverse effects of drugs	1	50	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.7 Cessation of treatment due to adverse effects	1	50	Risk Ratio (IV, Random, 95% CI)	1.57 [0.32, 7.81]
27.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.13 Pulmonary oedema	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.15 Palpitations	1	50	Risk Ratio (IV, Random, 95% CI)	0.13 [0.04, 0.39]
27.16 Headaches	2	110	Risk Ratio (IV, Random, 95% CI)	4.88 [0.88, 26.94]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
27.17 Nausea or vomiting	1	60	Risk Ratio (IV, Random, 95% CI)	1.50 [0.47, 4.78]
27.18 Tachycardia	1	60	Risk Ratio (IV, Random, 95% CI)	0.05 [0.01, 0.32]
27.19 Maternal cardiac arrhythmias	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.20 Maternal hypotension	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.21 Perinatal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.23 Neonatal death before 7 days	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.24 Neurodevelopmental morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.25 Gastrointestinal morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.26 Respiratory morbidity	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.27 Mean birthweight	1	50	Mean Difference (IV, Random, 95% CI)	399.00 [110.46, 687.54]
27.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
27.30 Gestational age at birth	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
27.31 Neonatal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Analysis 27.1. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 1: Delay in birth by 48 hours

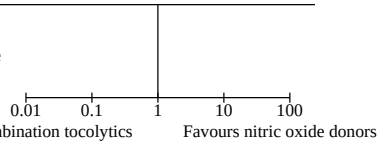
Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
He 2002	27	30	24	30	100.0%	1.13 [0.91 , 1.39]
Total (95% CI)		**30**		**30**	**100.0%**	**1.13 [0.91 , 1.39]**
Total events:	27		24			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.28)
Test for subgroup differences: Not applicable



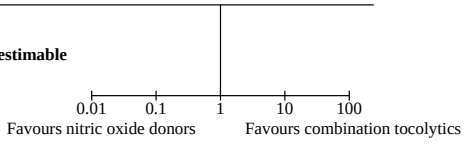
Analysis 27.2. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



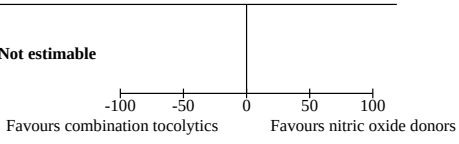
Analysis 27.3. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



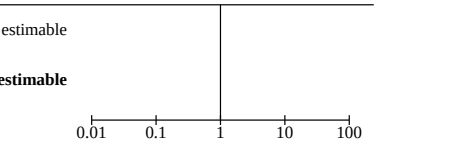
Analysis 27.4. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Nitric oxide donors Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



Analysis 27.5. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 5: Serious adverse effects of drugs

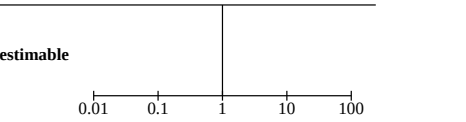
Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schleussner 2003	0	28	0	22		Not estimable
Total (95% CI)		**28**		**22**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



Analysis 27.6. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 6: Maternal infection

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

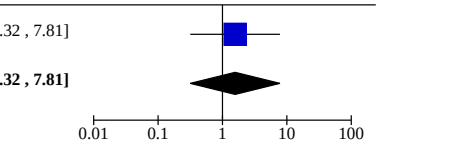
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.7. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schleussner 2003	4	28	2	22	100.0%	1.57 [0.32 , 7.81]
Total (95% CI)		**28**		**22**	**100.0%**	**1.57 [0.32 , 7.81]**
Total events:	4		2			

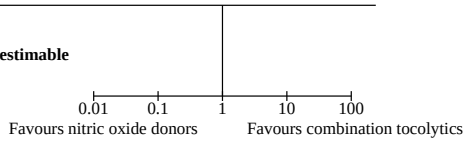
Heterogeneity: Not applicable
Test for overall effect: Z = 0.55 (P = 0.58)
Test for subgroup differences: Not applicable



Analysis 27.8. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 8: Birth before 28 weeks' gestation

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

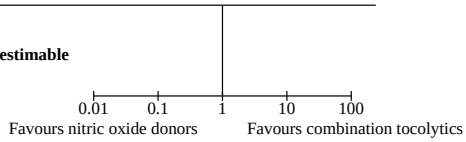
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.9. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

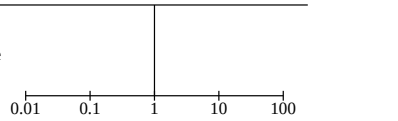
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.10. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

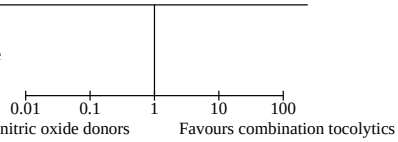
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.11. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

