

Effects of race and ethnicity on perinatal outcomes in high-income and upper-middle-income countries

IPPIC Collaborative Network

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Effects of race and ethnicity on perinatal outcomes in high-income and upper-middle-income countries: an individual participant data meta-analysis of 2 198 655 pregnancies

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Summary

Background Existing evidence on the effects of race and ethnicity on pregnancy outcomes is restricted to individual studies done within specific countries and health systems. We aimed to assess the impact of race and ethnicity on perinatal outcomes in high-income and upper-middle-income countries, and to ascertain whether the magnitude of disparities, if any, varied across geographical regions.

Methods For this individual participant data (IPD) meta-analysis we used data from the International Prediction of Pregnancy Complications (IPPIC) Network of studies on pregnancy complications; the full dataset comprised 94 studies, 53 countries, and 4 539 640 pregnancies. We included studies that reported perinatal outcomes (neonatal death, stillbirth, preterm birth, and small-for-gestational-age babies) in at least two racial or ethnic groups (White, Black, south Asian, Hispanic, or other). For our two-step random-effects IPD meta-analysis, we did multiple imputations for confounder variables (maternal age, BMI, parity, and level of maternal education) selected with a directed acyclic graph. The primary outcomes were neonatal mortality and stillbirth. Secondary outcomes were preterm birth and a small-for-gestational-age baby. We estimated the association of race and ethnicity with perinatal outcomes using a multivariate logistic regression model and reported this association with odds ratios (ORs) and 95% CIs. We also did a subgroup analysis of studies by geographical region.

Findings 51 studies from 20 high-income and upper-middle-income countries, comprising 2 198 655 pregnancies, were eligible for inclusion in this IPD meta-analysis. Neonatal death was twice as likely in babies born to Black women than in babies born to White women (OR 2·00, 95% CI 1·44–2·78), as was stillbirth (2·16, 1·46–3·19), and babies born to Black women were at increased risk of preterm birth (1·65, 1·46–1·88) and being small for gestational age (1·39, 1·13–1·72). Babies of women categorised as Hispanic had a three-times increased risk of neonatal death (OR 3·34, 95% CI 2·77–4·02) than did those born to White women, and those born to south Asian women were at increased risk of preterm birth (OR 1·26, 95% CI 1·07–1·48) and being small for gestational age (1·61, 1·32–1·95). The effects of race and ethnicity on preterm birth and small-for-gestational-age babies did not vary across regions.

Interpretation Globally, among underserved groups, babies born to Black women had consistently poorer perinatal outcomes than White women after adjusting for maternal characteristics, although the risks varied for other groups. The effects of race and ethnicity on adverse perinatal outcomes did not vary by region.

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Introduction

Inequalities and inequities faced by pregnant women contribute to the differential rates of adverse perinatal outcomes.^{1–3} In countries with multiethnic populations, the variations in perinatal outcomes between different racial and ethnic groups reflect the underlying health inequalities in maternity care.⁴ This difference has an impact on the health of future generations in the short and long term.⁵

To date, studies documenting racial and ethnic inequality and poor maternal and offspring outcomes have focused on specific groups of women,⁶ or had a country-specific focus.^{7,8} This makes it challenging to investigate the degree of inequality and inequities faced

globally by women from various underserved and under-represented racial and ethnic groups. The disparities in pregnancy outcomes are particularly stark in high-income and upper-middle-income countries, where the overall quality of health care is high and mortality rates are low. In the UK, the *Mothers and Babies: Reducing Risk through Audits and Confidence Enquiries across the UK* report on confidential enquiries showed that the rates of neonatal death and stillbirth in babies of Black and Asian women are double those of White women.¹⁹ Similar trends are seen in the USA, with high rates of preterm birth and low birthweight in babies of Black women compared to babies of White women.¹⁰

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See [Online](#) for appendix

Research in context

Evidence before this study

Individual studies done in countries with multiethnic populations suggest associations between underserved racial and ethnic backgrounds and adverse perinatal outcomes. Studies reporting the effects of race and ethnicity on adverse perinatal outcomes generally do not isolate the causal effect of race and ethnicity by adjusting for other factors such as socioeconomic background and health conditions. We did a MEDLINE search with no language restrictions from database inception to Jan 31, 2022, for systematic reviews on race and ethnicity and adverse perinatal outcomes, using the search terms “ethnicity” OR “race” AND “neonatal mortality” OR “stillbirth” OR “preterm” OR “SGA” OR “small for gestation”. Two systematic reviews analysing the relationship between race and ethnicity and preterm birth reported increased risks of preterm birth in Black women (odds ratio 1.5–2.0) compared to non-Black and White women, mostly from studies done in the USA. To the best of our knowledge, no study has so far provided a global overview of the effect of race and ethnicity on neonatal deaths, stillbirth, preterm birth, and small-for-gestational-age babies, and whether this effect varies by region.

Added value of this study

In this meta-analysis we provided a global outlook of the magnitude of the association between race and ethnicity and adverse perinatal outcomes across high-income and

upper-middle-income countries. Our individual participant data meta-analysis of more than two million pregnancies from multiple cohorts worldwide showed that Black women are at higher risk of adverse perinatal outcomes of neonatal death, stillbirth, preterm birth, and small-for-gestational-age babies than White women, even after adjusting for maternal characteristics. These racial disparities in perinatal outcomes are consistently observed across all geographical regions. Our study is, to the best of our knowledge, the first to assess the effect of race and ethnicity on perinatal outcomes across high-income and upper-middle-income countries.

Implications of all the available evidence

The disparities and inequalities in pregnancy outcomes observed in women from underserved and under-represented racial and ethnic groups across geographical regions highlight the need for a global approach to this problem. We require a holistic approach that complements multifaceted antenatal interventions, with a life course approach tackling race-related and ethnicity-related barriers faced by girls and young women, particularly Black women, who are the most affected. Race and ethnicity data, and relevant confounders (eg, maternal education), should be routinely collected in detail alongside qualitative evaluations, to identify the magnitude of the risks faced by women in various racial and ethnic subgroups and plan appropriate interventions for those with the highest need.

Research into the causal relationship of race and ethnicity with adverse health outcomes is challenging, particularly when considering regression models investigating the effects of race and ethnicity. Consideration of causal pathways and the relationship between variables is crucial to isolate the causal effect of race and ethnicity, a social construct present before the index pregnancy, on perinatal outcomes by controlling for other confounding variables.¹¹ This approach of using a causal pathway when investigating perinatal outcomes challenges the certainty of the degree of influence a woman's underlying socioeconomic background and health status, and the health-care system, has on her clinical outcome, compared to the inequalities related to race and ethnicity.

We aimed to quantify the effects of race and ethnicity in women from underserved groups in high-income and upper-middle-income countries on neonatal deaths and stillbirths primarily, and on preterm births and small-for-gestational-age babies secondarily, after adjusting for confounders in the causal pathway. We also aimed to determine the variations in the effects of race and ethnicity on offspring outcomes across studies from various geographical regions.

