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Weight Loss Intervention for Breast Cancer Survivors: A Systematic Review

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Abstract

To determine the effectiveness of weight loss intervention for breast cancer survivors. From October 2012 until March 2013, Pubmed was searched for weight loss intervention trials that reported body weight or weight loss as a primary outcome. Fifteen of these studies are included in this review. Of the 15 studies included, 14 resulted in statistically significant weight loss and 10 obtained clinically meaningful weight loss of ≥5 % from baseline. Evidence was provided of the feasibility of using several methods of weight loss intervention (telephone, in person, individual, group). Successful intervention used a comprehensive approach, with dietary, physical activity, and behavior modification components. Weight loss improved cardiovascular risk factors and markers of glucose homeostasis. However, there is insufficient evidence to identify the components of this intervention that led to successful weight loss, or to determine the weight loss necessary to affect biomarkers linked to breast cancer prognosis. The small number of randomized controlled trials shared several limitations, including small study sample sizes and lack of follow-up beyond 6 months. Intervention with longer follow-up revealed weight regain, showing the importance of considering strategies to promote long-term weight maintenance. Weight loss

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intervention for breast cancer survivors can lead to statistically significant and clinically meaningful weight loss, but the limited number of interventional studies, small sample sizes, and short duration of follow-up in many studies limit our ability to draw conclusions regarding the most efficacious weight-loss intervention after a breast cancer diagnosis. The findings to date are encouraging, but research on the effect of weight loss on breast cancer recurrence and mortality, and on prevention of weight gain for women newly diagnosed with breast cancer, is needed.

Keywords

Obesity; Overweight; Weight; Weight loss; Physical activity; Exercise; Diet; Nutrition; Breast cancer; Survival; Trial

Introduction

Breast cancer is the most common female cancer after non-melanoma skin cancer [1, 2]. As a result of early detection and more effective treatment, the number of breast cancer survivors is rapidly increasing[3]. Obesity at diagnosis is associated with greater risk of disease recurrence, and of breast cancer-specific and all-cause mortality [4•, 5–10]. Compared with women of normal weight, obese women have poorer survival, irrespective of hormone receptor type or menopausal status [11]. Some evidence also suggests that women who gain weight after breast cancer diagnosis are at increased risk of breast cancer recurrence, irrespective of baseline body mass index (BMI) [12•]. Weight gain is most common for women who undergo menopause as a result of cancer therapy, and is often accompanied by changes in body composition causing fat gain and muscle loss [13]. Being overweight or obese, or gaining weight and abdominal fat after diagnosis, is associated with co-morbidity, for example diabetes, osteoporosis, cardiovascular disease, and other cancers. Cardiovascular risk factors are of particular concern because of the cardio-toxic effects of many breast cancer treatments. Poorer surgical outcome and greater treatment intolerance have also been reported for obese than for normal-weight patients. Other negative effects associated with being overweight and with obesity include fatigue, functional decline, and reduced quality of life [14•, 15–19].

Biological mechanisms through which obesity could lead to poor breast cancer outcomes include changes to hormones involved in glucose and energy metabolism (e.g. insulin, leptin, and adiponectin), cellular growth factors (insulin-like growth factors and their binding proteins), steroid hormone metabolism, inflammatory mediators, and DNA oxidative damage [8, 20, 21]. Lifestyle intervention which incorporates dietary modification and physical activity promotion has the potential to enhance survival and improve the quality of life after a breast cancer diagnosis, and is recommended as part of cancer care [14•]. However, although randomized controlled trials of weight loss by healthy overweight or obese adults have led to improvement of mechanisms associated with obesity and cancer [22], application of intervention to populations of breast cancer survivors has been rare. There are limited studies addressing the potential of weight-loss intervention to improve breast cancer outcomes [23•]. Breast cancer survivors are motivated to seek strategies to

improve their prognosis, and intervention leading to successful weight loss among this population has the potential to have a substantial effect on public health.

The objective of this systematic review is to examine research on behavioral weight loss intervention that specifically targets women who have been diagnosed with breast cancer.

Methods

Study inclusion criteria were:

1. the primary objective of the study was weight loss intervention with a focus on changing body weight (measured as change in weight, BMI, percentage (%) body fat, or percent overweight), and;
2. the study was conducted exclusively on women diagnosed with breast cancer.

All interventional study designs (randomized or quasi-experimental, controlled or pre-post test) and age groups (pre and post-menopausal) were included. Intervention included any combination of diet, physical activity, and/or behavioral components with a focus on weight loss. Intervention could be in-person, by telephone, via the internet, or via smart-phone application, and in a one-to-one or group setting.

The electronic database Pubmed was searched from October 27th, 2012, to March 13th, 2013. Pubmed MeSH search terms included: “weight loss” AND “breast neoplasms” OR “breast cancer” AND “survivor”. References were imported into reference-management software and checked for duplicates. The first reviewer used inclusion and exclusion criteria to screen titles and abstracts. A second reviewer assessed the resulting reference list, and consensus was reached regarding articles for full-text review. Full reference checks were conducted for each full-text publication to assess other studies relevant to the research question.

Data extracted by the first reviewer included study design, intervention design (diet component, physical activity component, behavioral and/or cognitive component), duration, analysis strategy, participants and eligibility, exposure and outcome measures, retention, and changes to body weight, BMI, or fat percentage. Secondary outcomes were also extracted. Weight-loss targets were recorded, and success in meeting study weight-loss targets was calculated if the data were not presented.

Results

Literature Search (Table 1)

Eighty-one references were identified in Pubmed, with eight studies duplicating results. Initial screening by title yielded 73 references potentially meeting the review criteria. Fifty-four citations were excluded at abstract level; the full text of the other 19 was then reviewed for results. A further five studies were excluded. Reasons for exclusion included:

- participants were not breast cancer survivors (3);
- study outcomes did not include a measure of weight, BMI, or body fat (20);

- the study did not involve intervention (35);
- the study was still in progress (1); or
- the study reported duplicate findings (8).

Study Results (Table 2)

Fourteen studies met the inclusion criteria for the review. A further study was obtained by reference review, yielding the total of 15 studies included in this systematic review.

Study Design

Of the intervention reviewed, eight was in randomized controlled trials (*n*=23–239) [24–31]. Four studies were single-cohort, experimental intervention studies [15, 31–33], one was a controlled, non-randomized trial [34], one study was a randomized, crossover trial [35], and two studies were randomized, parallel intervention trials[36, 37].

Intervention

Eleven studies used a multi-component intervention design, incorporating diet, physical activity, and behavior modification [15, 25–28, 31–34, 36, 37]. Five types of intervention combined personalized lifestyle telephone counseling with face-to-face group-based education. Three studies based their intervention on those with previously established efficacy for other overweight and obese populations, including the diabetes-prevention program (DPP) [15, 36] and the commercial Weight Watchers (WW) program [25]. Telephone plus in-person group counseling was used for education on diet, physical activity, and behavior modification in two studies [27, 28]. Group teleconferencing was used for similar multi-component intervention for remote, rural breast cancer survivors [32].

Half the studies incorporated one-to-one, in-person multi-component intervention, including group-based counseling [26, 31, 33], and one-to-one counseling [34, 37]. Four studies provided dietary intervention without physical activity or behavior modification, by use of in-person dietary counseling [24, 29, 30, 35].

Weight Loss Success

Fourteen studies reported statistically significant weight loss (loss of 3–12.5 % of baseline body weight). Four studies reported significant weight change after intervention [15, 31–33], and eight studies achieved statistically significant weight loss in the intervention group compared with the control group [24–28, 34, 37, 38]. Two studies achieved substantially greater weight loss with one intervention than with a comparison intervention [35, 36]. One intervention, using a single dietary constituent for weight loss (green tea), had no significant effect on weight [30]. Ten studies achieved greater than 5 % weight loss, including two, three, four, and six-month weight loss phases [15, 24, 25, 27, 28, 32, 34, 35, 37, 38]. Five studies achieved less than 5 % weight loss [26, 30, 31, 33, 36]. Studies with follow-up and measurement of weight-loss maintenance after the weight-loss phase revealed weight regain [15, 25, 26, 36]. However, when participants were analyzed on the basis of weight loss success, those who lost ≥5 % body weight during the intervention continued to lose weight for up to 18 months [28].

Exposure and Outcome Measures

The primary outcome for most studies was weight loss or percentage change in body weight from baseline. Weight loss targets included: ≥5 % [28, 35], 7 % [15, 36], 10 % [25, 32], 1–2 lbs/week [34, 37], 10 kg from baseline [24], or achieving a healthy body weight for height [38], or were not specified [26, 27, 30, 31]. Mean baseline BMI was similar for studies in which participants achieved ≥5% weight loss (range 28–35 kg m^{-2}) and those in which participants achieved <5 % weight loss (range 30–34 kg m^{-2}) from baseline. Baseline characteristics and weight change are summarized in Table 3. Four studies met their intervention targets for weight loss [25, 27, 28, 32]. Seven studies achieved ≥5 % weight loss in the intervention group. Weight loss success was associated with meeting attendance and intervention adherence [15, 25, 26].