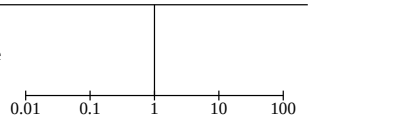
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.12. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 12: Maternal death

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

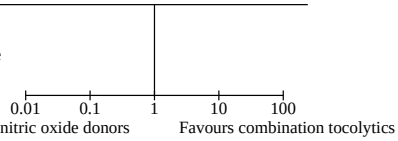
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.13. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 13: Pulmonary oedema

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

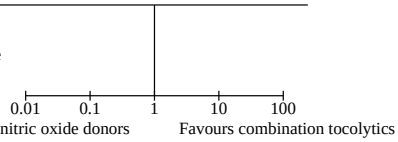
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.14. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 14: Dyspnoea

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

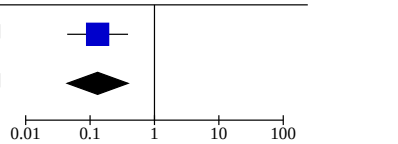
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.15. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 15: Palpitations

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schleussner 2003	3	28	18	22	100.0%	0.13 [0.04 , 0.39]
Total (95% CI)		**28**		**22**	**100.0%**	**0.13 [0.04 , 0.39]**
Total events:	3		18			

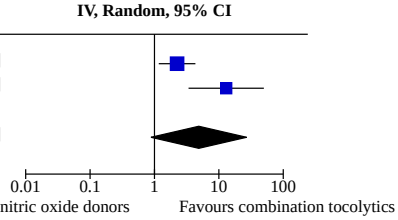
Heterogeneity: Not applicable
Test for overall effect: Z = 3.66 (P = 0.0002)
Test for subgroup differences: Not applicable



Analysis 27.16. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 16: Headaches

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Schleussner 2003	20	28	7	22	55.8%	2.24 [1.17 , 4.32]
Szulc 2000	26	30	2	30	44.2%	13.00 [3.38 , 49.96]
Total (95% CI)		**58**		**52**	**100.0%**	**4.88 [0.88 , 26.94]**
Total events:	46		9			

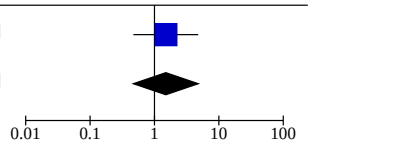
Heterogeneity: Tau² = 1.25; Chi² = 5.29, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 1.82 (P = 0.07)
Test for subgroup differences: Not applicable



Analysis 27.17. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 17: Nausea or vomiting

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Szulc 2000	6	30	4	30	100.0%	1.50 [0.47 , 4.78]
Total (95% CI)		**30**		**30**	**100.0%**	**1.50 [0.47 , 4.78]**
Total events:	6		4			

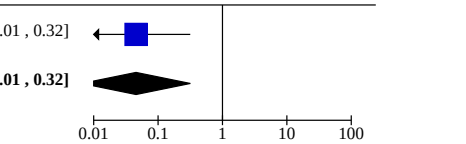
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable



Analysis 27.18. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 18: Tachycardia

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Szulc 2000	1	30	22	30	100.0%	0.05 [0.01 , 0.32]
Total (95% CI)		**30**		**30**	**100.0%**	**0.05 [0.01 , 0.32]**
Total events:	1		22			

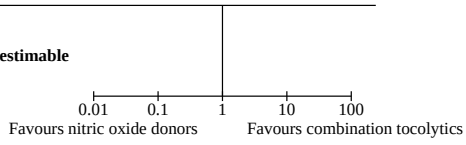
Heterogeneity: Not applicable
Test for overall effect: Z = 3.12 (P = 0.002)
Test for subgroup differences: Not applicable



Analysis 27.19. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

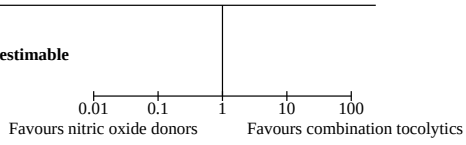
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.20. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 20: Maternal hypotension

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

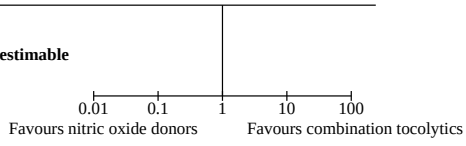
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.21. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 21: Perinatal death

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

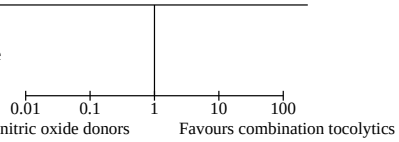
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.22. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 22: Stillbirth

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

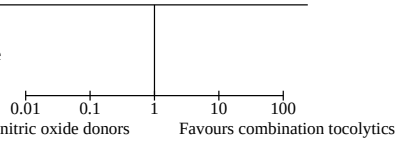
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.23. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

