

Effectiveness of weight loss interventions in breast cancer survivors

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BMJ Open Effectiveness of weight loss interventions in breast cancer survivors: a systematic review of reviews

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ABSTRACT

Background Elevated body mass index (BMI) in breast cancer survivors (BCS) is associated with cancer recurrence and poorer treatment response. Guidelines recommend 5%–10% weight loss for overweight or obese BCS.

Objectives To assess effectiveness of lifestyle interventions for female BCS on weight loss, BMI, body composition, health-related quality of life (HRQoL), physical functioning, psychosocial measures, biomarkers.

Design Systematic review of reviews and meta-analyses.

Setting All clinical settings.

Participants Adult female BCS (active treatment or post-treatment).

Methods Medline, Embase, CINAHL, PsycINFO, Cochrane Library (including Database of Abstracts of Reviews of Effects) were searched for systematic reviews published in English between 1990 and 2022, with weight, BMI or body fat as primary outcome. Narrative reviews, editorials, letters, conference abstracts were excluded. Review quality was assessed using the Joanna Briggs Institute quality assessment tool.

Results 17 reviews were included. Twelve reported significant reductions in one or more anthropometric outcomes: weight -1.36 kg (95% CI: -2.51 to -0.21) to -3.8 kg (95% CI: -5.6 to -1.9); BMI -0.89 kg/m² (95% CI: -0.15 to -0.28) to -3.59 kg/m² (95% CI: -6.29 to 0.89) or body fat -1.6% (95% CI: -2.31 to -0.88) to -2.6% (95% CI not reported). Significant reductions in two or more anthropometric outcomes were reported in 7/12 reviews, with effective interventions comprising aerobic exercise/aerobic exercise plus resistance training (n=5), or diet and exercise with or without counselling (n=2). Significant improvements were also reported for HRQoL (8/11 reviews), mental health (4/7) and physical functioning (2/3). Group interventions comprising aerobic exercise or aerobic exercise plus resistance training were most likely to improve outcomes.

Conclusions Lifestyle interventions can significantly improve outcomes for BCS. Multimodal interventions are likely to have the greatest impact in reducing weight, BMI and body fat. Further research must define the optimal combination, intensity and duration of effective interventions.

PROSPERO registration number CRD42021283481.

BACKGROUND

Breast cancer is the most frequently diagnosed female cancer, accounting for 25% of

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ To the best of our knowledge, this systematic review of reviews is the first to assess the effectiveness of lifestyle interventions in improving outcomes for breast cancer survivors.
- ⇒ We assessed a large volume of international evidence across diverse interventions and outcomes.
- ⇒ Our methodological approach was systematic and conformed to best practice.
- ⇒ Reviews of reviews do not allow us to look at the context in which interventions are implemented but permit a broad overview of the evidence that would not be possible at primary study level alone.
- ⇒ Heterogeneity of intervention design, duration, intensity and follow-up prohibited meta-synthesis across reviews.

all female cancers. There were 2.3 million new cases worldwide in 2020, and in the UK 55 900 new breast cancers are diagnosed each year.¹ Breast cancer survivors (BCS) are the largest group of cancer survivors, with 7.8 million women alive worldwide in 2020 following a breast cancer diagnosis in the previous 5 years, and with 500 000 women in the UK.^{1 2} The number of BCS continues to rise, and multiple aspects of their health pose challenges to the health service. One aspect of growing concern is the proportion of BCS who are overweight and obese. Over the last 20 years, levels of obesity have risen, particularly in Europe and in the UK, and now over 50% BCS in Western countries are overweight or obese. BCS who are overweight (body mass index (BMI) 25–29.9) or obese (BMI >30) have poorer outcomes than those with a normal BMI <25, with higher recurrence rates, poorer responses to treatment and increased secondary cancer rates.^{3 4} A recent meta-analysis concluded that women living with obesity have a one-third increased risk of breast cancer mortality and a 41% increased risk of overall mortality compared with women with breast cancer who have a normal weight.⁵

In addition to breast cancer recurrence, women with breast cancer often experience numerous short-term and long-term disease or treatment delayed physiological and psychosocial outcomes such as premature menopause, infertility, weight gain, altered body image and fatigue.^{6–8} These adverse effects can have a negative impact on quality of life and physical functioning and can be more significant in BCS who are overweight and obese by reducing treatment efficacy, decreasing the range of surgical options available for reconstruction and making surgery more challenging.⁴ Overweight and obese BCS may also experience prolonged recovery times and impaired ability to return to normal life.^{6,9}

Evidence suggests that BCS who follow a healthy lifestyle by increasing physical activity and by modifying diet may improve their quality of life.⁹ This may lead to positive impacts on their general health and a subsequent reduction in healthcare burden. Observational data suggest that higher levels of physical activity in BCS are associated with reduced risk of dying from breast cancer or from any cause.^{10,11} Lack of physical activity has been shown to relate to weight gain after cancer diagnosis and poorer survival.¹²

Current recommendations suggest that BCS should return to normal daily activities as soon as possible (recognising limitations associated with certain types of surgery or potential postoperative complications), and engage in 150 min of moderate-intensity aerobic exercise per week.¹³ The National Institute for Health and Care Excellence guidelines in England and Wales also recommend physical activity and diet changes to ensure a healthy lifestyle.¹⁴ Leading cancer organisations also recommend that cancer survivors achieve and maintain a healthy body weight and suggest weight loss of 5%–10% for those who are overweight or obese.¹⁵ However, breast clinicians can find it difficult to engage in advice concerning weight management or lifestyle modification: unlike with treatment regimens such as chemotherapy, at present there is no clear algorithm or pathway of individualised lifestyle intervention. Empowering BCS to modify their own health with a structured exercise, diet and counselling programme as part of their treatment plan may be a vital part of improving outcomes from breast cancer. This systematic review of reviews sought to understand which diet, physical activity and lifestyle interventions were most effective in facilitating weight loss, reducing BMI, improving body composition, alongside effects on health-related quality of life (HRQoL), physical functioning, psychosocial measures and biomarkers for female BCS.