Secondary outcomes included waist circumference (WC), BMI, waist and hip measurements, and percentage body fat. Beneficial changes to these variables in response to weight loss were reported in seven studies [15, 27, 28, 32, 35, 36, 38], and particularly in studies in which participants lost >10 % of body weight [25]. Several studies reported statistically significant improvements in measures of blood lipid (total cholesterol, HDL-cholesterol, triglycerides) [27, 28, 34, 37, 38], and two studies did not achieve significant improvements [15, 26]. In the Cancer Survival Through Lifestyle Change (CASTLE) study, reductions of triglyceride levels were significant for group-based intervention only versus telephone-based intervention [36]. A plant-based olive oil diet led to lower triglycerides and higher HDL-cholesterol than a low-fat diet (p=0.001) [35]. The green tea intervention resulted in elevated HDL-cholesterol levels (p=0.003) [30]. Six studies measured biomarkers associated with breast cancer risk and prognosis (fasting glucose, glucose homeostasis (HOMA-IR), insulin-like growth factor-I (IGF-I) and its binding proteins (IGF-BP1 and IGF-BP3), insulin, leptin, adiponectin, ghrelin, C-reactive protein, estrone, estradiol, and sex hormone-binding globulin (SHBG)). Improvements were obtained for measures of glucose metabolism, adipokines, and SHBG [26, 28, 32, 37].

Four studies assessed psychosocial quality of life (QOL), including use of symptom checklists, fatigue inventory, depression severity, and body image, revealing improvements in response to the intervention. Two types of multi-component intervention that achieved QOL improvements also achieved ≥5 % weight loss and significant improvements in measures of physical activity [15, 32]. One study reported high baseline QOL, and improvements were not significant [31]. Despite <5 % weight loss, lifestyle intervention led to significant improvements in QOL measures for women undergoing treatment for breast cancer in one multi-component intervention [33].

Dietary intake was measured by use of the 24-hour recall method [32], the three-day diet record [15, 25, 35], and the food frequency questionnaire (FFQ) [26, 31, 34]. Physical activity was measured by use of a questionnaire [26, 31, 32], by maximum-graded treadmill testing [15], recorded minutes per week of moderate–vigorous activity [33], and seven-day physical activity recall (PAR) [27]. On the basis of the studies that reported dietary intake at baseline and follow-up, calorie intake was reduced by approximately 300–500 kcal/day in the intervention groups [25, 26, 30, 31, 37, 38]. Fruit and vegetable intake increased by 1–

3.7 servings/day [31, 32]. Percentage of calorie intake from fat was substantially reduced in four studies [15, 31, 32, 38]. Physical activity was reported to increase substantially in five studies [15, 27, 31–33].

Discussion

This review summarizes the evidence for effects of weight loss intervention for breast cancer survivors. Over half of women with a breast cancer diagnosis are overweight or obese [14•], and adjuvant chemotherapy contributes to weight gain after diagnosis [4•, 39]. As well as increasing the risk of other chronic conditions, including type II diabetes and cardiovascular disease, being overweight or obese combined with progressive weight gain is associated with reduced breast-cancer-specific and overall survival [10]. These findings support the hypothesis that intervention to promote attainment of a healthy body weight or to delay progressive weight gain have the potential to affect prognosis, although little is currently known regarding the effect on breast cancer recurrence and mortality of intentional weight loss conducted in a randomized-controlled-trial setting.

Weight loss was proved feasible for populations of overweight or obese breast cancer survivors. More success was reported from use of multiple-component (diet, physical activity, and behavior modification) rather than single-component intervention. Weight loss was facilitated by both in-person and telephone counseling in either a one-to-one or group setting.

Most weight loss intervention achieved over 5 % weight loss from baseline. A 10 % weight loss target has been adopted in many weight loss trials [40]. However, weight loss of 5 % or more is believed clinically meaningful by the United States Preventive Services Taskforce [41]. Future studies will need to address gaps in the literature regarding the effect of intentional weight loss on breast cancer recurrence and mortality, to determine the most appropriate weight loss target of clinical benefit to women who have been treated for breast cancer.

Weight loss intervention attendance and completion are associated with improved weight loss outcomes [42], and the results in this review support this conclusion. Overall, enrollment was similar (range 20–93 %) in studies that led to ≥5 % versus <5 % weight loss, and retention was also similar (in the range 61–97 %). These figures reflect both the difficulty of minimizing loss to follow-up in weight loss studies, which commonly report dropout as high as 80 % [42], and the high motivation of breast cancer survivors to improve their health status. However, women who have been treated for breast cancer report poor compliance with exercise and dietary change, revealing the need for intervention that promotes compliance [43].

The method of intervention varied between studies, including in-person counseling, telephone counseling, or both. A greater proportion of studies that resulted in ≥5 % weight loss used both methods. In-person counseling for weight loss has been regarded as the best method; however, telephone and internet-based intervention may improve reach and reduce costs of implementation, improving feasibility [44]. Evidence also supports the effectiveness

for healthy populations of mobile or cell phone technology intervention that incorporates self-monitoring (diet, physical activity), feedback on performance, networks of social support, and design of the intervention for short-term weight loss [45]. Telephone-based lifestyle intervention also results in significant weight change for overweight and obese adults [46].

Systematic comparisons of group-based and individual-based weight loss intervention have obtained mixed results as a result of intervention heterogeneity. However, a recent meta-analysis of RCTs of obesity treatment for healthy adults that included at least one group-based and one individual-based treatment group found that group-based intervention was more effective up to 12 months [47]. Group-based intervention is also more cost-effective; given the need for long-term follow-up to support weight loss maintenance, it may be a more feasible mode of delivery. The findings of this review support both strategies for promoting weight loss for breast cancer survivors.

Multi-component weight loss intervention (diet plus physical activity) has been shown to achieve significantly greater weight loss than single component intervention (diet or exercise only) [40, 48]. Current weight-management guidelines recommend comprehensive and high-intensity (12 to 26 sessions per year) multi-component intervention for weight loss in the general population [41]. All but three [30, 34, 36] of the types of intervention that led to clinically meaningful weight loss in this review combined counseling on diet, physical activity, and behavior modification. Most studies that resulted in ≥5 % weight loss achieved calorie intake reduction of approximately 300–500 kcal/day, and substantially increased physical activity from baseline. Two of the successful types of intervention modified weight loss programs and resources with previously established efficacy, including the diabetes prevention program (DPP) and Weight Watchers program [15, 25]. Intervention materials for the DPP have been adapted to ascertain effectiveness for different populations at community level [49] and offer an established model that could potentially be used in future clinical intervention for breast cancer survivors.

Intervention that targets health-behavior change, including changes to diet and physical activity, should be based on theories of behavior change. Theory-based intervention targets causal determinants of behavior change, provides the basis for evaluation of effectiveness [50], and enables assessment of the predictors of attrition [42]. Two studies that resulted in >5 % weight loss based their intervention design on theoretical frameworks, including the transtheoretical stages of change model [15] and social cognitive theory [25]. Lifestyle intervention strengthened by theory will improve understanding of which components of intervention contribute to weight loss success for breast cancer survivors, which is unclear from this review.

Five studies did not achieve clinically meaningful weight loss of 5 %. Four of these used in-person counseling only [26, 30, 31, 33] and one used a combination of individual telephone and in-person group counseling [36]. Although not clinically meaningful, three did achieve statistically significant weight loss. Four studies used multi-component intervention, with two underpinned by theory. The study that did not result in statistically meaningful or

clinically significant weight loss used diet intervention only [30]. Calorie prescription was comparable with that for studies that resulted in clinically meaningful weight loss.

Baseline characteristics of participants in studies resulting in <5 % weight loss differed from those in studies achieving at least 5 % weight loss. Half of the studies targeted African American or Hispanic women, and four enrolled both pre and post-menopausal women in comparison with the primarily non-Hispanic white, postmenopausal populations investigated in the studies achieving ≥5 % weight loss. African American women have been shown to lose less weight than other sub-groups receiving behavioral weight loss intervention [51]. Factors contributing to higher calorie intake and reduced physical activity in this population include the cultural influence of food, a lack of social support, socioeconomic status, and limited access to opportunities for physical activity and to healthy food. Personal weight loss targets may also differ with ethnicity and affect success [31]. One intervention was tested for women currently undergoing treatment for breast cancer [16], and findings may not generalize to post-treatment breast cancer survivors.