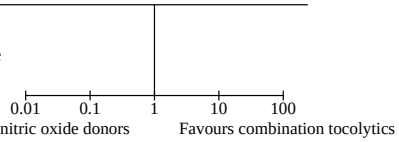
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.24. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

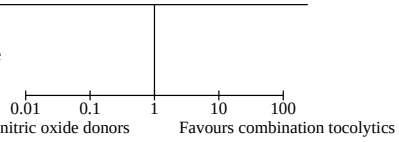
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.25. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**	
Total events:	0		0				

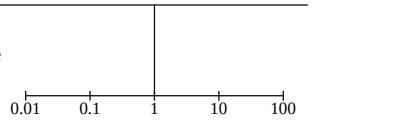
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.26. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 26: Respiratory morbidity

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

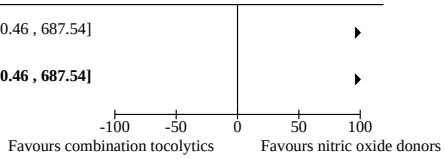
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.27. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 27: Mean birthweight

Study or Subgroup	Nitric oxide donors Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Schleussner 2003	3245	560	28	2846	480	22	100.0%	399.00 [110.46 , 687.54]
Total (95% CI)			**28**			**22**	**100.0%**	**399.00 [110.46 , 687.54]**

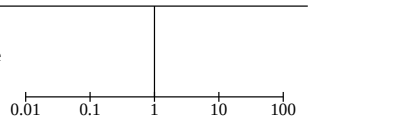
Heterogeneity: Not applicable
Test for overall effect: Z = 2.71 (P = 0.007)
Test for subgroup differences: Not applicable



Analysis 27.28. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

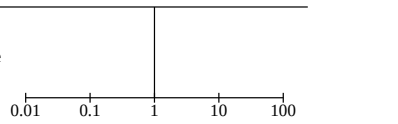
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.29. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Nitric oxide donors Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

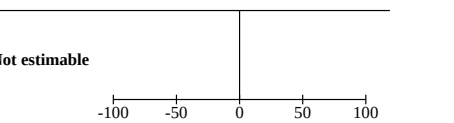
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



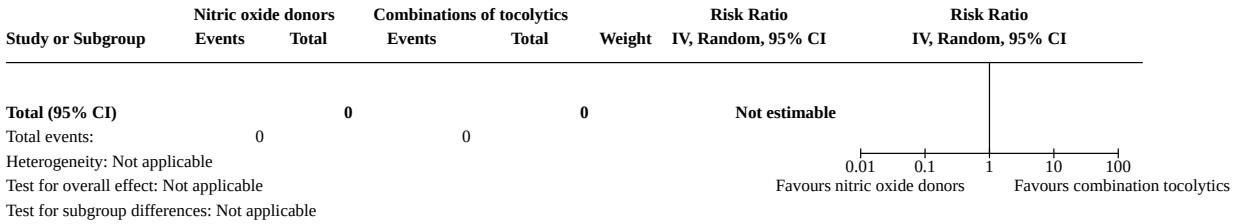
Analysis 27.30. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 30: Gestational age at birth

Study or Subgroup	Nitric oxide donors Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Total (95% CI)			**0**			**0**		**Not estimable**

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 27.31. Comparison 27: Nitric oxide donors vs combinations of tocolytics, Outcome 31: Neonatal infection