Methods

Search strategy and selection criteria

Our individual participant data (IPD) meta-analysis was based on a prospectively registered protocol,¹² and we

reported our findings in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses of Individual Participant Data (PRISMA-IPD) statement (appendix pp 1–3).¹³

Eligible studies were identified from the International Prediction of Pregnancy Complications (IPPIC) IPD Network without any language restrictions (figure 1).^{14,15} The studies in the network were identified by searching major databases such as MEDLINE, Embase, Cochrane (Wiley) CENTRAL, Science Citation Index (Web of Science), CINAHL (EBSCO), the ISRCTN Registry, UK Clinical Trials Gateway, WHO International Clinical Trials Portal, and ClinicalTrials.gov, specialist abstract and conference proceeding resources (British Library's ZETOC and Web of Science Conference Proceedings Citation Index) for outcomes such as pre-eclampsia, fetal growth restriction, and birthweight (from database inception to August, 2019). Details of the search, identification, inclusion of studies, and IPD harmonisation for the IPPIC database are provided elsewhere.^{15,16} The IPPIC dataset (comprising 53 countries, 94 studies, and 4539640 pregnancies) contains IPD from observational studies and cohorts nested within randomised studies reporting various maternal and perinatal outcomes.¹⁶ Studies obtained data on race and ethnicity through various methods, including self-reporting by the woman, routine data collected in medical records, or as recorded by the research team with prespecified definitions.

We included IPD on singleton pregnancies in the IPPIC dataset providing data on adverse perinatal outcomes (neonatal death, stillbirth, preterm birth, and small-for-gestational-age babies) in at least two racial and ethnic groups. We included only studies from high-income and upper-middle-income countries, as per the World Bank classification.¹⁷ Although race and ethnicity can be defined separately, they are overlapping concepts and are often used interchangeably.¹⁸ Therefore, throughout the Article, we use the terms race and ethnicity in line with current recommendations,¹⁹ acknowledging that these are social constructs. In the IPPIC dataset, we harmonised the various definitions used to define the race and ethnicity of participants as White, Black, south Asian, Hispanic, and other groups (including those of multiracial, multiethnic, and east Asian origin). Black women comprised those of African origin, including African American and African Caribbean women; the south Asian group comprised women from the Indian subcontinent; and the Hispanic group comprised women in the USA of Spanish-speaking or Latin American descent or heritage. We categorised all women of Hispanic identity, irrespective of their racial identity (White Hispanic, Black Hispanic, Asian Hispanic, and other Hispanic) as a single group.^{19,20} We considered Black, south Asian, Hispanic, and other populations to be underserved as reflected in the disparities and inequalities in health outcomes.¹⁹

We extracted data on women's characteristics such as age in years, parity (ie, nulliparous or multiparous), the highest level of maternal education attained (primary, secondary, or tertiary education), BMI, pre-existing or new-onset diabetes or hypertension, renal disease, autoimmune disease, and previous obstetric history of stillbirth or preterm birth. The primary outcomes were neonatal mortality (first 28 days of life)²¹ and stillbirth (≥ 20 weeks' gestation).²² Secondary outcomes were preterm birth (< 37 weeks' gestation)²³ and small-for-gestational-age baby (birthweight < 10 th centile).²⁴

Two independent reviewers (JS and TK) assessed the methodological quality of the included studies by use of the Newcastle Ottawa Scale for selection, comparability, and outcome ascertainment bias.²⁵ Studies were considered to have a low risk of bias if they achieved four stars for selection, two for comparability, and three for ascertainment of the outcome. Studies achieving two or three stars for selection, one for comparability, and two for outcome ascertainment, were considered to have a medium risk of bias. When studies achieved one star for selection or outcome ascertainment, or zero stars for any of the three categories, this was regarded as a high risk of bias. The summary risk of bias for the study was determined by the total number of stars, where seven to nine stars was considered low risk, four to six was considered medium risk, and less than four stars meant the study was regarded as having a high risk of bias.

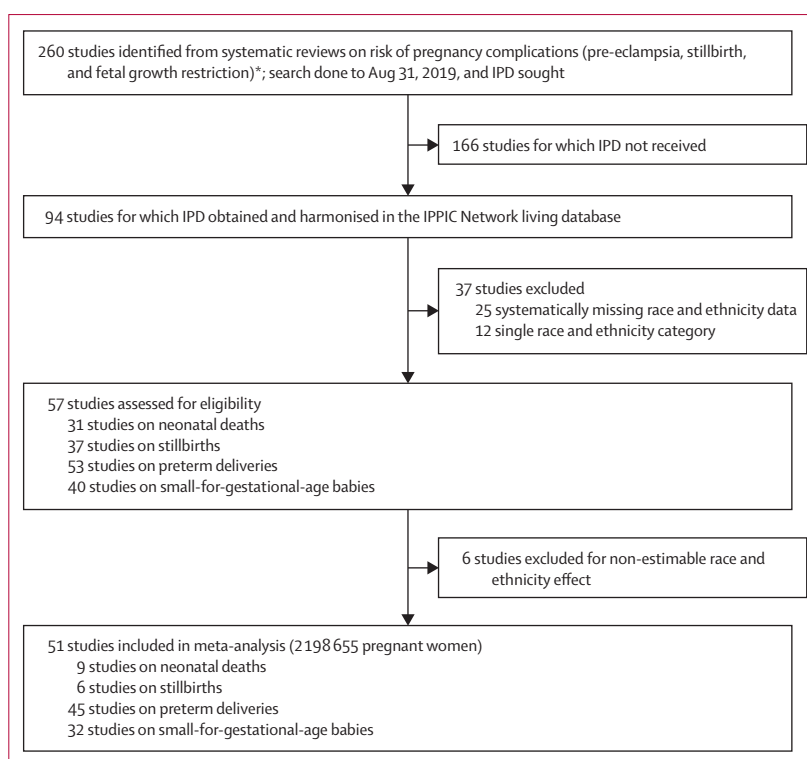


Figure 1: Study selection

IPD=individual participant data. IPPIC=International Prediction of Pregnancy Complications. *Townsend et al,¹⁴ Allotey et al,¹⁵ and Allotey et al (unpublished).

Data analysis

We did a two-step random-effects IPD meta-analysis. First, we did multiple imputations assuming a missing-at-random mechanism, and chained equations were used to generate 100 imputed datafiles for each cohort. Linear regression models were used for imputing continuous variables, logistic regression for binary variables, and multinomial logistic regression (or predictive mean matching in the presence of convergence issues) for categorical variables. We used outcome data in the imputation models to impute missing data on confounders.²⁶ However, when estimating the effects of race and ethnicity, we did not consider the imputed outcomes.²⁷ We did not impute when the values were completely missing or when more than 50% were missing.