It may be that prevention of weight gain during treatment is as important to breast cancer prognosis as weight loss after treatment. Few studies have addressed prevention of weight gain for women receiving adjuvant chemotherapy. A diet and physical activity feasibility study found reduced body weight (p=0.002) and percentage fat mass (p=0.01) for nine women undergoing treatment compared with a historic control [52]. These results were supported by the Survivor Training for Enhancing Total Health (STRENGTH) trial, which tested a calcium-rich diet plus exercise intervention versus calcium-rich, high fruit and vegetable, low-fat diet plus exercise, compared with a calcium-rich diet control group, on ninety pre-menopausal women on adjuvant chemotherapy. Participants in the multi-component intervention gained substantially less percentage body fat compared with the other groups (p=0.047) [53]. Future studies must examine how to prevent weight gain by women newly diagnosed with breast cancer.

Limitations

The lack of randomization in a number of studies may have contributed to selection bias and an inability to account for known, unknown, and unmeasurable confounding factors [54]. Four studies lacked a control group, making it difficult to determine which interventional components contributed to weight loss success. Most study samples were small, with 14 to 239 participants. Eight studies enrolled fewer than 50 participants. Future well-powered studies will enable assessment of a broader set of biomarkers associated with risk of breast cancer recurrence and correlates of weight loss success.

All studies resulting in clinically meaningful weight loss enrolled primarily non-Hispanic white, post-menopausal women. This limits generalizability to ethnically diverse populations and ability to assess the effects of weight loss for pre versus post-menopausal women. Estrogen receptor-negative tumors, which are more aggressive than estrogen receptor-positive tumors and are believed to be less responsive to changes in adiposity, are much more common in African American and Asian women [55]. Recent findings have found that the effects of obesity on breast cancer risk for pre versus post-menopausal women may also depend on breast cancer receptor status [56], although a recent meta-analysis found

increased cancer risk for both pre and post-menopausal obese women [10]. Whether menopausal status has an effect on weight loss success for women after treatment for breast cancer is unclear from this review.

Whereas some studies reported calorie intake, adherence was primarily assessed by amount of weight lost. However, accurate nutrition assessment will be important in future studies with the objective of determining the most appropriate dietary prescription for weight loss success for breast cancer survivors. Dietary intake was measured by use of tools that rely on self-reporting. Under-reporting of calorie intake by people who are obese is a limitation of commonly used methods of nutrition assessment [57]. An unannounced multi-pass 24-hour recall with portion size estimation is less prone than other methods to under-reporting by obese populations [58].

Ten studies included physical activity as a means of weight loss. The physical activity reported included many different types (aerobic training, circuit training, strength training), frequencies, and durations. The methods used (supervised, non-supervised, and lifestyle approaches to increase PA) also varied among studies. Because of the diverse procedures used in these studies, this review was unable to determine the optimum physical activity stimulus (type of exercise, duration, intensity, and volume) necessary to provide weight loss benefits to breast cancer survivors. To enable clinical recommendations, future studies should provide details of all intervention components including which type and how much physical activity participants perform. It is clear from the varied intervention and outcomes that additional research is needed to specify the exact physical activity associated with the most efficient weight loss for breast cancer survivors. This review was unable to determine the beneficial effects of physical activity, irrespective of weight loss, from the biomarkers that were assessed.

Future Directions

Appropriately powered randomized controlled intervention is needed to establish whether weight loss by overweight or obese women that have been treated for breast cancer affects breast cancer outcomes (recurrence and mortality), and to determine which components of intervention contribute to weight loss success. With the field of cancer survival gaining increasing attention, several clinical trials are in progress to test the efficacy and effectiveness of weight loss intervention for breast cancer survivors. As of March 2013, twelve studies in progress or pending publication were registered on ClinicalTrials.gov (Table 4) [59]. These studies may overcome some of the limitations noted in this review.

Conclusion

The results of this review suggest that statistically significant and clinically meaningful weight loss via diet, physical activity, and behavioral intervention is feasible for breast cancer survivors. Multimodal approaches (in-person, telephone, individual, and group counseling) can lead to successful outcomes. Intervention achieving greater success incorporated more than one component (diet, physical activity, and behavior modification). Community-based weight loss intervention, with established efficacy, is one means of wider implementation to involve the growing number of breast cancer survivors who may benefit

from weight loss. Intervention that achieved clinically meaningful weight loss involved a greater proportion of non-Hispanic white, post-menopausal participants than that which did not. Future studies should investigate how these factors affect weight loss success. The limited number of well-powered randomized trials highlights the need for future studies to determine whether weight loss improves outcomes for breast cancer survivors, and which components of weight loss intervention are effective. Because weight gain is common after breast cancer diagnosis, studies on prevention of weight gain in the first year after diagnosis are also warranted.

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Table 1

Search terms and number of citations included

Search terms	Number of citations
(“weight loss”[MeSH Terms] OR (“weight”[All Fields] AND “loss”[All Fields]) OR “weight loss” [All Fields]) AND (“breast neoplasms”[MeSH Terms] OR (“breast”[All Fields] AND “neoplasms”[All Fields]) OR “breast neoplasms” [All Fields] OR (“breast”[All Fields] AND “cancer”[All Fields]) OR “breast cancer”[All Fields]) AND (“survivors” [MeSH Terms] OR “survivors”[All Fields])	81
Number of citations searched	81
Number of citations reviewed by title	81
Number of citations excluded at title level	8
Outcome not weight loss or fat loss	1
Not an intervention	7
Number of citations reviewed by abstract	73
Number of citations excluded at abstract level	54
Participants not breast cancer survivors	3
Outcome not weight loss or fat loss	19
Not an intervention	28
Duplicate reporting of study findings	4
Number of citations reviewed for results at full text level	19
Number of citations excluded at full text level	5
Duplicate reporting of study findings	4
Study in progress	1
Number of citations included for review	15[a]

[a] One additional reference obtained from reference list review

Table 2

Table of studies

	Study design	Participants and eligibility	Exposure and outcome measures	Results
Befort et al. 2012 [32]	*Design*: Single-arm, experimental, pre-post test intervention feasibility study *Intervention*: Multi-component weight loss intervention. 24 consecutive weekly telephone conference meetings (60-minute duration). Group telephone conference call technology delivery to enable rural access and real-time peer support. Weight loss target: 10 % weight loss from baseline. *Diet* Reduced calorie diet (reduction of 1,000 kcal/day); participant-purchased, investigator-approved pre-packaged frozen entrees and study-provided shakes; dietary counseling to increase fruit and vegetable intake (>5 servings/day) *Physical Activity (PA)* Target: 225 min/week moderate intensity exercise (brisk walking); pedometer use and physical activity log. *Behavioral* Self-regulation skills: target setting, self-monitoring, problem solving for barriers (accessing PA, healthy foods, social eating setting, stimulus control). Social support to improve diet and PA behavior, move toward self-efficacy. *Duration*: 6 months *Analysis*: Intent to treat (ITT) and per procedure (completers) pre-post analysis of intervention. Exploratory analyses for baseline correlates of % weight loss (history of chemotherapy, anti-hormone therapy, large vs. small rural community, education).	*Study Population:* Overweight or obese breast cancer survivors *Study Sample: N* = 34 Breast cancer (Stage I–IIIc) diagnosed past 10 years; ≥ 3 months post treatment; weight stable (<10 lb fluctuation previous 3 months); postmenopausal, aged <75 years; BMI 27–45 Kg m^{-2}. *Setting*: Living in remote rural locations in and around Kansas, USA	*Primary Outcome*: Weight *Secondary Outcomes*: Waist circumference (WC); serum biomarkers (fasting insulin, leptin, adiponectin); QOL (assessed by use of the breast cancer prevention trial symptom checklist); the brief fatigue Inventory; the patient health questionnaire PHQ-9 assessing depression severity; the 32-item body image and relationships scale *Exposure Measures*: Dietary intake (assessed using 2 × 24-hour dietary recalls, including one week and one weekend day); PA (assessed using Minnesota physical activity questionnaire)	*Enrollment and retention*: 83 % enrollment; 91 % retention (attending 75 % intervention sessions and completing data collection). *Outcomes:* Significant changes ($P < 0.001$) in: ITT: Weight (−11.6 ± 6.5 kg or −12.8 ± 6.8 % weight loss) Among completers: Weight (−12.4 ± 5.8 kg, 13.9 % weight, $P < 0.001$) ITT: WC (−9.4 ± 6.3 cm, $P \leq 0.001$) Daily energy intake (−349 ± 550 kcal/day, $P \leq 0.001$) VF intake (+3.7 ± 4.3 servings/day, $P \leq 0.001$) Fat intake (−12.6 ± 8.6 %, $P \leq 0.001$) PA (+1235 ± 832 kcal week) Fasting insulin (−16.7 %, $P = 0.006$) Leptin (−37.1 %, $P \leq 0.001$) Improvements in QOL
Campbell et al. 2012 [15]	*Design*: Single-cohort, experimental pre-post test intervention feasibility study *Intervention*: Weight loss target: 7 % from baseline 24-week group-based lifestyle intervention modeled on the diabetes prevention program (DPP). Weekly group session for 2 months; bi-weekly group sessions for 3–6 months. *Diet* Individually prescribed, reduced energy diet with <20 % calories from fat; no specific calorie target but counseling to reduce calorie intake; 16 diet sessions led by a registered dietitian. *Physical Activity* 150 min/week moderate-to-vigorous exercise (e.g. walking). Telephone-based counseling to promote home-based activity plus two supervised 45-min exercise sessions per week for 24 weeks.	*Study Population*: Overweight or obese breast cancer survivors *Study Sample: N* = 14; early-stage breast cancer survivors (stage I–IIIa) diagnosed past 5 years; post-menopausal; BMI 25–35 kg m^{-2}; adults >18 years; prior completion of adjuvant treatment *Setting*: Recruitment from British Columbia Cancer Agency (Vancouver, BC, Canada)	*Primary Outcome*: % weight loss from baseline *Secondary Outcomes*: BMI; % fat (DEXA); waist circumference; hip circumference; aerobic fitness (maximum graded exercise test); QOL (functional assessment of cancer therapy–breast); blood biomarkers associated with CVD and diabetes risk (total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, C-reactive protein (CRP), c-peptide, glucose, insulin).	*Enrollment and retention*: 43 % enrollment 67 % retention *Outcomes*: 6-month: Weight loss (−3.8 ± 5.0 kg; P=0.01) BMI (−1.4 ± 1.9 g m^{-2}; $P = 0.01$) WC (−4.2 ± 6.6 cm; $P = 0.03$) HC (−5.5 ± 5.3 cm; $P < 0.01$) Fat mass (−3.3 ± 3.7 kg; $P < 0.01$) % body fat −2.4 ± 2.7 %; $P < 0.01$) Lean body mass (−0.6 ± 1.9 kg; $P < 0.001$) 9-month: Total 6 % weight loss from baseline (+2.6 % to −18.9 %) Aerobic fitness increased 11 % (VO2 peak by maximum graded treadmill test +0.2 L min^{-1}; $P < 0.001$)