METHODS

Registration and protocol

This systematic review of reviews was registered on PROSPERO (International Prospective Register of Systematic

Reviews) (19 October 2021; ref: CRD42021283481), and the protocol is available in online supplemental file 1. Findings are reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for systematic review and meta-analysis results (online supplemental file 2).¹⁶

Background to systematic review of reviews

Reviews of reviews are designed to synthesise evidence from multiple systematic reviews of interventions into a single review, using the findings and conclusions of included systematic reviews as the raw data.¹⁷ They do not repeat the searches, assessment of eligibility, assessment of risk of bias or meta-analysis from included reviews, nor do they aim to extract additional outcomes from studies, but they are a useful tool when the evidence base is broad and are of particular relevance for decision makers who need a synthesis of the most up-to-date and reliable data relating to the effects of different interventions on a specific outcome or range of outcomes.

Eligibility criteria

We included all systematic reviews of weight loss interventions in adult female BCS, published in the English language from 1990 to date, in which weight loss or percentage reduction in BMI or body weight was reported as a main outcome. Eligible reviews could include randomised controlled trials (RCTs), feasibility studies, non-randomised and observational study designs. The year 1990 was chosen following scoping searches that suggested there was little or no systematic review evidence about the effectiveness of weight loss interventions for BCS before 1990. It was also expected that most systematic reviews focusing on this topic will have been published in English, even if individual reviews included primary research written in languages other than English. No reviews were excluded on the basis of the language of their source material.

Reviews that were not published in English; where the study population was not female, adult BCS; reviews published before 1990; narrative reviews with unsystematic methodologies, editorials, opinion pieces, commentaries, letters, meeting abstracts or conference proceedings, were excluded.

PICO

Participants were female, adult (aged 18+ years) BCS who had been involved in weight loss intervention(s) following their initial breast cancer diagnosis or secondary breast cancer diagnosis.

Interventions could be individual or multicomponent interventions focusing on dietary modifications involving referral to a dietician or weight loss support group such as Weight Watchers or Slimming World; physical activity (whether individually targeted or in a group) or surgical weight loss interventions such as laparoscopic sleeve gastrectomy, gastric band or bypass surgery.

Comparison groups could include usual care (ie, participants who had not had dietary advice or physical activity interventions), comparison with another intervention or (for participants where the intervention was bariatric surgery) who had lifestyle intervention alone.

Outcome measures: all eligible reviews reported weight loss measured as a reduction in BMI or weight in pounds/kg or in waist circumference or as a percentage (%) of body weight loss or body fat or waist circumference. Other outcome measures of interest included HRQoL, measures related to physical functioning, psychosocial measures (eg, emotional and mental well-being) and biomarkers.

Search strategy

Relevant systematic reviews were identified through searching electronic bibliographic databases, and the manual checking of the reference list of each review which met the eligibility criteria. The following electronic databases were searched: Medline (Medline database and Medline in process), Embase, CINAHL, PsycINFO, Cochrane Library (including the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects). A search of PROSPERO was also undertaken to ensure that there was no duplication of other planned systematic review research. Searches were undertaken in November 2021.

The search strategy (strategy for Medline provided as online supplemental file 3) focused on terms related to breast neoplasms and weight loss or obesity or exercise or lifestyle or diet, with an English language and review/systematic review filter applied. Medical Subject Headings (MeSH) terms used breast neoplasm, weight loss, obesity, exercise, lifestyle, diet, review and systematic review. Other terms used as main headings: weight loss and lifestyle. Keywords for this search included: (“Breast Neoplasms”(MeSH) AND “Weight loss”(MeSH) or “Obesity”(Mesh) or “Exercise”(MeSH) or “Lifestyle”(MeSH) or “Lifestyle” or “Diet”(MeSH) AND Review (MeSH) or Systematic review(MeSH)).

Study selection

Search results were transferred to the Rayyan QCRI central electronic reference management application (<https://www.rayyan.ai>) and duplicates removed.¹⁸ Two independent reviewers (BL, SD) screened titles and abstracts for relevance against the eligibility criteria. Where both reviewers agreed that a review was not relevant, it was excluded. Where both reviewers agreed that a review should be included, full-text copies of the review were obtained and the review was taken forward for full-text screening. Disagreements were resolved by discussion. Full-text screening for all potentially eligible reviews was then independently undertaken by two reviewers (BL, SD). Disagreements were again resolved by discussion and consultation with the wider research team if uncertainty over eligibility remained.

Data extraction

Data on population characteristics, interventions being assessed and outcomes were extracted from each eligible review using a standardised data extraction form (online supplemental file 4). Data extracted included authors, year and country of publication, study types included in review, overall review question and methodological characteristics, study population, detailed description of intervention and follow-up regime and all primary and secondary outcomes. Included reviews were split equally between the two reviewers (BL, SD), and for each half of the set, one reviewer undertook the data extraction, which was checked against the original manuscript by the second reviewer. All disagreements were resolved by discussion or through arbitration by an additional reviewer.