We estimated the effects of race and ethnicity on perinatal outcomes by comparing pregnant women from underserved groups with White women in each individual cohort by fitting a multivariate logistic regression model in each imputed dataset. We assessed collinearity by estimating the variance inflation factor for all models.²⁸ Our proposed causal diagram and the assumptions are shown in the directed acyclic graph (figure 2).²⁹ We considered the exposure to be race and ethnicity, and that it affects the main outcomes of stillbirth and neonatal death through the causal pathway either directly, or is mediated through gestational age at

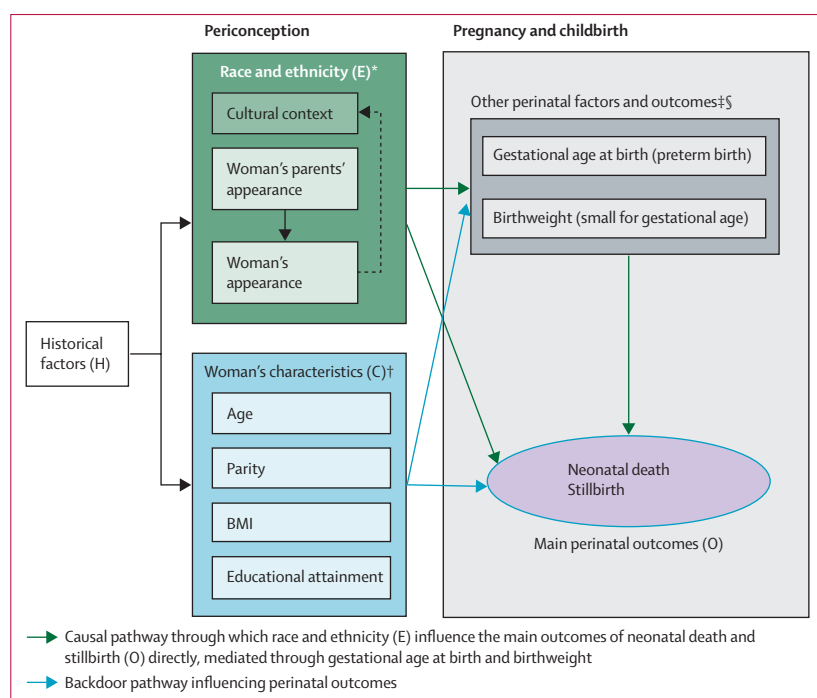


Figure 2: Causal diagram of race and ethnicity, and perinatal outcomes

The effects of race and ethnicity are considered to be the combined effects of the woman's appearance (phenotype including skin colour), her parents' appearance, and cultural context. The dashed line represents the potential influence of cultural context by the woman's appearance. Historical factors (H) include socioeconomic status of the family and neighbourhood at the time of the woman's conception. *Exposure. †Confounding is through a woman's characteristics such as age, parity, BMI, and educational attainment present at the time of her conception, which share a common history (H) with race and ethnicity (E); maternal educational attainment is a proxy for socioeconomic status. ‡Mediator is an intermediate variable between exposure (E) and outcome (O). §Collider is causally influenced by two or more variables.

birth and birthweight, which are proxies for the perinatal outcomes of preterm birth and a small-for-gestational-age baby. We also assumed that the woman's characteristics such as age, BMI, parity, and highest educational attainment that are present at the time of conception of her baby are related to complex historical factors (eg, family and neighbourhood socioeconomic status) present at the time of her own conception and birth.¹¹ As historical factors also have an influence on race-related and ethnicity-related factors, we used the woman's characteristics as confounding into the analysis to block the backdoor pathway from historical factors to perinatal outcomes. Since a woman's characteristics can also influence birthweight and gestational age at delivery (colliders), we refrained from adjusting for birthweight and gestational age in the analyses.³⁰ The effect of race and ethnicity was averaged over the imputed datasets by use of Rubin's rules within each cohort.³¹

In the second step, we used a random-effects model to pool the averaged effects estimated in the cohorts using the method of DerSimonian and Laird,³² with the estimate of heterogeneity being taken from the Mantel-Haenszel model. Odds ratios (ORs) with 95% CIs were selected as the effect measure, with White women

used as the reference group. This process was repeated to obtain unadjusted (crude) estimations of the effects of race and ethnicity to check the impact of adjustments on the overall estimation of race and ethnicity effect.

We did subgroup analyses where appropriate by geographical region on the effects of race and ethnicity on perinatal outcomes. We classified regions as the USA and Canada; the UK; northern, western, and southern Europe (including France, Germany, Greece, Italy, Netherlands, Norway, and Spain) based on the UN geoscheme,³³ and other regions (including Australia, Brazil, and multi-country studies). We evaluated the robustness of our assumptions about missingness through several sensitivity analyses where we imputed the main exposure variable (race and ethnicity) under extreme scenarios of all missing cases being White women, then Black women, and so on. Sensitivity analyses were done by limiting the analysis to high-risk women, defined as those with risk factors such as previous stillbirth, previous preterm birth, pre-existing or new-onset diabetes or hypertension, maternal age older than 40 years, or obesity (BMI ≥ 30 kg/m²). Sensitivity analyses were also done to assess the impact of the imputation strategies by restricting the analysis to complete cases, and the impact of the study period on the observed effects of race and ethnicity through meta regression by year of recruitment (midpoint of recruitment period). Further sensitivity analysis were done by excluding one study that recruited women between 1959 and 1965,³⁴ and by excluding one multi-country study that involved women from low-income and middle-income countries.³⁵ All analyses were done with Stata (version 17).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, writing of the manuscript, or the decision to submit the manuscript for publication.

Results

94 studies in the IPPIC IPD Network's database reported race and ethnicity, and adverse pregnancy outcomes. Of these, 51 provided the relevant IPD for 2 198 655 pregnant women from 20 high-income and upper-middle-income countries (figure 1; appendix p 4).

Of the 51 studies,^{34–84} 42 were observational studies (35 prospective^{34–45,47,48,50–54,56–61,63–66,70–75} and seven retrospective cohorts^{46,49,55,62,67–69}), including six birth registries^{48,63,73} and birth cohorts,^{41,60,61} and nine were cohorts nested within randomised controlled trials^{77–85} (appendix pp 5–20). Most studies were from the UK (13 studies),^{43,53,59–61,64,73,74,77,78,80,81,83} followed by the USA (nine studies),^{34,39,44,48,49,50,67,76,79} the Netherlands (six studies),^{41,54,55,69,70,75} and Canada (four studies).^{38,58,66,68} Regions were represented as follows: 17 studies were from northern, western and southern Europe; 13 were from the USA and Canada; 13 were from the UK; and eight were from other regions. 11 (22%) of the