	Study design	Participants and eligibility	Exposure and outcome measures	Results
	Behavioral Food records *Duration*: 6-month weight loss intervention; 9-month follow-up from baseline. *Analysis*: Pre-post test analysis. Independent samples t-test to compare differences in demographic factors and adherence between successful (7 % weight loss) and unsuccessful weight loss at 24 weeks.		*Exposure measures:* Dietary intake (3-day diet record)	PA metabolic equivalent hours/week increased 13.1 ± 12.3 ($P < 0.01$) No significant changes in blood biomarkers. 9-month follow-up: no significant changes in energy intake based on food records; decreased energy from fat ($P = 0.09$) and grams of fat ($P = 0.1$). Participants who lost >7 % weight were older and attended more diet and/or PA sessions.
De Waard et al. 1993 [24]	*Design:* Randomized controlled trial *Intervention:* Weight loss target: 10 kg from baseline 1) *Intervention* *Diet* Individualized dietary counseling with research dietitian. Calorie target of 1,500 kcal/day (1,000 kcal/day if participants did not achieve weight loss targets) *2) Control* Usual Care *Duration:* 6-month weight loss phase; 3 years follow-up *Analysis:* Wilcoxon two sample test for weight change in intervention versus control.	*Study Population:* Overweight or obese (at least 10 kg overweight) breast cancer survivors *Study Sample:* $N = 48$; adults 18–70 years; breast cancer diagnosis (Stage I–II) past 4 years; Chemotherapy and/or radiation therapy completed >3 months before. *Setting:* Recruitment from 3 hospitals in the Netherlands and Poland	*Primary Outcome:* Weight loss	*Enrollment and retention:* 93.1 % enrollment; 61.1 % retention in The Netherlands; 87.5 % retention in Poland. *Outcomes:* 6-month weight loss: −6 kg intervention group; +0.5 kg in the control group ($P <$ 0.001 at 1-year follow-up); highest quartile for weight loss −8 kg at 3 years; lowest quartile for weight loss +0.5 kg at 3 years.
Djuric et al. 2002 [25, 60]	*Design:* Randomized controlled pilot intervention trial *Intervention:* Weight loss target: 10 % from baseline Individualized telephone weight loss counseling with or without commercial Weight Watchers program versus control. Weekly dietitian counseling for 3 months, bi-weekly counseling months 3–6, monthly counseling 6–12 months. *Weight Watchers program* Weekly commercial weight watchers (WW) meetings. *1) Individualized cohort* *Diet* 500–1,000 kcal/day calorie intake reduction from maintenance requirements using the American Dietetic Association Exchange List diet plan. Fat target 20–25 % calories. Five servings fruit and vegetables per day. Emphasis on fiber and whole grain intake. Daily food records. *Physical Activity* Pedometers provided for self-monitoring/target setting. Daily PA records. *Behavioral* Behavioral approach using the LEARN program. Counseling based on Bandura's social cognitive	*Study Population:* Obese breast cancer survivors *Study Sample:* $N = 48$; adults 18–70 years; breast cancer diagnosis (Stage I–II) past 4 years; Chemotherapy and/or radiation therapy completed >3 months before. *Setting:* Komen Foundation Race for the Cure mailing list participants in the Detroit area, USA	*Primary Outcome:* Weight change *Secondary Outcomes:* % body fat (BIA); total cholesterol, LDL-cholesterol *Exposure measures:* Calorie and fat intake (3-day food records)	*Enrollment and retention:* 81 % retention *Outcomes:* Greatest weight loss with a comprehensive approach (individualized counseling plus social support and group meetings). Weight change: *Control* +0.85 ± 6.0 kg *Weight Watchers* −2.6 ± 5.9 kg (not significant) *Individualized counseling* −8.0 ± 5.5 kg ($P < 0.05$ at 12 months only) *Comprehensive group* −9.4 ± 8.6 kg ($P < 0.05$); achieved > statistically expected number of subjects losing 10 % body weight at 6 and 12 months (significantly higher % body fat at baseline). Weight loss not statistically significantly different from the Individualized group. Calorie intakes of intervention groups reduced vs. baseline (no significant differences between groups). Mean fat intake increased in the control group, and decreased in the intervention groups at 12 months.

	Study design	Participants and eligibility	Exposure and outcome measures	Results
	theory. Counseled regarding body image, self-image and self-acceptance theory. Counseled regarding body image, self-image and self-acceptance *2) Comprehensive cohort* Individualized counseling plus WW. *3) Control:* Received printed healthy eating materials. *Duration:* 12 months *Analysis:* Paired student's t-tests and ANOVA for significance between groups. Pearson Product correlations for measurement of associations.			Weight loss significantly correlated with attendance at WW meetings. Number of contacts made not significantly associated with amount of weight-loss. >10 % weight at 12 months associated with significantly lower: Body weight ($P < 0.05$); BMI ($P < 0.01$); % body fat ($P < 0.001$); calorie intake ($P < 0.05$); dietary fat % ($P < 0.05$); triglycerides ($P < 0.01$), and increased leptin ($P < 0.001$).
Flynn et al. 2010 [35]	*Design:* Randomized, non-controlled crossover pilot intervention *Intervention:* Weight loss target: 5 % from baseline. *Diet* 1,500 calorie diet using meal plans and recipes 1) National Cancer Institute (NCI) diet (15–30 % calories from fat, unlimited fruits and vegetables, minimum 5 servings fruits and vegetables/day, up to 7 oz lean meat/day, canola oil as a source of fat) 2) Plant-based olive oil diet (PBOO, >3 tbsp olive oil/day, unlimited vegetables, 3 servings/day fruit, up to 6 oz/week poultry, up to 8 oz/week seafood). Whole grains and legumes promoted on both diets. 3-day food records at weeks 4, 8, 12, and 24. *Duration:* Eight-week weight loss phase with randomized diet; 6-month follow-up with self-selection of study diet. *Analysis:* Crossover trial analysis; (1) paired t tests comparing baseline to end point differences in outcomes between the two diet trials, (2) independent samples t test for a period effect of administered trial, independent of diet type, (3) tests for interaction between treatment and period; comparison of proportions of women achieving >5 % weight loss between the two diets.	*Study Population:* Overweight breast cancer survivors *Study Sample: N*=44 Aged >50 years (post-menopausal); within 4 years adjuvant treatment; BMI 25–35 kg m^{-2} or weight gain of >10 kg from age 18 years for women with BMI < 25 kg m^{-2}. *Setting:* Participants recruited at physicians' offices and oncology treatment centers in Rhode Island, USA.	*Primary Outcome:* % weight loss *Secondary Outcomes:* Weight, BMI, % body fat; % fat free mass; waist circumference; hip circumference; total cholesterol; triglycerides; HDL-cholesterol; LDL-cholesterol; glucose; insulin; C-reactive protein; serum carotenoids. *Exposure measures:* Dietary intake (3-day food record)	*Enrollment and retention:* 63 % retention at 4 weeks. *Outcomes:* % weight change significantly greater for NCI vs. PBOO and vice versa depending on diet consumed first. NCI first: (NCI −4.6 ± 1.5 %, PBOO (−3.1 ± 1.7 %, $P = 0.001$) PBI first: (NCI: −3.3 ± 2.2 %, PBOO: −6.5 ± 1.6 %, $P = 0.001$). Period effect analysis (first-administered diet): 80 % achieved ≥ 5 % weight loss (PBOO) vs. 31 % (NCI diet) ($P < 0.01$). PBOO: Significantly greater percentage weight loss (−4.6 ± 1.5 NCI, −6.5 ± 1.6 PBOO, $P < 0.01$). Lower triglycerides (NCI 105 ± 46 mg dL^{-1}, PBOO 96 ± 37 mg dL^{-1}, $P = 0.06$) and higher HDL-cholesterol (NCI 64 ± 13 mg dL^{-1}, PBOO 68 ± 12 mg dL^{-1}, $P = 0.001$). No difference in change in fat-free mass.
Stendell-Hollis et al. 2010 [30]	*Design:* Randomized, double-blind, placebo-controlled trial *Intervention:* 2-week run-in period with daily intake of 960 mL herbal tea. Tea consumption on study site. *1) Intervention group* *Diet* Daily decaffeinated green tea consumption: 550–700 mg tea solids per tea bag (58.91 mg catechin, 32.21 mg EGCG, 6.68 mg caffeine per bag). *2) Control group* Daily citrus-based herbal tea consumption *Duration:* 6 months	*Study Population:* Overweight and obese breast cancer survivors *Study Sample: N* = 54 Breast cancer survivors (stage I–III); diagnosis at least 12 months earlier and <10 years prior; BMI 25–40 kg m^{-2}; had received chemotherapy for invasive breast cancer; adults 18–80 years *Setting*: Women residing in Southern Arizona, USA	*Primary Outcome:* Body weight and body composition (% body fat, % lean mass) change, DXA) *Secondary Outcomes:* Waist circumference; hip circumference; resting metabolic rate (RMR); fasting lipids; glucose; insulin; homeostasis model assessment for insulin resistance (HOMA-IR) *Exposure measures*:	*Enrollment and retention:* 73 % of enrolled women randomized 72 % retention *Outcomes:* Completers ($N = 39$): Average tea intake 5952±1176 mL/week; Green tea associated with significant reduction in calorie intake ($P = 0.02$). Change in body weight −1.2 kg (green tea) versus +0.2 kg (placebo) (not statistically significant). Decaffeinated green tea intake associated with elevated HDL ($P = 0.003$) and non-significant improvements in the HOMA-IR