Quality assessment

Two independent reviewers (BL, SD) assessed the quality of each included review using the Joanna Briggs Institute Critical Appraisal Checklist (online supplemental file 5).¹⁹ The checklist comprises 11 criteria including appropriateness of the review question, inclusion criteria and search strategy. The checklist also evaluates how the critical appraisal was done and by who and what methods were used to minimise data extraction errors and likelihood of publication bias. Any disagreements between the two reviewers over quality assessment (QA) in particular studies were resolved through consultation with an additional reviewer.

Data synthesis and analysis

In this systematic review of reviews, our goal was to evaluate the effectiveness of interventions described in the reviews in achieving weight loss, improving body composition, improving psychosocial outcomes and increasing quality of life. Study and intervention heterogeneity within included systematic reviews made synthesis impossible so data are presented narratively. This comprised a review of participants, interventions and outcomes, with a particular focus on the characteristics of effective interventions.

Where included reviews reported the results from meta-analysis, the relevant summary statistics for the outcomes of interest are reported. Where included reviews reported narrative findings only, we assessed outcome significance based on the authors’ own conclusions about the primary studies they included. An analysis of the overlap between primary studies in our included reviews was undertaken, focusing on the overlap between primary studies in each review in which one or more of our outcomes of interest was included.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

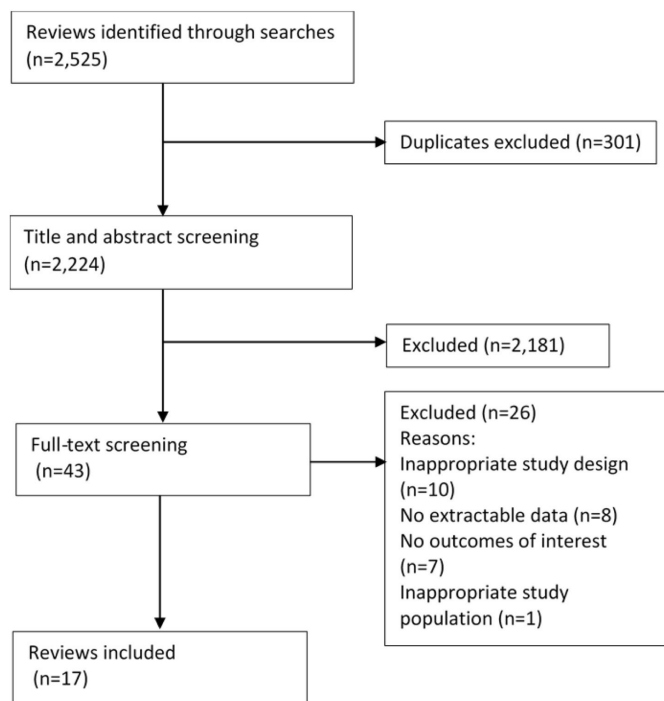


Figure 1 Flow diagram.

RESULTS

Study selection

Figure 1 summarises the search. A total of 2525 titles and abstracts were screened from which 301 duplicates were excluded. After screening titles and abstracts, a further 2181 were excluded, leaving 43 articles eligible for full-text screening. Twenty-six reviews were excluded following full-text screening for the following reasons: 10 studies had inappropriate study design, 8 studies had no extractable data, 7 studies had no outcomes of interest and 1 study had an inappropriate study population. Following full-text screening, 17 reviewed were deemed eligible and included in analysis.

Study characteristics

Of the 17 studies, 7 were systematic reviews,^{20–26} 9 were systematic reviews including meta-analysis^{27–35} and 1 was a systematic review and meta-regression.³⁶ The majority of primary studies included were RCTs. Other study types included non-RCTs, pilot studies, quasi-randomised trials, single-arm studies, cohort intervention studies, parallel intervention studies and crossover trials. A total of 199 primary studies assessing one or more of our outcomes of interest were included across the 17 reviews (range 4^{35–63}²⁸). The mean number of participants across the included reviews was 1823 (range 322³¹–6303³⁴). Six reviews were undertaken in Australia,^{25 26 30 32 33 36} two each from China,^{31 35} Brazil,^{27 34} the USA^{21 24} and one review each from Canada,²³ Korea,²⁹ England,²⁸ Ireland²² and Egypt.²⁰ Study characteristics are summarised in **table 1**.

Overlap between primary studies included in reviews

The degree of overlap between primary studies represented within each of the included systematic reviews

was assessed following methods suggested in a recent paper by Lunny *et al.*³⁷ Of the 199 primary studies represented across our 17 reviews that covered one or more of our outcomes of interest, 139 were unique that is, only appearing in a single review (69.8%). The remaining 60 primary studies (30.2%) appeared more than once across our reviews. Forty primary studies appeared two times (20.1%); 15 appeared three times (7.5%) and 4 were represented four times each (2.0%). The greatest number of repeat appearances of a single primary study was by Courneya *et al.*,³⁸ whose data were reported in 6 of our 17 reviews.^{22 23 28 30 33 34} The upper right area of **table 2** shows the number of shared primary studies in each review pair, expressed as a percentage, for example, Guinan *et al.*²² and Lahart *et al.*²⁸ share 4/55 primary studies, which equates to a proportion of 7.3%. The cells are colour coded, following the method outlined by Pieper *et al.*³⁹ for distinguishing thresholds of overlap (0%–5% overlap in green equates to low or slight overlap; 5%–10% overlap in yellow equates to moderate overlap; 11%–15% in pink suggests high overlap and 15% or greater, in darker red, indicates very high overlap between a given review pair). Of the 136 review pairs in **table 2**, the majority (n=119; 87.5%) have low to slight overlap in their primary studies. Nine pairs (6.6%) have moderate overlap, five pairs (3.7%) have high overlap and three pairs (Playdon/Reeves,^{24 25} Chlebowski/Shaiikh^{21 32} and Ingram/Soares Falcetta^{23 34}) have very high overlap.