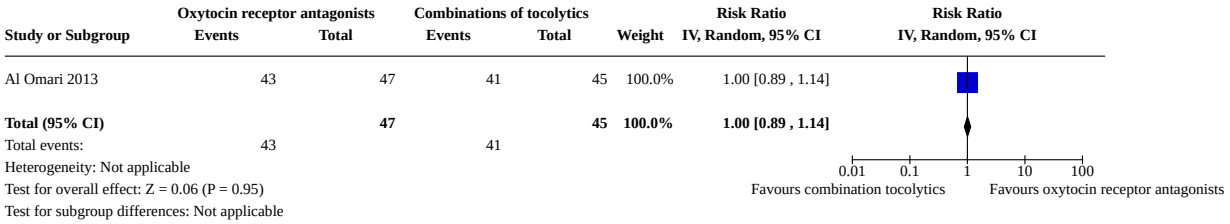


Comparison 28. Oxytocin receptor antagonists vs combinations of tocolytics

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
28.1 Delay in birth by 48 hours	1	92	Risk Ratio (IV, Random, 95% CI)	1.00 [0.89, 1.14]
28.2 Delay in birth by 7 days	1	84	Risk Ratio (IV, Random, 95% CI)	1.03 [0.89, 1.20]
28.3 Neonatal death before 28 days	1	92	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.4 Pregnancy prolongation (time from trial entry to birth in days)	1	92	Mean Difference (IV, Random, 95% CI)	-7.70 [-37.03, 21.63]
28.5 Serious adverse effects of drugs	1	92	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.6 Maternal infection	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.7 Cessation of treatment due to adverse effects	1	92	Risk Ratio (IV, Random, 95% CI)	0.19 [0.01, 3.89]
28.8 Birth before 28 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.9 Birth before 32 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.10 Birth before 34 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.11 Birth before 37 weeks' gestation	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.12 Maternal death	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.13 Pulmonary oedema	1	92	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.14 Dyspnoea	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.15 Palpitations	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
28.16 Headaches	1	92	Risk Ratio (IV, Random, 95% CI)	0.44 [0.18, 1.06]
28.17 Nausea or vomiting	1	92	Risk Ratio (IV, Random, 95% CI)	0.96 [0.14, 6.51]
28.18 Tachycardia	1	92	Risk Ratio (IV, Random, 95% CI)	0.30 [0.14, 0.64]
28.19 Maternal cardiac arrhythmias	1	92	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.20 Maternal hypotension	1	92	Risk Ratio (IV, Random, 95% CI)	0.30 [0.14, 0.64]
28.21 Perinatal death	1	63	Risk Ratio (IV, Random, 95% CI)	1.24 [0.42, 3.64]
28.22 Stillbirth	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.23 Neonatal death before 7 days	1	92	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.24 Neurodevelopmental morbidity	1	92	Risk Ratio (IV, Random, 95% CI)	0.19 [0.01, 3.89]
28.25 Gastrointestinal morbidity	1	92	Risk Ratio (IV, Random, 95% CI)	0.32 [0.01, 7.64]
28.26 Respiratory morbidity	1	92	Risk Ratio (IV, Random, 95% CI)	0.96 [0.44, 2.08]
28.27 Mean birthweight	1	92	Mean Difference (IV, Random, 95% CI)	230.00 [-499.21, 959.21]
28.28 Birthweight < 2000 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.29 Birthweight < 2500 g	0	0	Risk Ratio (IV, Random, 95% CI)	Not estimable
28.30 Gestational age at birth	1	92	Mean Difference (IV, Random, 95% CI)	0.40 [-1.10, 1.90]
28.31 Neonatal infection	1	92	Risk Ratio (IV, Random, 95% CI)	0.48 [0.13, 1.80]

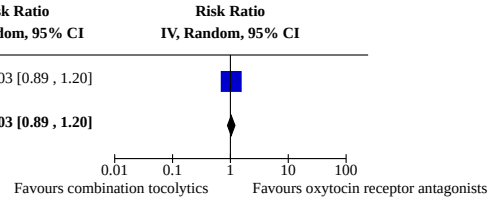
Analysis 28.1. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 1: Delay in birth by 48 hours



Analysis 28.2. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 2: Delay in birth by 7 days

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	39	43	36	41	100.0%	1.03 [0.89 , 1.20]
Total (95% CI)		**43**		**41**	**100.0%**	**1.03 [0.89 , 1.20]**
Total events:	39		36			

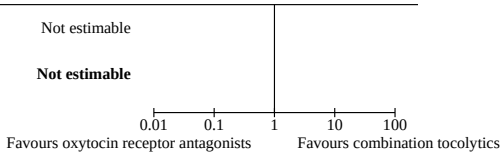
Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)
Test for subgroup differences: Not applicable



Analysis 28.3. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 3: Neonatal death before 28 days

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	0	45		Not estimable
Total (95% CI)		**47**		**45**		**Not estimable**
Total events:	0		0			

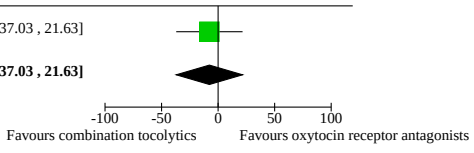
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.4. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 4: Pregnancy prolongation (time from trial entry to birth in days)

Study or Subgroup	Oxytocin receptor antagonists Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Al Omari 2013	42	61.7	47	49.7	80.2	45	100.0%	-7.70 [-37.03 , 21.63]
Total (95% CI)			**47**			**45**	**100.0%**	**-7.70 [-37.03 , 21.63]**

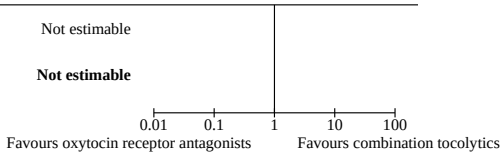
Heterogeneity: Not applicable
Test for overall effect: Z = 0.51 (P = 0.61)
Test for subgroup differences: Not applicable



Analysis 28.5. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 5: Serious adverse effects of drugs

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	0	45		Not estimable
Total (95% CI)		**47**		**45**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.6. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 6: Maternal infection