	Study design	Participants and eligibility	Exposure and outcome measures	Results
	Analysis: Pre-post intervention analysis of change in outcomes; independent Student t-tests to examine differences in demographic and clinical characteristics and 6-month changes in measures between groups.		Dietary energy and macronutrient intake (Arizona food frequency questionnaire); physical activity (Arizona activity frequency questionnaire, AAFQ)	(−1.1 ± 5.9: green tea; +3.2 ± 7.2: herbal) and the HDL-to-LDL ratio.
Goodwin et al. 1998 [33]	*Design:* Phase II non-randomized intervention trial *Intervention:* Weight loss target: weight maintenance for normal weight participants; 10 kg weight loss or achieve a healthy BMI for overweight or obese participants. Group-based counseling with individualized weight, nutrition, and physical activity targets. Weekly sessions for 10 weeks followed by monthly sessions for 10 months. *Diet* Education on Canada's food guide with guidance on meal planning. Individualized, written feedback. *Physical Activity* Counseled to increase incidental activity, guidance on strength and flexibility exercises three times/week, plus moderate aerobic activity (70 % maximum heart rate). *Behavioral* Motivational counseling, education on emotional eating, social support, coping strategies, problem solving, target setting and relaxation. *Duration:* One year *Analysis:* Intention to treat analysis of changes in variables between baseline and one year. Analysis of variance of characteristics of successful versus unsuccessful participants.	*Study Population:* Breast cancer survivors currently undergoing standard adjuvant treatment *Study Sample: N* = 61 Diagnosed Stage I–III breast cancer; BMI 20–35 kg m^{-2}; aged <70 years *Setting:* Participants recruited from University of Toronto Centers	*Primary Outcome:* Avoidance of weight gain in normal weight participants; weight loss in overweight or obese participants *Secondary Outcomes:* Skin fold thickness; physical activity (usual activity and functional limitation); psychosocial (profile of mood states, POMS; psychosocial adjustment to illness scale, PAIS; family environment scale, FES, mental adjustment to cancer scale, MAC, Courtauld emotional control scale (CECS), impact of events scale (IES), eating inventory (EI), eating habits questionnaire (EH), and European Organization for the Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ C-30) *Exposure measures:* Dietary intake (24-hour weighed food records on 3 randomly selected days)	*Enrollment and retention:* 70.9 % retention *Outcomes:* Mean weight loss −0.53 ± 3.72 kg. For overweight women, 70.9 % successful (lost 1.5 kg). Weight loss greater in women overweight at baseline: −1.63 ± 4.11 kg (P = 0.01 vs. normal weight) and women not receiving chemotherapy (+2.15 ± 2.83 kg, P = 0.0004). Physical activity increased significantly (63.5 ± 54.2 vs. 108.9 ± 58.7 min/week, P = 0.00005). Aerobic exercise predicted success (OR 1.73 for each additional 30 min of weekly exercise, P = 0.003). Calorie intake not significantly changed. Fat intake decreased; carbohydrate and fiber intake significantly increased. Total mood disturbance significantly improved (P < 0.001), IES (P < 0.03), PAIS (P = 0.009) and EORTC QLQ C30 GHRQL (P < 0.0005).
Greenlee et al. 2012 [26] The La Vida Activa/An Active Life study	*Design:* Randomized, controlled crossover pilot intervention trial *Intervention:* The Curves Weight Management Program *Diet* High-vegetable, low-fat, calorie-restricted diet plan plus weight loss education taught through six 1-hour group sessions over 6 weeks using books, DVDs and discussion. *Physical Activity* 30 minute exercise circuit 3 times/week (target 5 times/week); membership at Curves centers 1) *Immediate Cohort* (IA): 6 months Curves weight loss program followed by 6 months observation	*Study Population:* African American and Afro-Caribbean breast cancer survivors *Study Sample: N* = 42 9 % Hispanic, 21 % black; pre and post menopausal; overweight and obese adults; breast cancer survivors (stage 0–IIIa); >6 months post-treatment; sedentary; BMI >25 kg m^{-2} *Setting:* Hispanic and black women recruited from New York, USA	*Primary Outcome:* Weight change *Secondary Outcomes:* Body composition (DXA); cardiovascular fitness (VO2max); cholesterol, triglycerides, glucose, hs-CRP *Exposure measures:* Physical activity (Kaiser physical activity survey); dietary intake (Spanish and English 110-item NHANES block questionnaire)	*Enrollment and retention:* 37.5 % enrollment 91 % retention at 12 months *Outcomes:* Weight loss: IA: −3.3 ± 3.5 % WCA: −1.8 ± 2.9 (P = 0.04). Six months: Mean difference between groups: −1.8 kg (P = 0.03). No differences in weight loss by ethnicity. 12 months: weight regain in IA group, remained lower weight than baseline (P = 0.02). Higher adherence (Intervention Adherence Index) associated with more % weight loss.