Quality of included reviews

The mean QA score was 9.5/11. Four reviews (23%) scored 11/11.^{21 28 32 34} The criterion for which the largest number of reviews failed to score a point related to whether the review authors had described methods used to minimise errors in data extraction. Three reviews did not meet this criterion^{21 27 29} and it was unclear whether this criterion had been met in a further nine reviews.^{20 24–26 30 31 33 35 36}

Participant characteristics

The 17 reviews included patients who were either receiving active breast cancer treatment (n=5),^{26 27 29 31 36} post-treatment (n=6)^{20 25 28 32 34 35} or a combination of active and post-treatment (n=6).^{21–24 30 33} Active treatment was either active treatment with hormonal therapy either aromatase inhibitors or tamoxifen (n=4)^{21 22 27 30} or active treatment included either chemotherapy or radiotherapy and hormonal therapy (n=7).^{23 24 26 29 31 33 36} Post-treatment was defined by reviews as once all adjuvant therapy has been completed (n=12).^{20–22 24 25 28 30 32–35}

Most reviews included patients who had been diagnosed with early invasive breast cancer up to stage III node negative (n=12).^{20–23 26 27 30–32 34–36} Three reviews included patients with metastatic disease.^{25 28} Two reviews just stated breast cancer as the inclusion criteria and tumour stage was not described in the results.^{24 29} Only one review described more specific tumour characteristics as it included trials targeted to ER-positive tumours

Table 1 Characteristics of included reviews

Study, country	Review type, no. databases searched, restrictions	Study design(s), (number of studies included)	Number of participants, breast cancer treatment status	Intervention, control	Follow-up length
Bekhet <i>et al</i> ²⁰ Egypt	Systematic review N=6, no restrictions	RCTs (n=12)	1120 Post-treatment	Aerobic exercise, supervised or home-based Usual care	10 weeks to 12 months
Boing <i>et al</i> ²⁷ Brazil	Systematic review and meta-analysis N=5, English, Portuguese, Spanish	RCTs (n=5) Non-RCTs (n=3), pilot non-randomised clinical trials (n=2), pilot RCT (n=1)	368 Undergoing active hormonal therapy	Aerobic training alone (n=1) Aerobic and resistance exercise (n=8) Walking alone (n=2) Usual care (n=3), wait-list control (n=1), low-intensity stretching (n=1)	8–48 weeks
Chlebowski and Reeves ²¹ USA	Systematic review N=4, no restrictions	RCTs (n=8) (6 RCTs in breast cancer, 2 in endometrial cancer)	1325 Active treatment (n=1) Post-treatment (n=5)	12-week interventions: face-to-face group sessions (nutrition and PA) phone counselling (n=1) 6-month interventions: in-person face-to-face counselling and calorie reduction (n=1) 12-month interventions: individual tailored diet+exercise (n=1) 24-month interventions: lifestyle intervention (phone), calorie reduction (n=1), intense group based, calorie deficit, phone (n=1) Usual care (n=1), healthy eating (n=1), another intervention (n=1), leaflet/education (n=2), low-intensity general weight management, individualised counselling (n=1)	12 weeks to 24 months
Guinan <i>et al</i> ²² Ireland	Systematic review N=6, English only	RCTs (n=7) Non-RCTs (n=2)	435 Active or post-treatment	Aerobic exercise alone or combined with resistance training (n=7) Resistance training alone (n=1) Walking intervention (n=1) Usual care (n=7)	8 weeks to 6 months
Ingram <i>et al</i> ²³ Canada	Systematic review N=10, English only	RCTs (n=9) Non-randomised trials (n=5)	725 Active or post-treatment	Aerobic exercise (n=7) Aerobic and resistance exercise (n=5) Walking and Tai Chi (n=1) Timing of exercises for lymphoedema (n=1) Usual care (n=7), another intervention (n=2)	6–26 weeks
Lahart <i>et al</i> ²⁸ England	Systematic review and meta-analysis N=12, no restrictions	RCTs (n=60) Quasi-randomised trials (n=3)	5761 Post-treatment (3239 participants receiving intervention, 2524 controls)	Aerobic exercise only (n=28) Aerobic exercise and resistance training (n=21) Resistance training (n=7) Yoga (n=8) Qigong/Pilates/Tai Chi Chuan (n=1) Usual care (n=30), wait-list control (n=24), health education (n=2), telephone (n=1), physical therapy (n=1), psychosocial (n=1), stretching (n=1), attention control (n=1)	4–24 months
Lee and Lee ²⁹ Korea	Systematic review and meta-analysis N=2, no restrictions	RCTs (n=29)	2989 Active treatment	Aerobic and resistance exercise (n=17) Resistance exercise alone (n=4) Yoga (n=2) Moderate to vigorous intensity exercise (n=1) Aerobic exercise alone (n=2) Walking (n=3) Usual care	4 weeks to 12 months
Lopez <i>et al</i> ³⁶ Australia	Systematic review and meta-regression N=3, English only	RCTs (n=8) Single group studies (n=2)	985 Active treatment	Combined resistance and aerobic training (n=9) Resistance training only (n=1) Usual care (n=8)	4 weeks to 6 months
McNeely <i>et al</i> ³⁰ Canada	Systematic review and meta-analysis N=9, no restrictions	RCTs (n=14)	717 Active treatment (n=8), post-treatment (n=5), both (n=1)	Mixed aerobic and resistance exercise Usual care	7 weeks to 6 months
Pan <i>et al</i> ³¹ China	Systematic review and meta-analysis N=4, no restrictions	RCTs (n=9)	322 Active treatment	Tai Chi Chuan Usual care (n=3), psychosocial support (n=4), education (n=1), spiritual growth guidance (n=1)	10 weeks to 6 months