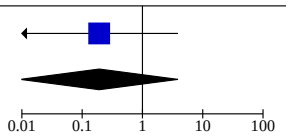
Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 28.7. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 7: Cessation of treatment due to adverse effects

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	2	45	100.0%	0.19 [0.01 , 3.89]
Total (95% CI)		**47**		**45**	**100.0%**	**0.19 [0.01 , 3.89]**
Total events:	0		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 28.8. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 8: Birth before 28 weeks' gestation

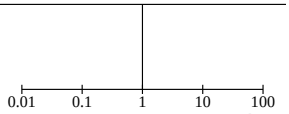
Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Analysis 28.9. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 9: Birth before 32 weeks' gestation

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

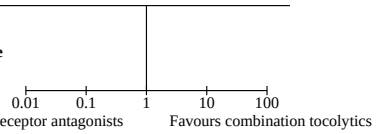
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.10. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 10: Birth before 34 weeks' gestation

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

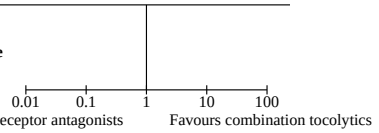
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.11. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 11: Birth before 37 weeks' gestation

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

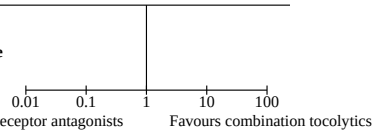
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.12. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 12: Maternal death

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

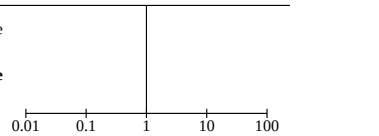
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.13. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 13: Pulmonary oedema

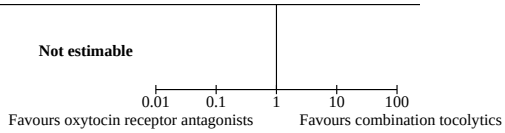
Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	0	45		Not estimable
Total (95% CI)		**47**		**45**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



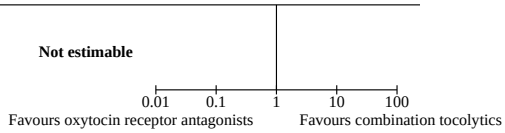
Analysis 28.14. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 14: Dyspnoea

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



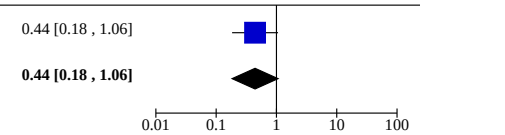
Analysis 28.15. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 15: Palpitations

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



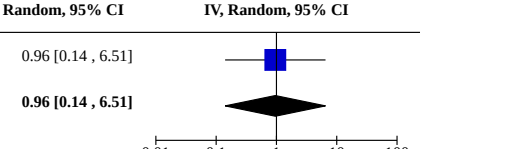
Analysis 28.16. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 16: Headaches

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	6	47	13	45	100.0%	0.44 [0.18 , 1.06]
Total (95% CI)		**47**		**45**	**100.0%**	**0.44 [0.18 , 1.06]**
Total events:	6		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.83 (P = 0.07)						
Test for subgroup differences: Not applicable						



Analysis 28.17. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 17: Nausea or vomiting

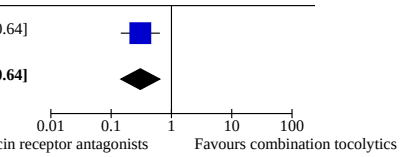
Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	2	47	2	45	100.0%	0.96 [0.14 , 6.51]
Total (95% CI)		**47**		**45**	**100.0%**	**0.96 [0.14 , 6.51]**
Total events:	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.04 (P = 0.96)						
Test for subgroup differences: Not applicable						



Analysis 28.18. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 18: Tachycardia

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	7	47	22	45	100.0%	0.30 [0.14 , 0.64]
Total (95% CI)		**47**		**45**	**100.0%**	**0.30 [0.14 , 0.64]**
Total events:	7		22			

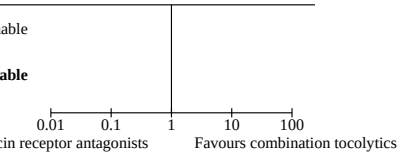
Heterogeneity: Not applicable
Test for overall effect: Z = 3.12 (P = 0.002)
Test for subgroup differences: Not applicable



Analysis 28.19. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 19: Maternal cardiac arrhythmias

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	0	45		Not estimable
Total (95% CI)		**47**		**45**		**Not estimable**
Total events:	0		0			

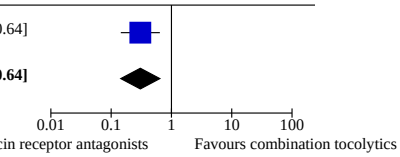
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.20. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 20: Maternal hypotension