	Study design	Participants and eligibility	Exposure and outcome measures	Results
	2) *Waitlist control cohort* (WCA): 6 months observation followed by 6 months Curves weight loss program (WCA): 6 months observation followed by 6 months Curves weight loss program (WCA): 6 months observation followed by 6 months Curves weight loss program *Duration:* 6-month intervention; 12-month follow-up. *Analysis:* Intent to treat (ITT). Generalized estimating equations (GEE) model with repeated measures using weight and height as covariates to examine intervention effects on weight change over 6 months.			No changes in metabolic biomarkers. Fat loss >2 %: statistically significant decreases in insulin, glucose, and HOMA-IR. Weight loss ≥5 %: statistically significant increase in IGF-BP-1 and decrease in glucose.
Harris et al. 2012 [36] The Cancer survival Through Lifestyle Change (CASTLE) study	*Design:* Randomized Clinical Trial (no non-intervention control) *Intervention:* Weight loss target: 7 % from baseline (1–2 lbs/week) In-person vs. telephone behavioral-based lifestyle weight loss program. Used the diabetes prevention program guidelines based on the stages of change theory and motivational interviewing. 1) *In-person*: 16 group-based weight loss education sessions *Diet* Counseling on calorie reduction. *Physical Activity* Counseling to increase physical activity. *Behavioral* Motivational enhancement techniques. Follow-up: monthly telephone calls (weight loss maintenance counseling). 2) *Telephone:* Weekly one-to-one weight loss counseling intervention telephone calls. Program incorporating behavioral stage of change model (pre-contemplation, contemplation, preparation, action, maintenance). Clinical testing laboratory blinded to intervention group. *Duration:* 6-month weight loss phase; follow-up to 12 months. *Analysis:* Repeated measure mixed models ANCOVA to test for differences in change in weight, waist circumference, and BMI between interventions.	*Study Population:* Overweight or obese breast cancer survivors *Study Sample: N* = 52 Stage I to IIIa breast cancer; BMI 25–45 kg m^{-2}; aged 30–75 years; completed treatment 2–36 months before baseline *Setting:* Recruitment from local cancer centers, physician referrals, and breast cancer survivor groups in Baton Rouge, LA, USA	*Primary Outcome:* Weight loss *Secondary Outcomes:* Waist circumference, lipids (cholesterol, HDL, LDL, triglycerides,) fasting glucose	*Enrollment and retention:* 56.52 % enrollment 78.8 % retention *Outcomes:* Significant within-group weight loss after 6-months for in-person (−3.3 kg ± 4.4, *P* = 0.002) and telephone groups (−4.0 kg ± 6.0, *P* = 0.01). Telephone group: Significant within-group change in BMI, waist circumference, and triglycerides In-person group: Significant within-group change in BMI and waist circumference in the in-person group. No differences in weight loss between groups. Significant weight regain during follow-up in the in-person group (+1.3 kg ± 1.7, *P* = 0.009).
Mefferd et al. 2007 [27, 61] The Healthy Weight Management (HWM) study	*Design:* Randomized, controlled intervention trial 1) *Intervention:* Cognitive behavioral therapy (CBT) with exercise and diet modification. *Diet* 500–1,000 kcal/day calorie deficit (emphasis on higher-fiber foods and adequate protein). *Physical Activity* Target: 1 hour/day moderate to vigorous PA and 2–3 muscle strengthening sessions per week. Pedometer use. *Behavioral*	*Study Population:* Overweight or obese breast cancer survivors *Study Sample: N* = 85 Aged ≥ 18 years; diagnosed stage I–IIIa breast cancer within 14 years of baseline; completion of adjuvant chemotherapy or radiation therapy; BMI ≥25 kg m^{-2}; 15 kg over ideal weight defined by Metropolitan Life Insurance tables *Setting:*	*Primary Outcome:* Weight loss *Secondary Outcomes:* Waist circumference, hip circumference, body composition (DXA); fasting cholesterol, triglycerides, HDL-cholesterol. *Exposure measures*: 7-day physical activity recall (PAR)	*Enrollment and retention:* 20 % enrollment 89 % retention *Outcomes:* Significant differences in change between groups; Intervention: Weight (−6.8 %, $P \leq 0.05$), BMI (−6.5 %, $P \leq 0.05$), % fat (−9.5 %, $P \leq 0.01$), trunk fat (−18.7 %, $P \leq 0.01$), leg fat (−18.8 %, $P <$ 0.01), waist and hip circumference ($P <$

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	Study design	Participants and eligibility	Exposure and outcome measures	Results
	Group-based CBT curriculum (standard behavioral treatment, self monitoring, setting, cognitive restructuring, attitudinal change). Self-monitoring using food diaries, exercise logs, and mood and/or feelings … 2) *Wait-list control group Duration:* 16 weeks *Analysis:* Group differences at 16 weeks	Women living in San Diego, CA, USA, recruited via community outreach and referral, and community event advertising.		0.05); triglycerides, total cholesterol, HDL cholesterol ($P \leq 0.05$)
Rock et al. 2013 Breast Cancer Survivors Health and Physical Exercise (SHAPE) study [28]	*Design* Randomized controlled trial *Intervention:* Weight loss target: ≥5 % 1) *Immediate intervention group* Weekly group sessions for 6 months and monthly to 18 months. Individualized telephone-based counseling twice-weekly for 2 weeks, weekly for 10 weeks, and monthly thereafter. *Diet* Modest reduction in energy intake. Weight loss and maintenance dietary guidance. *Physical Activity* Promotion of regular physical activity: planned aerobic exercise, increased daily physical activity, strength training. *Behavioral* Promotion of healthy eating attitudes and behaviors. 2) *Wait-list control group:* Mailed communication and monthly check-up calls. Provided with written materials and seminar. *Duration:* 6-month weight loss phase; follow-up to 18 months. *Analysis:* Independent *t*-tests to measure group differences; Regression analysis to assess biological factors and weight change.	*Study Population:* Overweight or obese breast cancer survivors *Study Sample:* $N = 220$ Stage 0–IIIa breast cancer within previous 10 years; aged ≥ 18 years; BMI >25 kg m^{-2}; 15 kg over ideal weight (defined by the Metropolitan Life Insurance tables) *Setting:* Women recruited from San Diego, California, USA	*Primary Outcome:* Serum estrogens, sex hormone binding globulin (SHBG), insulin, leptin *Secondary Outcomes:* Weight loss	*Enrollment and retention:* 85.3 % recruitment 96.8 % retention *Outcomes:* 6-month follow-up: ≥5 % weight loss ($n = 74$): −7.5 ± 3.3 kg ≤5 % weight loss ($n = 139$): +0.3 ± 2.9 kg ($P < 0.0001$) Mean weight loss −8.7 kg; Statistically significant decreases in insulin ($P < 0.0001$) and leptin ($P < 0.0001$); statistically significant increases in SHBG ($P = 0.004$).
Shaw et al. 2007 [29, 38]	*Design:* Randomized controlled trial *Intervention:* Weight loss target: achieve a healthy weight for height. *1) Intervention group:* *Diet* Individualized dietary counseling by a registered dietitian and diet plans to create 1,000 kcal/day deficit from pre-randomization diet-record derived intake. Recommendations to reduce fat and refined carbohydrate intake. Food exchange system to promote variety in intake. *2) Control group:* Written materials on healthy eating. *Duration:* 12 weeks	*Study population:* Women with lymphedema secondary to treatment for breast cancer. *Study Sample:* $N = 24$ Breast cancer survivors with diagnosed lymphedema; BMI ≥ 25 kg m^{-2}; completed chemotherapy or radiation therapy 12 months before baseline *Setting:* Women recruited from a hospital in London and the National Lymphedema Support Network	*Primary Outcome:* Arm volume *Secondary Outcomes:* Height; weight; skin-fold thickness. *Exposure Measures:* 7-day dietary records with visual prompts	*Enrollment and retention:* 48 % enrolment 87.5 % retention *Outcomes:* Control group: Weight loss −0 ± 2.97 kg; skin fold thickness −2.5 ± 9.2 mm Intervention group: Weight loss −3.3 ± 2.6 kg m^{-2} ($P = 0.02$); BMI: −1.3 ± 1.1 kg ($P = 0.016$); Skin fold thickness −5.0 ± 5.6 mm ($P = 0.426$)

	Study design	Participants and eligibility	Exposure and outcome measures	Results
	Analysis: Non-parametric Mann Whitney U-test for differences in outcomes between groups; Spearman Rank correlation coefficients.			
Stolley et al. 2009 [31] The Moving Forward Study	*Design:* Non-randomized, pre-post test intervention design. *Intervention:* *Diet* 2-weekly group education sessions related to portion control, meal planning, and healthy eating. Based on social cognitive theory and the health belief model. Culturally tailored. *Physical Activity* Two 60-minute exercise classes per week. *Duration:* 6 months *Analysis:* Per procedure analysis. Pre-post test analysis of change in outcome variables.	*Study Population:* Overweight or obese African American breast cancer survivors *Study Sample:* $N = 23$ $n = 20$ analyzed; Aged >18 years; African American; breast cancer diagnosis stage I–III, BMI >25 kg m^{-2}; completed chemotherapy or radiation therapy at least 6 months before baseline *Setting:* Women recruited from breast cancer support organizations in Chicago, USA.	*Primary Outcome:* Weight *Secondary Outcomes:* BMI; social support (social support for eating and exercise questionnaire); quality of life (functional assessment of cancer therapy, FACT-B) *Exposure measures:* Diet (block food frequency questionnaire; FFQ from NHANES food intake data); physical activity (international physical activity scale, long format, IPAQ);	*Enrollment and retention:* 60 % enrollment of eligible participants 87 % retention *Outcomes:* Mean weight change −5.6 lbs (−8.63 to −2.51, $P < 0.001$); Significant increases in vegetable intake (+1.6 servings/day, $P < 0.05$) and significant decreases in total fat intake (−23.6 g, $P < 0.03$); significant increases in median time spent in vigorous activity (from 0 min at baseline to 23.6 min at 6 months, $P < 0.02$); Significant improvement in social support.