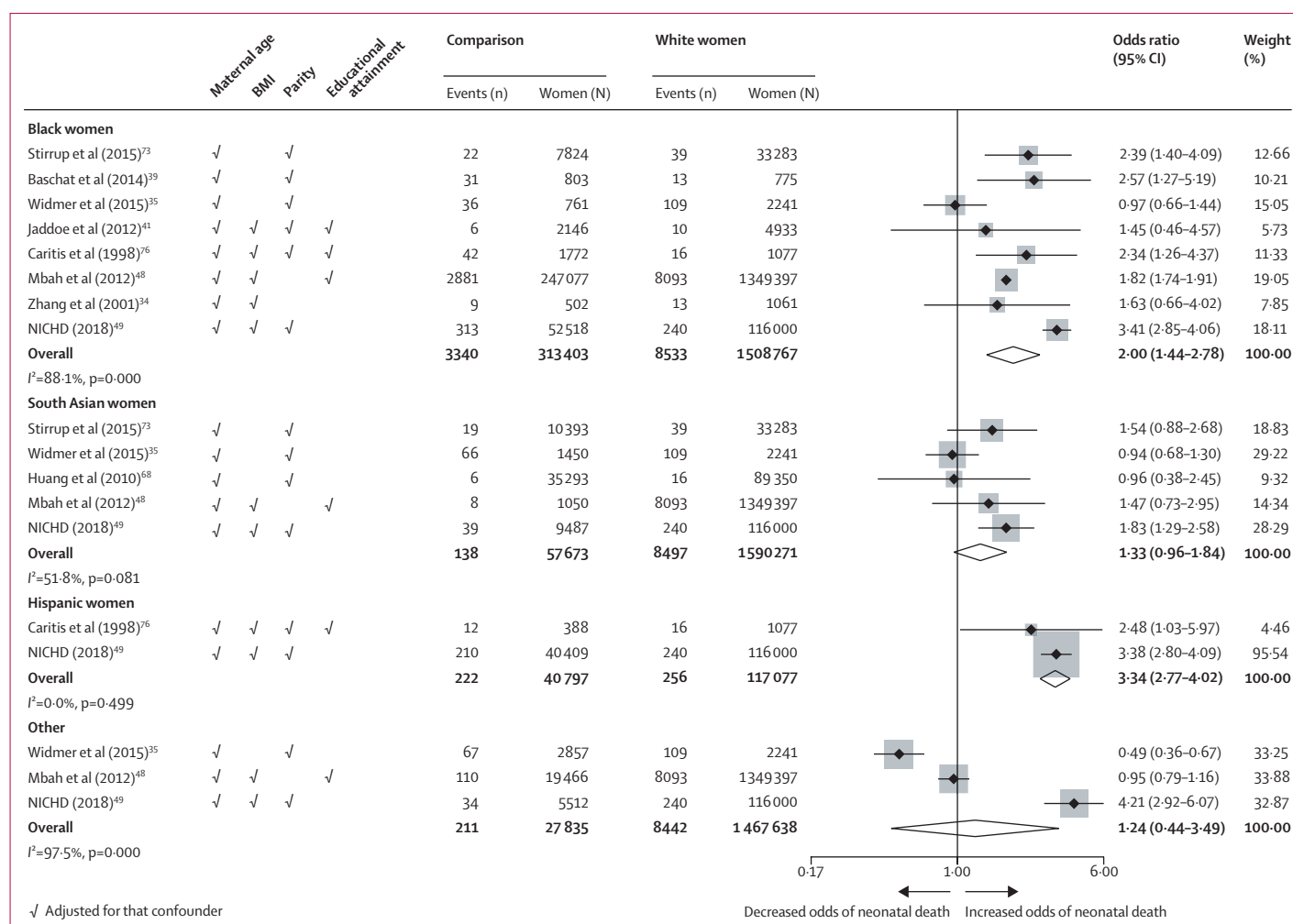


Figure 3: Effect of race and ethnicity on the risk of neonatal deaths

Weights are from random-effects analyses. Other category includes multiracial, multiethnic, east Asian women. White women were used as the reference for all comparisons. NICHD=Eunice Kennedy Shriver National Institute of Child Health and Human Development.

51 studies included only high-risk women, eight (16%) only included low-risk women, and the rest had mixed risk groups or did not specify. 20 (39%) of 51 studies provided perinatal outcomes between five racial and ethnic groups (White, Black, south Asian, Hispanic, and other), 25 (49%) studies included four racial and ethnic groups (White, Black, south Asian, and other), five (10%) studies^{34,42,51,65,72} included three groups, and one (2%) study⁶² allowed comparison of perinatal outcomes between two racial and ethnic groups. Six datasets^{42,48,51,70,79,84} provided data for more than 50% of the four confounders (maternal age, parity, BMI, and maternal educational attainment), 23 studies^{36,37,42,44-46,48-53,56-58,60,63,64,71,72,78,80,83} provided data on three confounders, 19 studies^{34,35,38-40,54,55,59,61,62,65,68,69,73-75,77,81,82} provided data on two confounders, and three studies^{67,66,67} provided data on one confounder. Neonatal deaths were reported in nine studies (from 2051844 pregnancies)^{34,35,39,41,48,49,68,73,76} and stillbirths were reported in six studies (from 380017 pregnancies)^{44,49,61,67,68,76} studies.

All comparative cohort studies evaluated with the Newcastle Ottawa Scale assessing the outcome of neonatal death had an overall low risk of bias (appendix pp 21-22). All studies had a low risk of bias for study selection and a medium risk of bias for comparability of cohorts. Six of nine studies had a low risk of bias for outcome assessment of the cohorts and three had a medium risk of bias. When assessing stillbirth, five of six studies had an overall low risk of bias, and one study had a medium risk of bias (appendix pp 21-22). All studies had a low risk of bias for study selection and a medium risk of bias for comparability of cohorts. Three studies had a low risk of bias for outcome assessment of the cohorts, two had a medium risk of bias, and one had a high risk of bias.

Nine studies provided IPD on race and ethnicity and neonatal deaths (12468 neonatal deaths, 2051844 pregnancies; 12 countries).^{34,35,39,41,48,49,68,73,76} Compared with White women, a higher risk of neonatal