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	7	47	22	45	100.0%	0.30 [0.14 , 0.64]
Total (95% CI)		**47**		**45**	**100.0%**	**0.30 [0.14 , 0.64]**
Total events:	7		22			

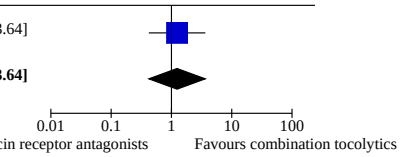
Heterogeneity: Not applicable
Test for overall effect: Z = 3.12 (P = 0.002)
Test for subgroup differences: Not applicable



Analysis 28.21. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 21: Perinatal death

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	6	31	5	32	100.0%	1.24 [0.42 , 3.64]
Total (95% CI)		**31**		**32**	**100.0%**	**1.24 [0.42 , 3.64]**
Total events:	6		5			

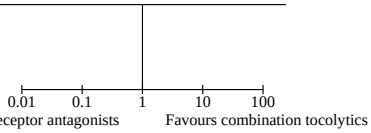
Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.70)
Test for subgroup differences: Not applicable



Analysis 28.22. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 22: Stillbirth

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

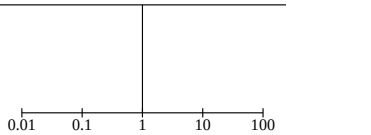
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.23. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 23: Neonatal death before 7 days

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	0	45		Not estimable
Total (95% CI)		**47**		**45**		**Not estimable**
Total events:	0		0			

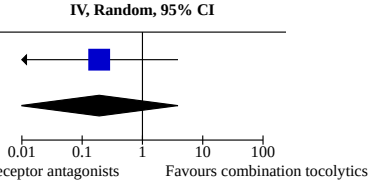
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.24. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 24: Neurodevelopmental morbidity

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	2	45	100.0%	0.19 [0.01 , 3.89]
Total (95% CI)		**47**		**45**	**100.0%**	**0.19 [0.01 , 3.89]**
Total events:	0		2			

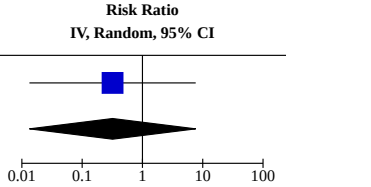
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 28.25. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 25: Gastrointestinal morbidity

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	0	47	1	45	100.0%	0.32 [0.01 , 7.64]
Total (95% CI)		**47**		**45**	**100.0%**	**0.32 [0.01 , 7.64]**
Total events:	0		1			

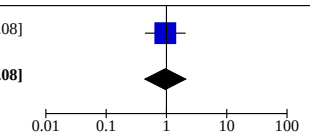
Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.48)
Test for subgroup differences: Not applicable



Analysis 28.26. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 26: Respiratory morbidity

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Al Omari 2013	10	47	10	45	100.0%	0.96 [0.44 , 2.08]
Total (95% CI)		**47**		**45**	**100.0%**	**0.96 [0.44 , 2.08]**
Total events:	10		10			

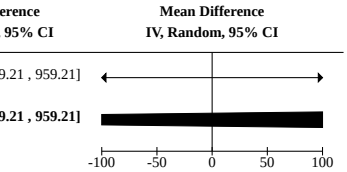
Heterogeneity: Not applicable
Test for overall effect: Z = 0.11 (P = 0.91)
Test for subgroup differences: Not applicable



Analysis 28.27. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 27: Mean birthweight

Study or Subgroup	Oxytocin receptor antagonists Mean	SD	Total	Combinations of tocolytics Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Al Omari 2013	3480	1440	47	3250	2060	45	100.0%	230.00 [-499.21 , 959.21]
Total (95% CI)			**47**			**45**	**100.0%**	**230.00 [-499.21 , 959.21]**

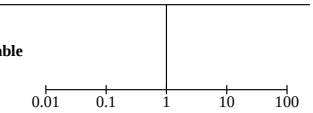
Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.54)
Test for subgroup differences: Not applicable



Analysis 28.28. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 28: Birthweight < 2000 g

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

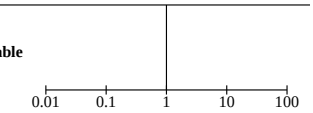
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



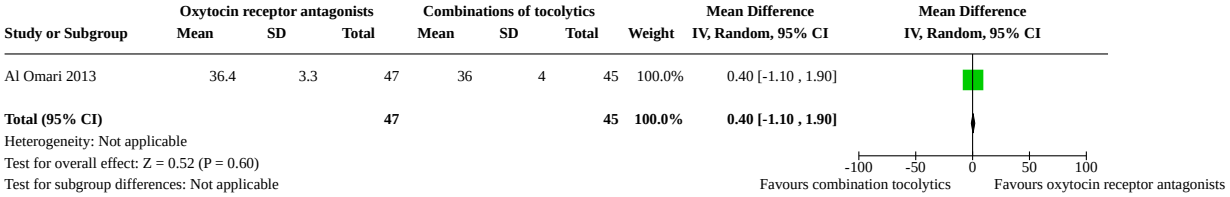
Analysis 28.29. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 29: Birthweight < 2500 g