	Study design	Participants and eligibility	Exposure and outcome measures	Results
Thompson et al. 2012 [34, 62] The CHOICE study	*Design:* Controlled, non-randomized trial *Intervention:* Weight loss target: 1–2 lbs per week (3,500 kcal per week calorie deficit through diet and/or physical activity). *Diet* 42-day cycle interchangeable menu and recipe-defined weight loss diet. Monthly dietary counseling and optional group-based education. Daily self-monitoring with food and physical activity records. 1) Low carbohydrate (LC) weight loss diet: 32 % carbohydrate, 20 % protein, 48 % fat 2) Low fat (LF) weight loss diet: 64 % carbohydrate, 20 % protein, 16 % fat 3) Usual care: optional provision of diet plan at the end of 6 months *Physical activity* Target of 10,000 steps per day; pedometer provided. *Duration:* 6 months *Analysis:* Current analysis: Per procedure analysis assessing change over time in outcome measures (lipid measures presented in this paper), with separate magnitude of change of outcomes calculated based on weight loss success. In Press: Differences across diet groups by global F test in one-way ANOVA stratified by disease stage and treatment type. Maximum likelihood method for repeated measures. Chi-square test for equal proportions for categorical data. Time-to-event (weight loss) by Kaplan-Meier log-rank test.	*Study Population:* Overweight or obese breast cancer survivors *Study Sample:* *N* = 239 BMI 25–34.9 kg m^{-2}; diagnosed stage I–III breast cancer; at least 4 months post-chemotherapy and radiation therapy *Setting:* Participants referred by physicians at a private oncology clinic in Denver, CO, USA	*Primary Outcome:* C-reactive protein *Secondary Outcomes:* Weight; BMI; waist-hip ratio; body composition (BODPOD); fasting blood glucose, lipids (total cholesterol, HDL-cholesterol, LDL-cholesterol); biomarkers of risk for breast cancer recurrence (inflammatory markers, markers of oxidation, glucose homeostasis, and sex hormones)	*Enrollment and retention:* Overall dropout rate 20 % (8 % control; 7 % low carbohydrate; 5 % low fat). *Outcomes:* Mean weight loss in both interventions −12.5 %; mean body fat loss −27.5 %; Mean waist circumference loss −9.5 %; minimum lean body mass loss (−1.3 %); >90 % of participants in the intervention arm achieved >5 % weight loss. Weight loss −9.3 ± 4.17 kg (LF); −10.46 ± 4.61 kg (LC), $P < 0.001$. Fat loss −8.85 ± 4.05 kg (LF); −9.69 ± 4.04 kg (LC), $P < 0.001$. % Fat loss −7.27 ± 3.64 kg (LF); −7.58 ± 3.62 kg (LC), $P < 0.001$. Lean mass −0.45 ± 1.42 kg (LF); −0.77 ± 1.64 kg (LC), $P < 0.001$. Waist circumference −8.55 ± 5.04 cm (LF); −9.26 ± 5.42 cm (LC), $P < 0.001$ (Henry Thompson, personal communication). No adverse effects on fasting blood lipids or glucose. Statistically significant decreases in cholesterol (4.7 %; $P = 0.0001$) and triglycerides (21.8 %; $P = 0.01$) for intervention versus control.
Thomson et al. 2010 [37]	*Design:* Randomized clinical trial (no non-intervention control group) *Intervention:* Weight loss target: 1–1.5 lb/week *Diet* Calorie-restricted diets creating a 500 kcal/day deficit. Clinic-based face-to-face counseling sessions. Sample menus, behavior change support materials, and macronutrient food logs provided. Weekly counseling for 6 weeks. 1) *Low-fat diet*: 55 % carbohydrate, 25 % fat, 15–20 % protein 2) *Low-carbohydrate diet* (modified Atkins): 35 % carbohydrate, 25–30 % protein, 35–40 % fat; carbohydrate reduction to <30 g/day for 2 weeks with increases to 35 % carbohydrate. *Duration:* 6 months *Analysis:* Changes in dietary intake and outcomes over time.	*Study Population:* Overweight, post-menopausal breast cancer survivors *Study Sample:* *N* = 40 Postmenopausal; aged 50–60 years; diagnosed stage I–II invasive, estrogen receptor positive breast cancer; completed treatment within previous 4 years; BMI 25–35 kg m^{-2} *Setting:* Participants recruited from the Arizona Cancer Center, USA.	*Primary Outcome:* Weight *Secondary Outcomes:* BMI; waist circumference; hip circumference; body composition (DXA); glucose; insulin; HnA1c; HOMA; lipids (total cholesterol, HDL, LDL, triglycerides); hs-CRP; blood pressure *Exposure measures* Dietary intake (Arizona food frequency questionnaire, AFFQ)	*Enrollment and retention:* 72 % enrollment from eligible participants 80 % retention *Outcomes:* Significant changes in weight, BMI, and waist circumference for both intervention groups. Average weight loss −6.1 ± 4.8 kg ($P < 0.001$). Reduced lean mass in both groups with Increased sarcopenia (+10 %, $P = 0.04$). Statistically significant improvements in metabolic indices in both diet groups (fasting insulin, HbA1c, HOMA, total cholesterol). No significant differences in change in metabolic indices by diet group.

kg kilograms; *PA* physical activity; *ITT* intention to treat; *WC* waist circumference; *QOL*, quality of life; *VF* vegetables and fruit; *BMI* body mass index; *HC* hip circumference; *WW* Weight Watchers; *ANOVA* analysis of variance; *NCI* National Cancer Institute; *PBOO* plant-based olive oil; *DXA* dual X-ray absorptiometry; *HOMA-IR* homeostatic model assessment; *HDL* high-density lipoprotein; *LDL* low-density lipoprotein; *WLC* wait list control arm; *GEE* generalized estimating equation; *IA* intervention arm; *SHBG* sex hormone binding globuli

Table 3

Summary of study populations and weight change (weight change is summarized for the intervention groups only)

Study	Design	Sample size	Average age (years)	Average BMI (kg m^{-2})	Average baseline weight (kg)	Average weight loss (kg)	Average % weight loss	% Caucasian	Weight loss phase (months)	% Post-menopausal
>5 % Weight loss										
Befort et al. [32]	F T D+PA+B	34	58.9 ± 7.8	33.7 ± 4.4	89.8 ± 13.6	11.6 ± 6.5	12.8[a]	97	6	100
Campbell et al. [15]	F IT+IPG D+PA+B	14	54.6 ± 8.3	30.1 ± 3.6	78.8 ± 10.7	3.83 ± 5	6	85	6	100
De Waard et al. [24]	RCT IP D	102	Not reported	Not reported	Not reported	6	Not reported	Not reported	6	100
Djuric et al. [25]	RCT IT+IPG D+PA+B	48	51.7 ± 8.4	35.5 ± 3.9	95.4 ± 13.6	2.6 ± 5.9[b] 8.0 ± 5.5[c] 9.4 ± 8.6[d]	70 % >10 %[d]	73	12	75
Flynn et al. [35]	RC D IP	44	59.2 ± 6.1	27.9 ± 2.8		(2.7 ± 1.4[e]) 3.6 ± 1.9[f]	(4.6[e]) 6.5[f]	Not reported	6	Not reported
Mefferd et al. "Healthy Weight Management" [27]	RCT IT+IPG D+PA+B	85	56.3 ± 8.2	31 ± 4.2	84.7 ± 12.6	5.7	6.8	71	2	100
Rock et al. "SHAPE" [28]	RCT IT+IPG D+PA+B	220	55 ± 10	30.4 ± 4.1 (≥5 % weight loss) 31.8 ± 5.0 (≤5 % weight loss)	82.4 ± 12.5 (≥5 % weight loss) 85.7 ± 15.3 (≤5 % weight loss)	7.5 ± 3.3 (≥5 % weight loss) 0.3 ± 2.9 (≤5 % weight loss)	9.1	83.6	6	85.9
Shaw et al. [29]	RCT IP D	24	60	32 ± 6	83.9 ± 16.7	5.0 ± 5.6	6.2	Not reported	3	Not reported
Thompson et al. "CHOICE" [34, 62]	CNR IP D+PA+B	239	56.6 ± 7.7	28.19 ± 2.44 [g] 29.35 ± 2.54 [h]	81.6 ± 10.1	9.3 ± 4.7 [g] 10.5 ± 4.61 [h]	12.5 95 %>5 %12.5	Not reported	6	Not reported
Thomson et al. [37]	RNC IP D+PA+B	40	56.2 ± 9.4	31.8 ± 4.3	84.1 ± 12.3	6.1 ± 4.8	7.2	82.5	6	100
<5 % Weight loss										