Continued

Table 1 Continued

Study, country	Review type, no. databases searched, restrictions	Study design(s), (number of studies included)	Number of participants, breast cancer treatment status	Intervention, control	Follow-up length
Playdon <i>et al</i> ²⁴ USA	Systematic review N=1, no restrictions	RCTs (n=8), cohort intervention studies (n=4), randomised parallel interventions (n=2), non-RCTs (n=1), crossover trial (n=1)	1028 Active treatment (n=2), post-treatment (n=14)	Weight loss intervention (any combination of diet, physical activity and/or behavioural components with a focus on weight loss) Usual care (n=1), printed healthy eating materials (n=2), wait-list (n=3), citrus herbal tea (n=1)	8 weeks to 12 months
Reeves <i>et al</i> ²⁵ Australia	Systematic review N=3, English only	RCTs (n=10) Single-arm trials (n=4)	654 Post-treatment	RCTs: diet and PA (n=6), diet alone (n=4) Single arm trials: group interventions (n=4) Usual care/healthy eating pamphlets (n=7), other intervention (n=3)	6–12 months
Shaikh <i>et al</i> ²² Australia	Systematic review and meta-analysis N=11, no restrictions	RCTs (n=17), randomised crossover trials (n=3)	2028 Post-treatment	Diet interventions only (n=3) Diet and exercise interventions (n=3) Diet, exercise and psychosocial support interventions (n=15) Other interventions (n=2) Usual care, written materials, wait-list	2 weeks to 24 months
Singh <i>et al</i> ³³ Australia	Systematic review and meta-analysis N=9, English only	RCTs (n=61)	5200 Active or post-treatment	Aerobic exercise only (n=20) Combined aerobic and resistance exercise (n=21) Resistance exercise only (n=6) Other modes of exercise (n=11) Separate aerobic and resistance exercise arms (n=3) Usual care	6 weeks to 12 months
Soares Falcetta <i>et al</i> ²⁴ Brazil	Systematic review and meta-analysis N=4, English only	RCTs (n=60)	6303 Post-treatment	PA interventions (with or without dietary intervention) Counselling or structured programmes with supervised and/or individualised exercise sessions Usual care	4 weeks to 24 months
Thomson and Reeves ²⁶ Australia	Systematic review N=4, no restrictions	RCTs (n=5)	381 Active treatment	Behavioural-based dietary intervention±PA and weight gain prevention Usual care (n=2), general cancer prevention recommendations (n=1), exercise recommendations (n=1), other interventions (n=1)	6–12 months
Wang <i>et al</i> ³⁵ China	Systematic review and meta-analysis N=10, no restrictions	RCTs (n=11)	666 Post-treatment	PA interventions (aerobic, flexible/endurance exercise, resistance training, yoga, stretching, dancing) Usual care	8–24 weeks
PA, Physical activity; RCT, randomised controlled trial.					

Table 2 Proportion of studies shared by pairs of reviews

	Bekhet	Boing	Chlebowski	Guinan	Ingram	Lahart	Lee	Lopez	McNeely	Pan	Playdon	Reeves	Shaikh	Singh	Soares-Falcetta	Thomson	Wang
Bekhet	7	0	0	4.8	0	4.2	0	0	0	0	0	0	0	3.4	3.5	0	0
Boing	14	7	0	0	0	2.1	0	0	0	0	0	0	0	0	3.5	0	0
Chlebowski	15	15	8	0	0	0	0	0	0	0	0	0	16.1	0	10.3	0	0
Guinan	21	21	22	14	4.0	7.3	0	0	9.5	0	0	0	0	4.5	9.4	0	0
Ingram	18	18	19	25	11	1.9	0	5.0	11.1	0	0	0	0	1.6	16.3	0	0
Lahart	48	48	49	55	52	41	1.9	0	6.3	2.1	0	0	0	11.8	13.2	0	0
Lee	20	20	21	27	24	54	13	9.5	0	0	0	0	0	7.7	1.6	0	0
Lopez	16	16	17	23	20	50	21	9	0	0	0	0	0	1.6	0	0	0
McNeely	14	14	15	21	18	48	20	16	7	0	0	0	0	1.7	5.3	0	0
Pan	14	14	15	21	18	48	20	16	14	7	0	0	0	0	0	0	0
Playdon	21	21	22	28	25	55	27	23	21	21	14	32.1	10.8	0	1.6	0	0
Reeves	21	21	22	28	25	55	27	23	21	21	28	14	13.5	0	4.7	0	0
Shaikh	30	30	31	37	34	64	36	32	30	30	37	37	23	0	12.3	0	0
Singh	59	59	60	66	63	93	65	61	59	59	66	66	75	52	6.9	0	0
Soares-Falcetta	57	57	58	64	61	91	63	59	57	57	64	64	73	102	50	0	1.9
Thomson	12	12	13	19	16	46	18	14	12	12	19	19	28	57	55	5	0
Wang	11	11	12	17	15	45	17	13	11	11	18	18	27	56	54	9	4