Study or Subgroup	Oxytocin receptor antagonists Events	Total	Combinations of tocolytics Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events:	0		0			

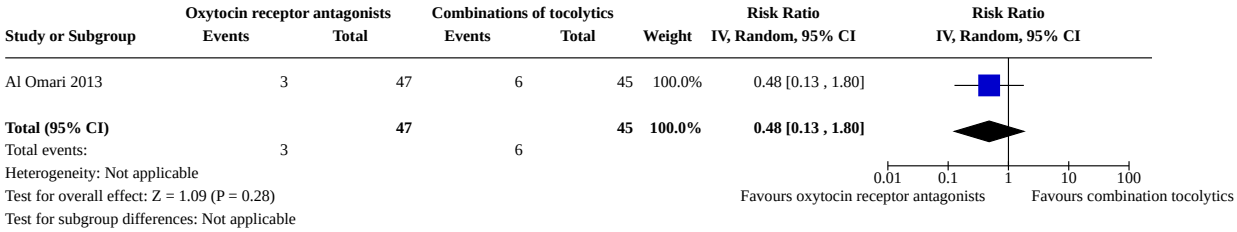
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 28.30. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 30: Gestational age at birth



Analysis 28.31. Comparison 28: Oxytocin receptor antagonists vs combinations of tocolytics, Outcome 31: Neonatal infection



APPENDICES

Appendix 1. Search methods for ClinicalTrials.gov

Advanced search

Interventional studies

Intervention field terms (sleeted from drop-down menu where available)

tocolytic

tocolysis

calcium channel blocker

calcium antagonist

betamimetics

nitricoxide

mononitrate

dinitrate

trinitrate

gtn

nitroglycerin*

oxytocin agonist

nifedipine

nicardipine

fenoterol

salbutamol

sulindac

atosiban

retosiban

isoxuprine

ritodine

hexoprenaline

terbutaline

magnesium sulphate

magnesium sulfate

mgs04

cox

celecoxib

indomethacin

indometacin

ketorolac

Condition field terms (selected from drop down manu where available)

preterm

premature

ruptured membranes

prom

pprom

Appendix 2. Screening eligible studies for scientific integrity/trustworthiness

All studies meeting the inclusion criteria will undergo further independent evaluation by two review authors against the criteria below.

Criteria questions	Assessment		Comments and concerns
	High risk	Low risk	
Research governance			
Was the study prospectively registered (for those studies published after 2010)?			
When requested, did the trial authors refuse to provide/share the protocol and/or ethics approval letter?			

(Continued)

Did the trial authors refuse to engage in communication with the Cochrane Review authors within the agreed timelines?
Did the trial authors refuse to provide individual participant data upon request, with no justifiable reason?
Baseline characteristics
Is there anything about the characteristics of the study participants that appear too similar? (E.g. distribution of the mean (standard deviation (SD)) excessively narrow or excessively wide, as noted by Carlisle 2017)
Feasibility
Is there anything about the study characteristics that, in your opinion, could be implausible? (E.g. large numbers of women with a rare condition (such as severe cholestasis in pregnancy) recruited within 12 months).
Results
Is there anything about the reported results of the study that could be implausible? (E.g. massive risk reduction for the main study outcomes with a small sample size?)
Do you have any concerns about the methods of randomisation such as unexpectedly even numbers of women 'randomised' including a mismatch between the numbers and the methods? (E.g. if the authors say 'no blocking was used' but still end up with equal numbers, or if the authors say they used 'blocks of 4' but the final numbers differ by 6.)
Are there (close to) zero losses to follow up without plausible explanation?
For abstracts only
Have the study authors confirmed in writing that the data to be included in the review have come from the final analysis and will not change?

Assessment after applying trustworthiness criteria high risk (awaiting classification) OR low risk (include)

Decision after attempting to contact authors high risk (awaiting classification) OR low risk (include)

Appendix 3. Summary of findings for secondary outcomes

https://www.birmingham.ac.uk/tocolytics-preterm-birth see trial documentation

HISTORY

Protocol first published: Issue 4, 2021

CONTRIBUTIONS OF AUTHORS

Ioannis D Gallos (IDG) and Olufemi T Oladapo (OTO) conceived the idea for this review. IDG, Amie Wilson (AW), Victoria A Hodgetts-Morton (VAH), Ella Marson (EM), Alexandra Markland (AM), Eva Larkai (EL), and Argyro Papadopoulou and Rachel K Morris (RKM) designed and

conducted the review. Malcolm J Price (MJP) provided statistical advice and input. Doris Chou (DC), Arri Coomarasamy (AC), RKM and OTO reviewed the manuscript and provided critical feedback. IDG is the guarantor for this review.