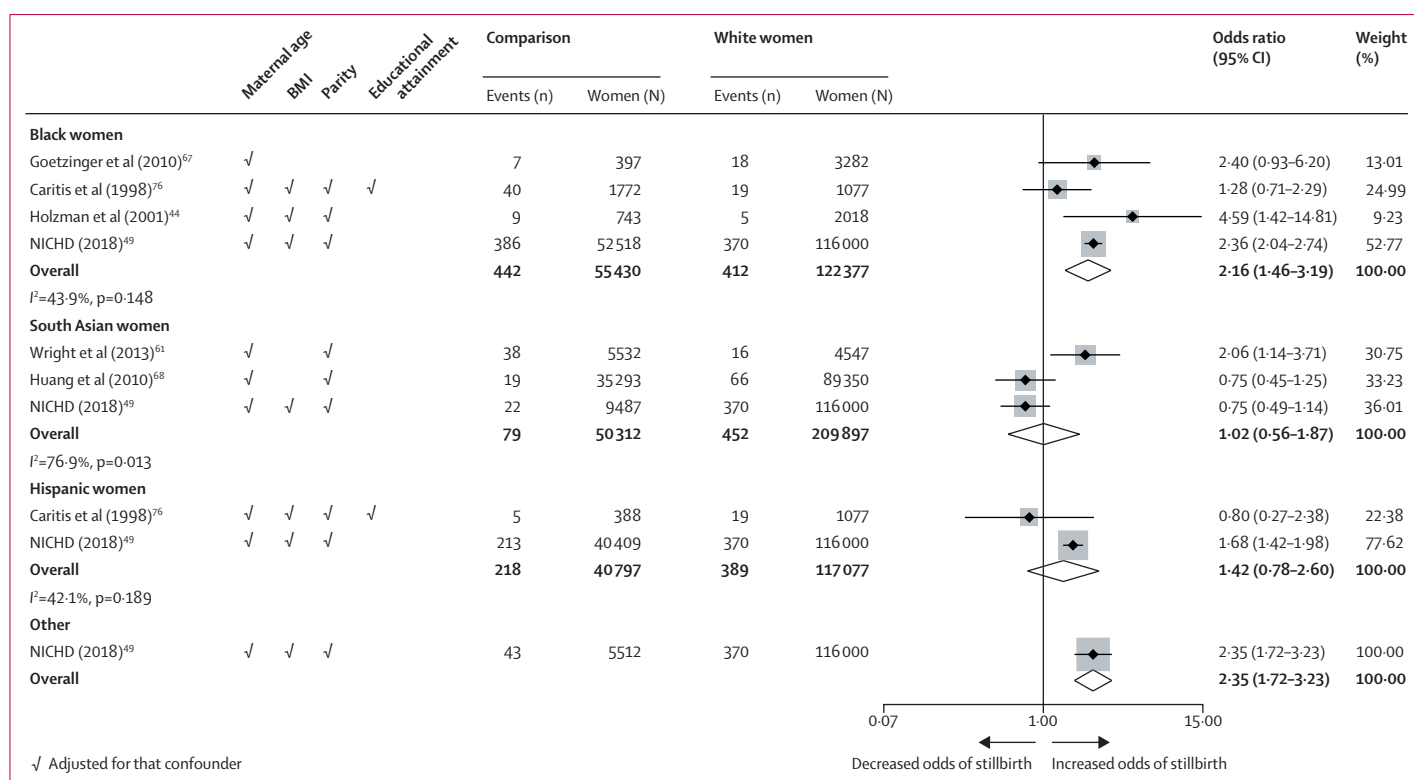


Figure 4: Effect of race and ethnicity on the risk of stillbirths

Weights are from random-effects analyses. Other category includes multiracial, multiethnic, east Asian women. White women were used as the reference for all comparisons. NICHD=Eunice Kennedy Shriver National Institute of Child Health and Human Development.

death was seen in Black women (OR 2.00, 95% CI 1.44–2.78) and Hispanic women (3.34, 2.77–4.02; figure 3). No differences were observed for south Asian women, when compared to White women, for neonatal death (OR 1.33, 95% CI 0.96–1.84).

Six studies provided IPD on race and ethnicity and stillbirths (1292 stillbirths, 380 017 pregnancies; three countries).^{44,49,61,67,68,76} The odds of stillbirth were two times higher in Black women (OR 2.16; 95% CI 1.46–3.19) and in other racial and ethnic groups (2.35, 1.72–3.23) when compared with White women (figure 4). No differences were observed in the odds of stillbirth in south Asian (OR 1.02, 95% CI 0.56–1.87) or Hispanic women (1.42, 0.78–2.60) when compared with White women. Subgroup analysis of neonatal death and stillbirth by geographical region was not possible because of the small number of studies.

45 studies provided IPD on race and ethnicity, and preterm birth (241 817 preterm births, 2 048 987 pregnancies; 21 countries).^{34–53,55–60,63–67,69,71–76,78–84} Compared with White women, a higher risk of preterm birth was seen in Black women (OR 1.65, 95% CI 1.46–1.88) and south Asian women (1.26, 1.07–1.48; appendix pp 23–25). 32 studies provided IPD on race and ethnicity and small for gestational age (266 302 small-for-gestational-age babies, 1 915 004 pregnancies; 19 countries).^{36–58,61,70,75–79} A higher risk of small-for-gestational-age babies was seen in

Black women (OR 1.39, 95% CI 1.13–1.72) and south Asian women (1.61, 1.32–1.95), when compared to White women (appendix pp 26–28). Subgroup analyses did not show significant variations in the effects of race and ethnicity on preterm births and small-for-gestational-age babies between regions (figures 5,6). Babies born to Black women were more likely to be preterm than those born to White women in the USA and Canada (OR 1.74, 95% CI 1.49–2.03), the UK (1.68, 1.23–2.31), and northern, western and southern Europe (OR 1.89, 95% CI 1.36–2.62) without any subgroup effect ($p=0.41$; figure 5A). The risks of preterm birth were high for south Asian women versus White women, with no variations between regions ($p=0.30$; figure 5B). The odds of small-for-gestational-age babies were increased for Black and south Asian women versus White women across regions, with no difference in the risk estimates between regions ($p=0.27$ for Black women and $p=0.66$ for south Asian women; figure 6).

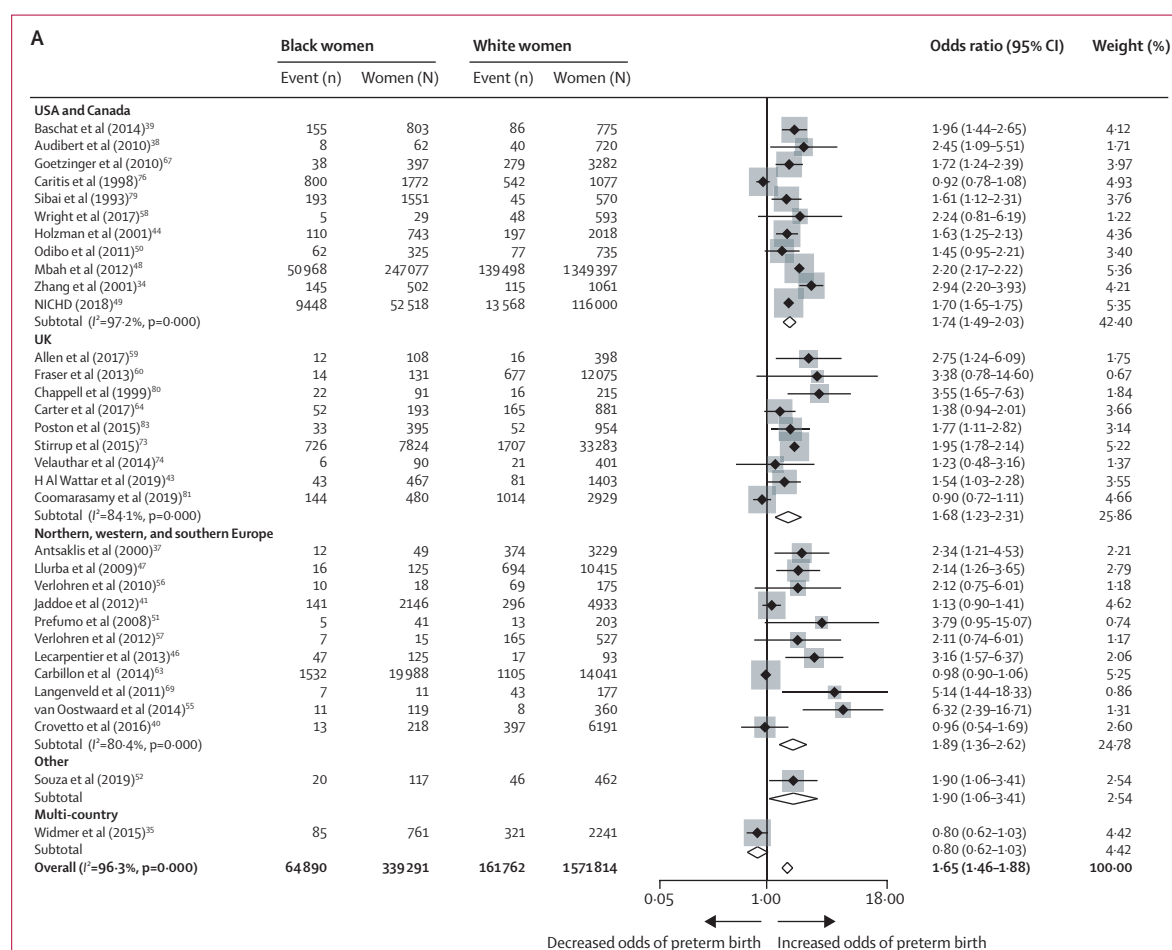
Sensitivity analyses for the various assumptions of missingness used to impute data were consistent with the main findings for the association between race and ethnicity and perinatal outcomes (appendix pp 29–30). We did not find any collinearity issues among the covariates in the models, with the variance inflation factor below 5 (ranging between 1.00 and 2.12) in all models. Findings were similar when the analyses were limited to high-risk