Grey cells indicate the number of primary studies in a given review that reported one or more of our outcomes of interest. White cells show the total number of primary studies in each pair of reviews which reported one or more of our outcomes of interest. In the upper right section of table 2, numbers indicate the proportion of primary studies in each pair of reviews that were the same (green cells indicate overlap <5%; yellow cells indicate overlap between 5% and <10%; pink cells show overlap of 10%–<15% and dark red cells indicate overlaps of 15% or greater).

only, triple negative breast cancer and Afro-Caribbean women only.²¹

Interventions

Participants received individual interventions (diet or exercise alone) (n=11)^{20 22 23 27-31 33 35 36}, a mixture of diet and exercise interventions (n=2)^{25 32} or multicomponent interventions comprising diet, exercise and behavioural change support such as counselling (n=4).^{21 24 26 34} Exercise interventions were varied. Five reviews did not describe the nature of the exercise interventions they included.^{24-26 32 34} One review focused solely on Tai Chi,³¹ and another described aerobic exercise interventions only.²⁰ The remaining 10 reviews reported data from primary studies that may have included aerobic exercise alone, resistance training alone or aerobic and resistance exercise in combination.^{21-23 27-30 33 35 36} Intervention duration ranged from 2 weeks to 24 months. Interventions were either entirely supervised (n=5),^{24 26 31 32 35} or comprised a mixture of supervised and unsupervised activities (n=6).^{20 21 23 27 30 34} Six reviews did not report whether or not interventions were supervised.^{22 25 28 29 33 36}

Dietary interventions were varied. Six reviews included dietary interventions.^{21 24-26 32 34} Calorie deficit was the most frequent dietary intervention,^{21 24-26 32 34} followed by low fat, high fruit and vegetables diet^{21 24-26 32 34} and calorie reduction.^{25 32 34} Other dietary interventions used were Weight Watchers,^{24 32} Curves diet,^{25 32} low carbohydrate,²⁵ very low calories <600,³² Green Tea,³² Modified Atkins,³² plant based,^{21 24} individualised tailored,^{21 24} combination of Mediterranean and macrobiotic²⁶ and the lean method.³⁴

Comparator groups

The most common control group was usual care alone (n=8).^{20 22 29 30 33-36} The other nine reviews used usual care and a mixture of other control groups, including waitlist controls, low-intensity stretching and healthy eating, one or more other interventions, health education, individualised counselling, physical therapy, psychosocial support, stretching, attention control, spiritual growth guidance, printed healthy eating materials, citrus herbal tea, general cancer prevention recommendations and exercise recommendations.

Outcomes

Outcome measures measured included BMI (n=11),^{22 23 28-36} weight (n=11),^{20 21 23-26 28 30 32-34} body composition (n=12),^{22-29 32-34 36} HRQoL (n=11),^{20 21 24 25 28-34} mental health (n=7),^{21 28 29 31-34} physical functioning (n=3)^{28 30 31} and biomarkers (n=3)^{20 22 25} (online supplemental file 6). The majority of reviews (n=15) assessed multiple outcomes of interest, ranging from two outcomes³⁶ to six.²⁸ Only two reviews looked at a single outcome measure of interest.^{27 35} Overall, 13 reviews (76%) reported a nominally statistically significant result (either positive or negative) for at least one outcome (online supplemental file 7).

Weight

Seven of 11 reviews (n=17137 participants) showed a significant reduction in weight.^{21 24-26 28 32 34} The range of weight loss reported was between 3% and 12.5% of baseline weight; from a loss of 1.36 kg (95% CI: -2.51 to -0.21)³⁴ to a loss of 3.8 kg (95% CI: -5.6 to -1.9).²¹ Of the other four reviews, two showed no difference in weight between groups^{30 33} and two showed mixed significance, whereby some primary studies showed a significant reduction in weight, and others did not.^{20 23} Only one review evaluated maintenance of weight loss over time, reporting that when stratified by weight loss success, participants who lost >5% of their body weight during the intervention period continued to lose weight for up to 18 months.²⁴

Chlebowski and Reeves²¹ performed a subgroup analysis (4 studies, 1266 participants), focusing on the association between intervention duration and weight loss. A 6-month intervention comprising counselling, calorie reduction and physical activity (delivered in-person or by telephone) was associated with significant weight loss of -1.7 kg (95% CI: -3.2 to -0.3); a 12-month intervention demonstrated weight loss significantly greater in the group receiving individually tailored diet and aerobic exercise (150 min duration, -3.77 kg±4.8 kg) and a 24-month intervention showed significant weight loss with an intervention comprising calorie reduction and unsupervised exercise, delivered over the telephone (-5.5% of body weight±6.4%). The most substantial weight loss was achieved among participants receiving intensive group-based sessions as part of a 24-month intervention comprising three sessions of 60 min activity, moderate-intensity physical activity, a calorie-deficit diet and telephone support (-6.0% of body weight).