DECLARATIONS OF INTEREST

This project was supported by the National Institute for Health Research, via ESP Incentive Award Scheme funding to Cochrane Pregnancy and Childbirth (award number NIHR150766).

Ioannis D Gallos: The World Health Organization provided payment to Ioannis Gallos for working on this review. Ioannis is a health professional at Birmingham Women's Hosptital. Ioannis is an Associate Editor for Cochrane Pregnancy and Childbirth, but had no involvement in the editorial processing of this review. Ioannis was also awarded an NIHR ESP incentive award for completion of this review (NIHR150766).

Amie Wilson: works as a Midwife at Birmingham Women's and Children's Hospital Foundation Trusth, and has no declarations of interest.

Victoria A Hodgetts-Morton: works as a NIHR clinical lecturer in O&G at the University of Birmingham and Birmingham Women's Hospital. Victoria reports personally receiving funds from Hologic, LLC as an Independent Contractor.

Ella Marson: has no declarations of interest.

Alexandra Markland: has no declarations of interest.

Eva Larkai: has no declarations of interest.

Argyro Papadopoulou: is currently a PhD student at the University of Birmingham, UK. Her tuition fees are paid by Tommy's charity, Tommy's National Centre for Miscarriage Research. Tuition fees are directly paid to the University of Birmingham. Argyro works as a Resident at Alexandra University Hosptial, Athens, Greece.

Arri Coomarasamy: has no declarations of interest.

Aurelio Tobias: has no declarations of interest.

Doris Chou: in terms of guideline and recommendation synthesis, I manage the maternal/perinatal living guideline process within the World Health Organization. The technical group may consider this review in deliberations related to the use of tocolytics. During these meetings, I do not carry any voting capacity.

Olufemi T Oladapo: is an Editor with Cochrane Pregnancy and Childbirth, but had no involvement with the editorial processing of this review.

Malcolm J Price: has no declarations of interest.

Katie Morris: has acted as an Independent Contractor for the British Maternal and Fetal Medicine Society, NHS England, Royal College of Obstetricians and Gynaecologists and Tommy's Baby Charity and did not receive funds personally for this work. Kate has also acted as an Independent Contractor for Surepulse and received consultant fees personally for this work. Her institution received funds for a National Institute for Health Research grant, which she held. Kate has published several invited reviews and book chapters related to preterm birth and works as a Consultant in Maternal Fetal Medicine at Birmingham Womens and Childrens Hospital NHS Foundation Trust.

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Internal sources

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Due to the limited detail reported in the trial characteristics we were unable to perform the prespecified subgroup analyses for the following.

1. Gestational age at trial entry (less than 32/40 completed weeks versus 32/40 completed weeks or more)
2. Status of amniotic membranes (women with ruptured membranes versus women with intact membranes)
3. Number of fetuses (singleton versus multiple pregnancy)

In addition to the prespecified subgroup analysis conducted according to the duration of tocolysis use (suppression alone versus suppression plus long-term maintenance), we also conducted a post-hoc subgroup analysis according to the use of rescue tocolysis (when the first tocolytic fails and an additional tocolytic is given).

We conducted all prespecified sensitivity analysis stated in the protocol. For the primary outcomes, these included the following.

1. Risk of bias (restricted to studies with low risk of bias only): studies were ranked as 'low risk of bias' if they were double-blinded and had allocation concealment with little loss to follow-up (less than 10%). We considered protocol publication in advance of the results to be an unsuitable criterion for sensitivity analyses, because protocol publication only became widespread in recent years.
2. Co-intervention (we removed trials where participants received co-interventions such as progesterone)
3. Choice of relative effect measure (risk ratio versus odds ratio)
4. Use of fixed-effect versus random-effects model
5. Randomisation unit (cluster versus individual)

We assessed differences by evaluating the relative effects and assessment of model fit. There were no cluster-randomised trials included to allow us to perform a sensitivity analysis based on randomisation unit. Other planned sensitivity analyses were performed but no differences were detected in terms of the overall results.

In addition to the prespecified sensitivity analysis, we also carried out a post-hoc sensitivity analysis by removing trials published before 1990.

INDEX TERMS

Medical Subject Headings (MeSH)

Adrenergic beta-Agonists; Birth Weight; Calcium Channel Blockers [therapeutic use]; Headache; Magnesium Sulfate [therapeutic use]; Network Meta-Analysis; Nitric Oxide Donors [therapeutic use]; *Premature Birth [prevention & control]; Randomized Controlled Trials as Topic; Receptors, Oxytocin; *Tocolytic Agents [adverse effects] [therapeutic use]; Vomiting [drug therapy]

MeSH check words

Child; Female; Humans; Infant, Newborn; Pregnancy