pregnancies for all outcomes, except for increased odds of neonatal death in south Asian women versus White women (OR 1.85, 95% CI 1.05–3.26) and stillbirths in Hispanic versus White women (1.91, 1.45–2.51; appendix pp 31–34). The increased risk of small-for-gestational-age babies observed in south Asian versus White women was no longer present. Sensitivity analyses for complete cases (data not shown), by time of recruitment (appendix p 35), and after exclusion of one study³⁴ that was an outlier for recruitment period (1959–65; appendix p 36) showed findings similar to the main analysis for the outcomes. When one multi-country study that included women from low-income and middle-income countries was excluded,³⁵ the findings were similar to the main analysis for all outcomes, except for the risk of neonatal death, which became significant for south Asian versus White women (OR 1.62, 95% CI 1.25–2.10; appendix p 36).

Discussion

In high-income and middle-income countries, women from underserved and under-represented racial and

ethnic groups are at increased risk of adverse perinatal outcomes. Black women are consistently at higher risk of all complications such as neonatal death, stillbirth, preterm birth, and small-for-gestational-age babies than White women. The effect varied for other racial and ethnic groups. Adverse outcomes such as preterm birth and small-for-gestational-age babies were higher in Black and south Asian women than in White women irrespective of the geographical region, and over time. Our work highlights the magnitude of disparities facing pregnant women from underserved racial and ethnic backgrounds irrespective of geographical region, emphasising the need for a broad global outlook to tackle these problems. To the best of our knowledge, our IPD meta-analysis is the largest and most comprehensive assessment to date of the magnitude of the association between race and ethnicity and adverse perinatal outcomes across high-income and upper-middle-income countries. Our work was based on a prospectively registered protocol with predefined aims and objectives. The harmonised IPPIC IPD data from multi-country cohorts provided us with a large sample size, facilitating



(Figure 5 continues on next page)

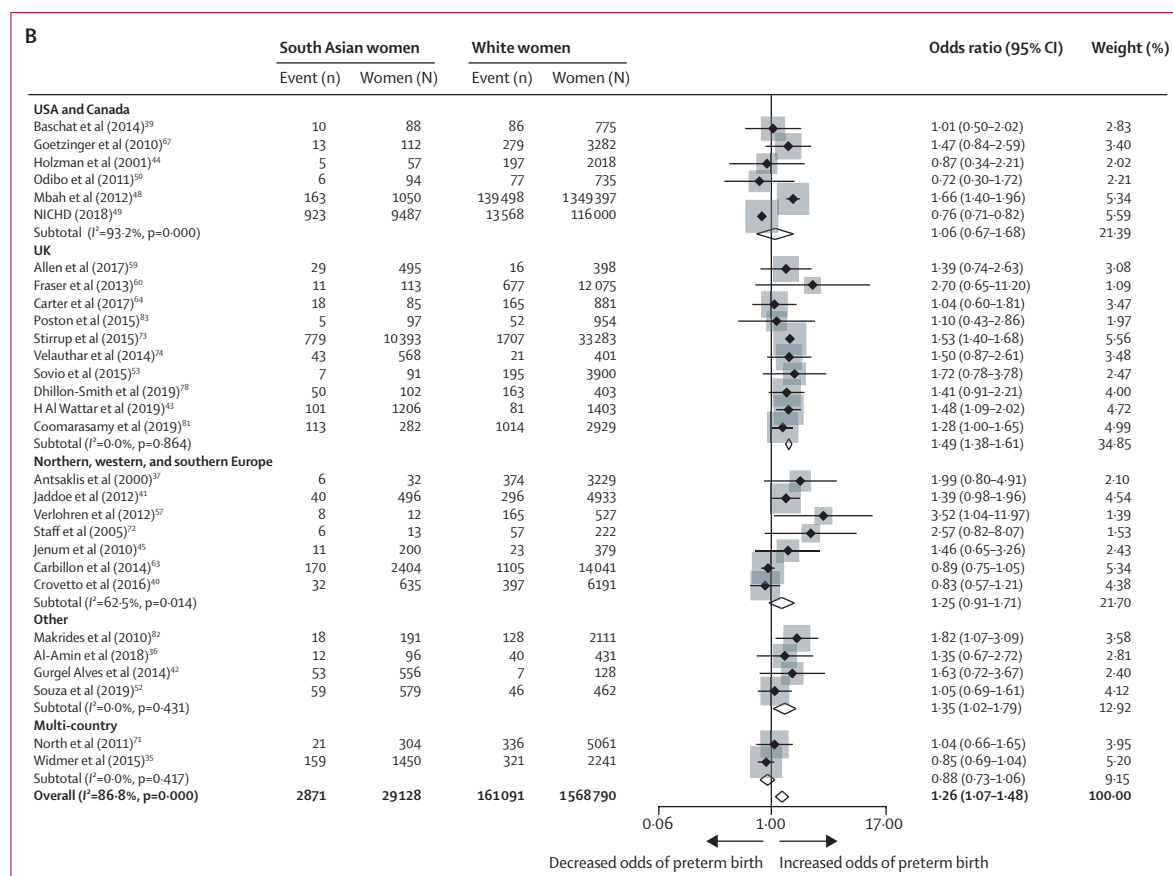


Figure 5: Subgroup analysis of the effect of race and ethnicity on the risk of preterm births by region

Weights are from random-effects analysis. Adjusted for maternal age, BMI, parity, and maternal educational attainment. Other category includes studies from Australia and Brazil. (A) Effects of race and ethnicity on preterm births for Black women. Subgroup effect: $p=0.408$. (B) Effects of race and ethnicity on preterm births for south Asian women. Subgroup effect: $p=0.296$. White women were the reference group in all comparisons. NICHD=Eunice Kennedy Shriver National Institute of Child Health and Human Development.

high precision in the findings and increasing the generalisability of these results. We used multiple imputations to deal with missing variables, thereby avoiding the loss of useful information.