Study	Design	Sample size	Average age (years)	Average BMI (kg m^{-2})	Average baseline weight (kg)	Average weight loss (kg)	Average % weight loss	% Caucasian	Weight loss phase (months)	% Post-menopausal
Harris et al. "CASTLE" [36]	RNC IT+IPG D+PA+B	52	50.3 ± 6.3	31.8 ± 4.5	85.5 ± 16.4	3.3 ± 4.4 [i] 4.0 ± 6[j]	4.1 [i] 3.9 [j]	Not reported	6	Not reported
Stendell-Hollis et al. [30]	RCT IP D	54	57.1 ± 8.2	30.1 ± 4.2	80.2 ± 13.3	1.2 ± 4.1	0.01 %	92	6	Not reported
Greenlee et al. "La Vida Activa" [26]	RCT IP D+PA+B	42	52.6 ± 8	33.4 ± 6.6	85.1 ± 12.5	2.9 ± 3.2	3.3 ± 3.5	0[k]	6	77.3
Goodwin et al. [33]	F IP D+PA+B	61	41.3 ± 9.1	Not reported	Not reported	0.5 ± 3.7	Not reported	Not reported	12	Not reported
Stolley et al. "Moving Forward" [31]	RCT IP D+PA	23	51.4 ± 8.9	34.7 ± 7.8	87.7	2.5	3 ± 3.7	0[l]	6	Not reported

F feasibility; *RCT* randomized controlled trial; *RNC* randomized non-controlled trial; *CNR* controlled, non-randomized; *RC* randomized crossover; *D* diet; *PA* physical activity; *B* behavioral therapy; *T* telephone; *IP* in-person; *G* group

[a] Completers

[b] Weight Watchers group

[c] Individualized group

[d] Comprehensive group

[e] National Cancer Institute (NCI) diet

[f] Plant-based olive oil (PBOO) diet

[g] Low fat

[h] Low carbohydrate

[i] In-person group

[j] Telephone group

[k] 22.7 % African–American, 77.2 % Hispanic

[l] 100 % African American

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Table 4

Weight loss intervention for breast cancer survivors (in progress or pending publication)

Study	Sample size	Study design	Sample	Duration (months)	Outcomes	Intervention	Control
Basen-Engquist et al. [59]	60	Parallel assignment feasibility intervention	Aged 18 years or older Stages 0–IIIa breast cancer (also recruiting colon, endometrial and prostate cancer) BMI 27–50 kg m^{-2}	6	Recruitment and dropout rates	**1** Standard Arm: print materials on diet and exercise, weekly telephone counseling, mailed progress reports **2** Online print information, group discussion forum, emailed counseling, emailed progress reports	
Dittus et al. (iWEB) [59]	72	RCT	Aged 40–65 years Breast cancer stage 1–III BMI 27–50 kg m^{-2} Completed chemotherapy 6–48 months before study baseline	6	Weight, fat-free mass, fat mass, total and active energy expenditure, calorie intake, oral glucose tolerance test, compliance (% completing lessons & program), SF-36, FACT-fatigue survey	1) Behavioral weight control treatment via the internet; 2) behavioral weight control treatment via the internet plus resistance training program	Usual care
Dittus et al. [59]	48	Pre-post test	Aged 21–69 years Breast cancer stage I–III BMI 27–40 kg m^{-2} Completed chemotherapy 2–12 months before study baseline	6	Feasibility (length of time to obtain approval at multiple cancer center sites), total calorie and fat gram intake, change in weight, BMI, % body fat, step count, IL-6, hsCRP, HOMA	Effectiveness trial; pre-post test Distance weight loss and exercise program; weekly on-line chats with study facilitator.	NA
Greenlee et al. [59]	45	Randomized, crossover pilot	Aged 21–70 years Stage 0–IIIa breast cancer Hispanic or African descent BMI > 25 kg m^{-2} Sedentary Completed surgery, chemotherapy and radiation therapy ≥6 months before baseline	12	Weight change, adherence, barriers to or predictors of adherence, anthropometric measures, fitness, hormonal biomarkers, metabolic markers, psychological and QOL measures	Combined resistance training and aerobic exercise program plus 6-week nutrition counseling class	Delayed physical activity and dietary change intervention
Greenlee & Hershman et al. [59]	50	Single group assignment	Female stage I–III breast cancer BMI >25 kg m^{-2}	12	Attendance, change in fruit and vegetable consumption, weight,	Behavioral dietary intervention and counseling intervention by telephone, exercise intervention at	NA

Study	Sample size	Study design	Sample	Duration (months)	Outcomes	Intervention	Control
			Sedentary		BMI, waist circumference, hip circumference, % body fat (DXA), minutes spent per week in moderate- to-vigorous intensity aerobic activity, dietary intake (24-hour recall), fasting insulin, fasting glucose, HbA1c, estradiol, testosterone, adiponectin, anxiety, depression, fatigue, sleep, satisfaction with social roles, pain, physical function, DNA methylation patterns	Curves, and online QOL assessment	
Irwin et al. (LEAN Study) (personal communication)	100	RCT	Pre and post-menopausal women Breast cancer stage I–III BMI ≥25 kg m^{-2} Completed treatment before study baseline	6	Weight, fat mass, lean mass, fat %, waist circumference, hip circumference, biomarkers associated with breast cancer survival, psychological and QOL measures	**1** Telephone-based lifestyle counseling (diet and physical activity) **2** In-person lifestyle counseling **3** Usual care control	Healthy eating, physical activity print materials
Mathews et al. (My Lifestyle Intervention of Food and Exercise, MyLIFE) [59]	220	Randomized, parallel assignment intervention	Aged 21–65 years Stage I–III breast cancer BMI 27–45 kg m^{-2} Completed primary treatments for breast cancer within 3–24 months of consenting	6	Change in body weight, BMI, inflammatory and/or metabolic disease markers associated with breast cancer recurrence, total, HDL and LDL-cholesterol, TAG, blood glucose, BP, calorie intake (ASA-24), body composition, waist circumference, physical activity (triaxial accelerometer and IPAQ), QOL, self-efficacy (WEL questionnaire), Weight management questionnaire (WMQ)	Tailored lifestyle intervention (TLI): 3-month weight management program tailored to specific needs (nutrition, physical activity, and behavioral weight management)	Active comparator: commercial weight loss program (CLWP), e.g. Weight Watchers
Patterson et al. (Reach for Health Study) [59]	340	2 × 2 Factorial	Postmenopausal women Breast cancer stage I–III Not scheduled for or currently undergoing chemotherapy	6	Biological markers associated with breast cancer survival	**1** Metformin **2** Lifestyle (telephone-based dietary and physical activity	Placebo

Study	Sample size	Study design	Sample	Duration (months)	Outcomes	Intervention	Control
			BMI ≥25 kg m^{-2} Adults			intervention) plus placebo **3** Lifestyle intervention plus metformin	
Rock et al. (ENERGY Trial) [23•]	800	RCT	Aged 21 years or older Breast cancer stages I–III diagnosed 6 months–5 years before therapy completion BMI 25–45 kg m^{-2}	6	Weight loss, QOL, fatigue	Intensive group: print materials on diet and exercise; weekly group sessions for 4 months; bi-weekly for 2 months, monthly for 6 months up to one year.	Less intensive group: print materials on diet and exercise and two individual counseling sessions.
Schmitz et al. (The Women In Steady Exercise Research (WISER) Survivor Trial) [63]	555	Randomized, parallel assignment intervention	Female breast cancer survivor BMI >25 kg m^{-2} At least 2 months post surgery, chemotherapy or radiotherapy	12	Clinical lymphedema exacerbation rate, QOL, biomarkers of breast cancer recurrence	**1** Exercise only: twice-weekly supervised weight lifting training plus 180 minutes/week aerobic exercise. **2** Weekly dietary counseling from a registered dietitian plus meal provision (NutriSystem) of 1200–1500 calories/day	NA
Swisher et al. (Fit for the Fight Trial) [59]	30	Single group assignment intervention	Aged 18–80 years ER/PR/HER2neu negative breast cancer At least 3 months post-treatment for breast cancer BMI >25 kg m^{-2}	3	Weight loss, QOL, markers of inflammation	Diet and aerobic exercise intervention	NA
Vitolins et al. [59]	25	Single group assignment intervention	Aged 21 years and older Stage I–III ER/PR negative breast cancer Completed treatment for breast cancer ≥6 months before baseline BMI >27 kg m^{-2}	3	Adherence, body weight, bioelectrical impedance, waist circumference, glucose, insulin, hsCRP, IGF, IGFBP-3, lipids, QOL	Soy-based, meal-replacement (Almased) weight loss intervention (target-oriented, cognitive-behavioral therapy plus physical activity counseling and social support)	NA

RCT randomized controlled trial; *BMI* body mass index; *IL-6* interleukin-6; *hsCRP* high-sensitivity C-reactive protein; *HOMA* homeostatic model assessment; *QOL* quality of life; *DXA* dual energy X-ray absorptiometry; *HbA1c* glycated hemoglobin; *HDL* high-density lipoprotein; *LDL* low-density lipoprotein; *TAG* triglyceride; *BP* blood pressure; *ASA-24* automated self administered 24-hour recall; *WEL* weight efficacy lifestyle questionnaire; *ER* estrogen receptor; *PR* progesterone receptor; *HER2neu* human epidermal growth factor receptor 2; *IGF* insulin-like growth factor; *IGFBP-3* insulin-like growth factor binding protein 3