Body mass index

Six of 11 reviews (n=17619 participants) showed a significant reduction in BMI,^{22 29 32-35} ranging from a reduction of 0.89 kg/m²³¹ (95% CI: -0.15 to -0.28) to a reduction of 3.59 kg/m² (95% CI: -6.29 to -0.89).³² Of the other five reviews, four showed no difference in BMI between intervention and comparator groups,^{28 30 31 36} and one reported mixed significance.²³

Body composition

Eight of 12 reviews assessing body composition (n=18425 participants) showed a significant reduction in body fat or waist circumference,^{22 23 25 28 29 32-34} with percentage reduction in body fat ranging from -1.6%³⁴ (95% CI: -2.31 to -0.88) to -2.6% (95% CI not reported).²³ The other four reviews that assessed body composition showed no difference between intervention and control groups.^{24 26 27 36}

Overall anthropometric outcomes (weight/BMI/body composition)

Overall, 12 out of 17 reviews reported significant reductions in one or more of the anthropometric outcomes of weight, BMI or body composition (body fat or waist

circumference).^{21–26 28 29 32–35} Seven of those 12 reviews showed significant reductions in two or more anthropometric outcomes.^{22 25 28 29 32–35} Effective interventions used in these seven reviews focused on either aerobic exercise alone or a combination of aerobic exercise and resistance training (n=5),^{22 25 28 29 33} or a combination of diet and physical activity interventions with or without behavioural change support (counselling) (n=2).^{32 34}

The two reviews which reported statistically significant reductions across all three anthropometric outcomes (n=8331 participants),^{32 34} included multicomponent interventions comprising lifestyle advice, physical activity and dietary modification. Shaikh *et al*³² was a systematic review and meta-analysis of 17 RCTs and 3 randomised crossover trials which included a total of 2028 women post-treatment. Interventions lasted between 2 weeks to 24 months, and typically involved diet, exercise and psychosocial support. This review showed significant reductions in body weight (standardised mean difference (SMD) -2.25 kg; 95% CI: -3.19 to -1.3); significant reduction in BMI (SMD: -1.08 kg/m²; 95% CI: -1.61 to -0.56) and a significant reduction in waist circumference (SMD: -1.73 cm; 95% CI: -3.17 to -0.29). Shaikh *et al* also compared 15 studies with multicomponent interventions against either diet only (n=3), or diet and exercise (n=3) and found that multimodal weight loss interventions (diet, exercise and psychosocial support) resulted in greater reductions in body weight, BMI and waist circumference compared with dietary change alone: body weight: (SMD -2.88 kg; 95% CI: -3.98 to -1.77), BMI: (SMD -1.44 kg/m²; 95% CI: -2.16 to -0.72), waist circumference: (SMD: -1.66 cm; 95% CI: -3.49 to -0.16).

Soares Falcetta *et al*³⁴ reported a meta-analysis of 60 RCTs comprising a total of 6303 women post-treatment. Intervention duration ranged from 4 weeks to 24 months and involved physical activity interventions with or without diet, counselling and structured programmes. This review showed significant weight loss (-1.36 kg; 95% CI: -2.51 to -0.21), significant reduction in BMI (-0.89 kg/m²; 95% CI: -1.50 to -0.28) and significant reduction in percentage body fat (-1.6%; 95% CI: -2.31 to -0.88).

Health-related quality of life

Eight out of 11 reviews assessing HRQoL (n=25 351 participants) showed a significant improvement.^{21 24 28–30 32–34} Of these eight reviews, interventions included aerobic exercise or combined aerobic/resistance exercise (n=4),^{28–30 33} or a combination of diet and physical activity with or without counselling (n=4).^{21 24 32 34} Of the other three reviews, two showed no difference between groups^{20 31} and one showed mixed significance.²⁵ One review showed a possible link between HRQoL and weight loss with studies in which participants experienced a significant improvement in HRQoL also demonstrating >5% weight loss.²⁴

Mental health

Four of seven reviews (n=15 209 participants) showed a significant improvement in mental health,^{28 30 33 34} with a particular effect on levels of anxiety and depression (range of SMD 0.28–0.77). Effective interventions included aerobic exercise or combined aerobic and resistance training (n=3)^{28 30 33} and combined diet/physical activity with or without counselling support (n=1).³⁴ One review showed mixed significance, with improvements in the HRQoL mental health component, but no difference in anxiety and depression levels.²⁵ Another review showed a decline in mental health following an intervention that combined diet and physical activity, with significantly higher depression levels reported in the intervention group.²¹ Singh *et al*³³ carried out subgroup analysis by exercise type and supervision and showed significant reductions in anxiety and depression for combined exercise (p<0.01) and for aerobic exercise (p<0.01), but with no significant effect for resistance exercise (anxiety p=0.68, depression p=0.79). In terms of exercise supervision, there were significant improvements in quality of life and anxiety/depression for both supervised and unsupervised interventions (p<0.01).