We considered race and ethnicity to be social constructs without biological meaning and reported these terms in line with current recommendations to minimise bias.¹⁹ We used the terms race and ethnicity as a lens through which to study the disparities in pregnancy outcomes in women from underserved and under-represented groups because of differential treatment and access to health care. We considered the effects of race and ethnicity to include the effects of a woman's appearance (phenotype including skin colour) that influences how she is perceived by others, and also the understanding of her appearance affecting her identity and behaviour, her parents' appearances, and the cultural context.¹¹ Given the different ways in which women of African origin might self-identify their origin, and the varied reporting of these women, we categorised the grouping as Black for the purpose of our analysis, as recommended by current guidance.¹⁹ Our subgroup analysis assessed the variations

in outcome disparities in Black women by geographical region. The term Asian is broad and includes numerous countries of origin (eg, Bangladesh, China, India, Indonesia, Japan, and Pakistan). Given the significant differences between the various Asian ethnic groups in terms of rates of diabetes, hypertension, and other adverse outcomes, instead of pooling in one category, we reported them separately as south Asians and east Asians.⁸⁵ Because of the small sample size of east Asians in the IPPIC dataset, we included them in the "other" group for the purpose of analysis. We classified all women of Hispanic identity under the underserved and under-represented race and ethnic category, including those who might identify as White Hispanic. We did so on the basis of how women might be perceived by others, which can affect their experiences and expose them to inequalities in care. In a survey, Hispanic adults said that they are described by most people as Hispanic rather than White.²⁰ In our study, we considered White women to be the reference group through the lens of societal context, irrespective of their majority or minority status,¹⁸ where White experience is one of privilege and power across

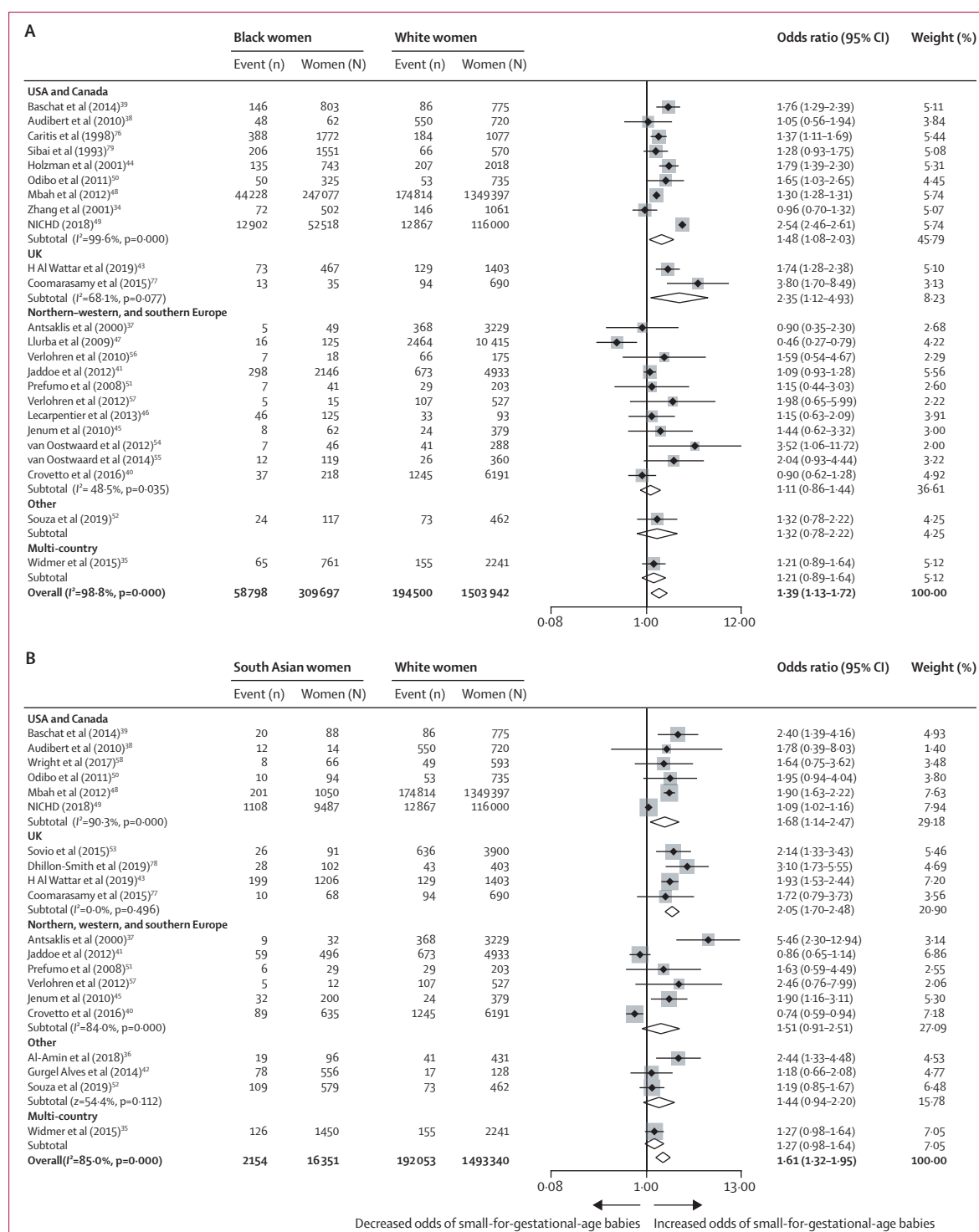


Figure 6: Subgroup analysis of the effect of race and ethnicity on the risk of small-for-gestational-age babies by region

Weights are from random-effects analysis. Adjusted for maternal age, BMI, parity, and maternal educational attainment. Other category includes studies from Australia and Brazil. (A) Effects of race and ethnicity on small-for-gestational-age babies for Black women. Subgroup effect: $p=0.267$. (B) Effects of race and ethnicity on small-for-gestational-age babies for south Asian women. Subgroup effect: $p=0.661$. White women were the reference group in all comparisons. NICHD= Eunice Kennedy Shriver National Institute of Child Health and Human Development.

regions and settings⁸⁶ and White women are expected to have optimal outcomes compared with other groups.

Confounding variables adjusted for in our analysis were identified *a priori* by use of a directed acyclic graph, and unlike previous studies in this area^{87–90} we refrained from the unnecessary adjustment of gestational age and birthweight due to their collider status.^{30,91} By adjusting for the highest educational level attained as a measure of socioeconomic status, we avoided overadjusting for other factors along the pathway.⁹² Since the highest educational attainment achieved by an individual is usually reached in early adulthood and is the main marker for upward mobility,⁹³ we consider it to be a key marker of social status such as income, employment, and living environment.^{93–96} Studies show that the association between education and health is driven by increases in human capital, with people who have lower levels of education experiencing a faster health decline than those with higher levels of education.⁹⁷

Our study had some limitations. We only included cohorts of pregnant women shared and harmonised as part of the IPPIC project, and data from studies not in the IPPIC data repository were not considered in the analysis. There were high levels of missing data in variables in some of the cohorts used for the IPD meta-analysis. However, our sensitivity analysis on complete cases resulted in similar results to our imputed dataset. Some of the cohorts included pregnant women over many decades, and the risk of adverse perinatal outcomes could have changed over time. Stillbirth was also variably defined within individual cohorts, which might have affected estimates in our analysis. Our analysis did not consider unmeasured factors that could confound the association between race and ethnicity and perinatal outcomes. The definitions of race and ethnicity differed between studies according to the databases used, the geographical regions, and time of data collection within the included IPPIC cohorts. We were only able to assess for variations in disparities due to race and ethnicity in perinatal outcomes between geographical regions, and not by health systems (private sector, government funded, or mixed models) because of the paucity of reported data.

We acknowledge that the experiences and challenges faced by women from ethnic groups such as south Asians might vary between regions due to differences in historical immigration patterns (eg, migration to escape civil war, for economic reasons, or to join family members) and policies.⁹⁸ But overall, we did not observe significant differences between the subgroups categorised by region for increased risk of small-for-gestational-age babies in women of south Asian ethnicity. It is likely that the effects of race and ethnicity on perinatal outcomes might be different within subgroups such as African and African Caribbean women born in a high-income country (eg, the UK, USA, or Canada) compared to first-generation migrants to that country, and also between various south Asian groups (eg, those of Bangladeshi, Indian, and

Pakistani origin) who have been reported to have varied health outcomes, such as the highest levels of infant mortality rates in babies born to women of Pakistani origin.^{99–101} However, we were limited by the paucity of relevant data in the primary studies and were not able to undertake this analysis. We were able to adjust for only one measure of a woman's socioeconomic status, maternal educational attainment, and not for other measures such as income and occupation, because of the availability of sparse and heterogeneous data in the IPPIC repository. Since the studies involved in our meta-analyses were not specifically done to assess the effects of race and ethnicity on perinatal outcomes, it is difficult to interpret the likelihood of the publication of a study included in our IPD meta-analysis with the magnitude of the association we estimated or the precision of these estimates. Therefore, we refrained from assessing the risk of publication bias.¹¹

Since the 1980s, neonatal mortality rates have been on the decline in most countries, but this overall trend hides underlying differences within individual racial and ethnic groups.¹⁰² For example, in the UK, a 12% fall in stillbirths among White women between 2013 and 2018 contrasts starkly with a contemporaneous 5% rise in stillbirths among Black women.¹ The effect of race and ethnicity has often been shown to be associated with adverse perinatal outcomes, but this has mostly been presented in the light of it being modified by socioeconomic status.¹⁹ Studies such as the UK National Maternity and Perinatal Audit⁹ and those from the USA^{103,104} report higher rates of adverse perinatal outcomes in Black and Asian women, as well as women from other underserved groups, than in White women even after adjusting for socioeconomic deprivation,⁹ implying the contribution of other factors.¹⁰⁵

Our study shows that after controlling for the effect of maternal characteristics, including a woman's educational attainment, the association between race and ethnicity and adverse perinatal outcomes persists. Complex multifactorial characteristics influence these outcomes in women from underserved racial and ethnic groups. The unique set of challenges posed by pregnancy is further worsened in individuals who are disadvantaged by their sex, race, and ethnicity.¹⁰⁶ Racial discrimination is known to be associated with chronic stress that can influence pregnancy outcomes.⁴ Furthermore, women from underserved racial and ethnic groups encounter discrimination at various levels, contributing to adverse pregnancy outcomes: at the institutional level, leading to differential access to antenatal care; at the interpersonal level in their interactions with health-care professionals who do not acknowledge their concerns; and through internalised racism, where women from marginalised groups accept their perceived incompetence that limits them from seeking timely care.⁴ These problems are compounded by racial discrimination across generations and gaps in health literacy,⁴ which are in turn affected by the environment, social relationships, and employment

opportunities.⁵ Previous studies have incorrectly adjusted for birthweight and gestational age at delivery, which dampens the true effect of race and ethnicity on adverse perinatal outcomes.⁹

Our finding of disparities in perinatal outcomes across regions and over time in underserved racial and ethnic groups highlights the global need to address the structural, interpersonal, and internalised barriers faced by these women. In many countries, poor maternal and perinatal outcomes have been linked to structural racism^{7,107–110}—a system where public policies, institutional practices, cultural depiction, and other means contribute to and reinforce racial inequity.¹¹¹ The recent inquiry into racial justice and human rights in UK maternity care found that systemic factors such as negative stereotyping, microaggressions, race-based risk assumptions, and dehumanisation of women from underserved racial and ethnic groups contributed to their poor pregnancy outcomes.¹⁰⁷ Structural racism was also highlighted as a key contributing factor to poor outcomes in Black mothers in the testimonies submitted to the US House Oversight and Reform Committee for their hearing, *Birthing While Black*.¹¹²

Multifaceted antenatal interventions are urgently needed across all regions and countries to reduce the racial and ethnic inequities in pregnancy care and outcomes. Central to any such effort should be the removal of organisational and policy-level structural barriers contributing to poor perinatal outcomes.¹¹³ Interventions should focus on understanding why Black and south Asian babies die or develop complications at a disproportionate rate to White babies, and avoid clinical decisions guided by race and ethnicity that could exacerbate such inequalities.¹¹⁴ In the UK, the Royal College of Obstetricians and Gynaecologists has launched the Race Equality Taskforce to tackle racial disparities in women's health care, including pregnancy outcomes.¹¹⁵ This is supported by national strategies such as the Race and Health Observatory, the NHS England Equality strategy, and the Core20Plus5 approach.^{116–118} Similar efforts are underway in other countries.^{119,120}

The window of opportunity available to maternity services to tackle these disparities is brief but substantial, and requires resource-intensive and time-consuming changes in social and maternity care.¹⁰⁵ These efforts need to be complemented by a life course approach to optimising the health of, and underpinning determinants in, girls and women from underserved and under-represented groups. The curriculum and training offered to midwifery and medical students should integrate strategies to identify explicit and implicit racial biases in health-care settings and provide the tools to improve communication while caring for women from various backgrounds.¹²¹

Despite race and ethnicity being a risk factor for adverse health outcomes, particularly in pregnancy, there are no comprehensive research strategies or initiatives to address this problem. In addition to encouraging women

from various racial and ethnic backgrounds to participate in research,¹²² funding bodies need to prioritise topics that directly address the disparities in pregnancy outcomes that are related to race and ethnicity. The voices of women from relevant backgrounds should be central to lead and guide the efforts in this area. Given that race and ethnicity are key demographic variables, studies should aim to comprehensively collect and report these data in line with current recommendations at all stages of a woman's life.¹⁹ This will allow us to not only map the magnitude of disparities at various timepoints, such as childhood, adolescence, pre-pregnancy, and pregnancy, contributing to poor pregnancy outcomes and their long-term effects in later years, but also plan targeted interventions at crucial timepoints to improve the health of babies in the short and long term, with the impact spanning generations.

Contributors

ST, AK, JZ, and JA conceptualised the study. All authors were involved in the design of the study. JZ and BMF-F analysed the data. JS and TK quality assessed included studies. All authors interpreted the results. JS and JA are joint first authors. All co-authors contributed to the writing of the manuscript and approved the final version. ST, AK, JA, and JZ accessed and verified the data. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors had access to the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

All data requests should be submitted via email to the corresponding author for consideration. Access to available anonymised data might be granted following review by the IPPIC Data Sharing Committee and once appropriate agreements are in place.

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