Physical functioning

Two of three reviews that assessed some metric of physical functioning (n=6478 participants) showed significant improvements in physical functioning and well-being (range of SMD 0.33–0.84).^{28 30} One review showed no improvement in physical well-being.³¹

Biomarkers

Three reviews used biomarkers as an outcome; all showed no overall significant difference between intervention and control groups.^{20 22 25} Two reviews showed mixed significance: Guinan *et al*²² reported a reduction in insulin-like growth factor (IGF)-1, IGF-2 and no change in IGF-3, C reactive protein, interleukin-6, TNF α , adiponectin, glucose and insulin and insulin resistance. Reeves *et al*²⁵ reported a reduction in insulin and insulin resistance, no change in glucose, lipids or IGF-1. One review showed no difference in biomarkers between intervention and control groups.²⁰

DISCUSSION

This review has shown that lifestyle interventions can significantly improve anthropometric outcomes (weight, BMI and body composition) and improve both quality of life and mental health of BCS. Our analysis suggests that multimodal component interventions comprising lifestyle advice or counselling, physical activity and diet are likely to have the most significant impact in reducing weight, BMI and body fat/waist circumference. Two reviews with nearly 9000 participants showed a significant reduction in all three anthropometric measures.^{32 34} The other two reviews which included multimodal interventions both showed a significant reduction in weight.^{21 24}

This suggests that achieving weight loss or change in body composition or BMI may require all three facets of diet, physical activity and lifestyle support to be most effective. While only one review assessed the impact of intervention duration, this review suggested that longer interventions were most effective in achieving significant weight loss, with the most substantial losses achieved by a 24-month multimodal intervention with 60 min sessions of PA three times per week, calorie deficit and telephone support.²¹ Weight loss maintenance over time was assessed in a single review, in which a multicomponent intervention was used. This review demonstrated that participants who were able to lose >5% of their body weight during the intervention period continued to lose weight for up to 18 months.²⁴ This suggests that losing a substantial proportion of body weight may provide encouragement to maintain and lose more.

The type of physical activity with the most impact was group interventions of aerobic exercise alone or combined exercise aerobic and resistance exercise, which was shown to improve anthropometric measures, HRQoL and mental health. One review which performed subgroup analysis on the basis of exercise intervention type found that both aerobic and combined exercise improved anxiety and depression, but resistance exercise alone had no impact on mental health.³³ Evidence suggests that physical activity can promote multiple psychological benefits in BCS, including improved quality of life.⁷ Our analysis suggests that HRQoL can be improved by either physical activity alone, or through multicomponent interventions that include dietary advice and/or behavioural change support such as counselling. Mental health is a crucial aspect of any cancer survivors' journey and is key to managing the sequelae of the effects of treatment.⁴⁰ For BCS, this is particularly important in helping survivors to accept changes in body image, impacts on fertility and thus the subsequent ability to return to normal life.⁴¹ Mixed results were shown regarding the effects of lifestyle interventions on key biomarkers. Although increased physical activity levels have been associated with improved insulin sensitivity and increased IGF-1,⁴² the heterogeneity of our data and the fact that only three reviews had biomarkers as an outcome of interest may explain the lack of significant findings.

This review of reviews is, to the best of our knowledge, the first to be conducted in relation to the effectiveness of weight loss interventions for BCS. Our review allowed us to look at the large evidence base on all types of multimodal weight loss interventions for BCS during or after treatment. A limitation of our approach in conducting a review of reviews is the relatively high level of abstraction at which evidence is assessed, as the unit of analysis is the review rather than the primary study level. This may lose some of the nuanced evaluation of the context in which interventions are implemented, which poses challenges for making specific recommendations about which components of diet, physical activity and lifestyle interventions may be most effective in terms of their optimum

balance, intensity, duration and mode of delivery (ie, group-based or individualised). However, reviews of reviews are beneficial in allowing the assessment of a large volume of evidence across diverse interventions and outcomes.⁴³ This broader view of the evidence base rather than a focus on primary studies alone may increase the potential value of the findings for commissioners and healthcare practitioners. Our review showed some degree of overlap in the primary studies included in the 17 systematic reviews assessed. However, the evidence we included was of high quality and we believe that our review of reviews was performed with a high degree of methodological rigour and adherence to best practice guidelines.

This review of reviews has demonstrated that multimodal component lifestyle intervention is key to improving anthropometric outcomes in BCS. This mirrors findings from studies conducted in the general population.⁴⁴ Fifty per cent of BCS will either be overweight or obese, and elevated BMI has been shown to be associated with poorer long-term outcomes, less effective treatment response, reduced treatment options and longer return to normal life.^{9 25} Although patients with an elevated BMI are more likely to have a breast cancer recurrence or secondary cancer,³ it is still unclear whether losing weight will mitigate the risk for these patients. Our analysis has shown that with concomitant weight loss through weight loss interventions there can be benefits of improved HRQoL, mental health and physical functioning. This review of reviews suggests that lifestyle interventions comprising a mixture of dietary advice, physical activity recommendations and behavioural change support such as counselling should be part of the gold standard pathway for every breast cancer survivor, both during and after active treatment.

This study has suggested that the key to enabling BCS to lose weight could be through multicomponent interventions comprising dietary advice, physical activity and behavioural change support. Further research is required to determine the most effective combination/balance of these components, along with the optimum duration and intensity. Furthermore, studies with long-term follow-up are essential to assess whether positive impacts from intervention can be maintained in the long term, and crucially, whether or not this translates to a reduction in the likelihood of breast cancer recurrence. There was a paucity of evidence concerning the potential role of bariatric surgery as an effective weight loss intervention for BCS. It is likely that bariatric surgery is key to weight loss for certain groups of patients, and future research into surgical rather than simply lifestyle interventions is needed.

CONCLUSION

Further research is needed to define the optimum combination, intensity and duration of a multimodal component intervention for BCS. This would facilitate

the long-term goal of being able to provide every breast cancer survivor with an individualised treatment plan of lifestyle intervention as part of standard therapy. Part of this research would involve mapping out an algorithm to enable breast cancer clinicians to decide which lifestyle interventions are most suitable for each individual patient as part of a holistic needs assessment.

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