Preventing Obesity in Midlife Women

Systematic Review for the Women's Preventive Services Initiative

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INTRODUCTION

Obesity is an escalating epidemic in the United States[1] that is associated with increased mortality and multiple chronic conditions including cardiovascular disease, several types of cancer, and diabetes mellitus and its related complications.[2-4,5] It is estimated that by 2030, nearly half of adults in the United States will be obese, with highest rates among women, non-Hispanic Black adults, and low income adults.[6]

Obesity is most commonly assessed in the clinical setting by measuring body mass index (BMI), calculated as weight in kilograms divided by height in meters squared (kg/m^2). Adults with normal or healthy weight have BMI ranging from 18.5 to 24.9 kg/m^2. Overweight is defined as a BMI of 25 to 29.9 kg/m^2 and obesity is defined by a BMI of 30 kg/m^2 or higher.[7]

Prevalence rates of overweight and obesity are steadily increasing in women. The estimated prevalence of obesity in women is 36.5% for ages 20 to 39 years, 44.7% for ages 40 to 59 years, and 43.1% for ages 60 years and older, based on the 2015 to 2016 National Health and Nutrition Examination Survey.[8] In the U.S., nearly two-thirds of women ages 40 to 59 years and approximately three-quarters of women older than 60 years are overweight or obese (BMI >25 kg/m^2), with the average woman in midlife gaining 1.5 pounds (0.7 kg) per year.[9] Rates are generally higher among non-Hispanic Black, Alaska Native/American Indian, and Hispanic women, and lower among non-Hispanic white and Asian women.[10]

Obesity is associated with numerous health conditions.[2-4] For women with obesity in particular, incidence is higher for endometrial, gallbladder, esophageal, and renal cancer[11] and the risk of death from several types of cancer (i.e., uterine, kidney, and cervical cancer in women) increases with increasing BMI.[2,12] All-cause mortality also increases when shifting from normal to obese BMI categories.[13]

Women are particularly susceptible to weight gain during midlife. Weight gain during the menopausal transition is common and can be attributed to factors unique to this life phase including aging, hormonal changes, reduced physical activity, and changes in body composition, among others.[9,14] Compared with other hormonally driven life phase transitions in women, such as menarche and pregnancy, hormonal changes influencing weight gain during the menopausal

transition often correspond to increases in fat mass and abdominal adiposity-- independent risk factors for cardiovascular disease.[15,16] Additional contributors include individual factors, such as genetics, health behaviors, dietary patterns, and comorbid illnesses; and societal factors, such as environment, education and skills, income, and food marketing.[17] Obesity is easy to diagnose, as are many related risk factors, yet progress in prevention has been inadequate. For example, less than 20% of adult women meet recommendations for aerobic exercise or muscle strengthening activity.[18] In contrast, measures to prevent childhood obesity, such as healthy eating, breastfeeding, and physical activity, have been implemented by some states.[19]

Currently, there are no clinical recommendations on *preventing* obesity among normal weight or overweight women specifically. The U.S. Preventive Services Task Force (USPSTF) issued a B-level recommendation for clinicians to screen all adults for obesity and offer or refer patients with BMI of 30 kg/m^2 or higher to intensive, multicomponent behavioral interventions, and a B-level recommendation to screen adolescents for obesity and provide comprehensive, behavioral interventions to promote improvements in weight status (**Table 1**).[20-23] In addition, the USPSTF issued a B-level recommendation for intensive behavioral counseling interventions to promote a healthy diet and physical activity for cardiovascular disease prevention among adults with cardiovascular disease risk factors; and a C-level recommendation (i.e., individualized decisions) for interventions for adults without obesity or cardiovascular disease risk factors. The USPSTF recently issued a new B-level recommendation to offer pregnant persons effective behavioral counseling interventions aimed at promoting healthy weight and weight gain during pregnancy.[24]

Table 1. USPSTF Recommendations Related to Obesity[20-23]

Population	Recommendation	Rating
Obesity		
Adults	Offer or refer adults with a BMI of 30 kg/m^2 or higher to intensive, multicomponent behavioral interventions (2018).	B
Children and adolescents 6 years and older	Screen for obesity in children and adolescents 6 years and older and offer or refer them to comprehensive, intensive behavioral interventions to promote improvements in weight status (2017).	B
Cardiovascular disease (CVD) risk		
Adults who are overweight or obese and have additional CVD risk factors	Offer or refer adults with CVD risk factors* to behavioral counseling interventions to promote a healthy diet and physical activity (2020).	B
Adults without obesity who do not have known CVD risk factors	Individualize the decision to offer or refer adults without obesity who do not have CVD risk factors* to behavioral counseling to promote a healthy diet and physical activity (2017, in progress).	C
Pregnancy		
Pregnant persons	Offer effective behavioral counseling interventions aimed at promoting healthy weight gain and preventing excess gestational weight gain in pregnancy (2021).	B

Abbreviations: BMI=body mass index; CVD=cardiovascular disease

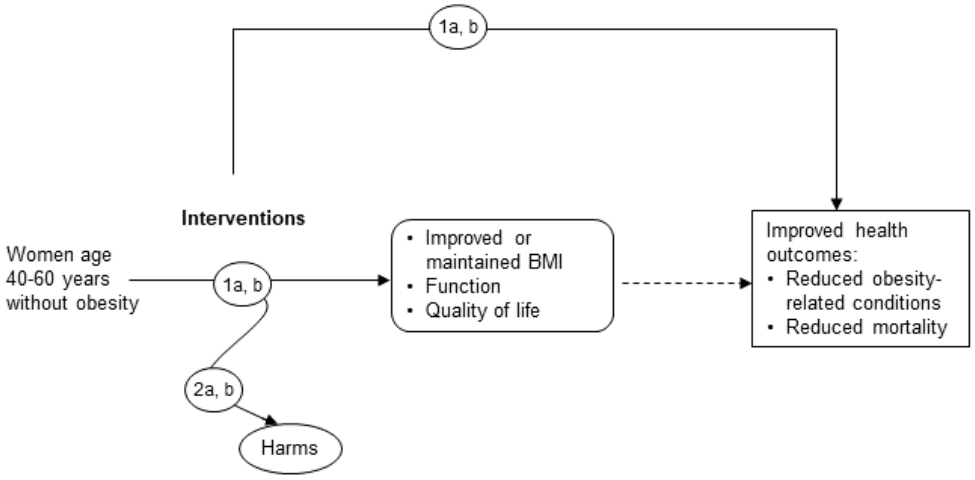
***** Hypertension, dyslipidemia, diabetes, metabolic syndrome, or an estimated 10-year CVD risk of 7.5% or greater.

Losing weight once obese is an important, although often difficult, effort to modify chronic health conditions with challenges for both achieving and maintaining weight loss.[25-27] Preventing obesity is an essential approach that currently lacks clinical guidance. This systematic review addresses this gap by evaluating evidence on the effectiveness and harms of behavioral interventions to prevent weight gain and obesity and improve function, quality of life, and obesity-related health outcomes in midlife women without obesity aged 40 to 60 years.

METHODS

The Women's Preventive Services Initiative (WPSI) Advisory Panel determined the scope and key questions for this review to inform the development of new screening recommendations. The protocol was developed according to established methods[28] with input from experts and the public. Investigators created an analytic framework outlining the key questions and patient populations, interventions, and outcomes (**Figure 1**). The target population includes women with normal and overweight (BMI <30 kg/m^2) BMI ages 40 to 60 years.

Figure 1. Analytic Framework



Key Questions

1. a. Among women without obesity, age 40 to 60 years, what is the effectiveness of interventions to prevent weight gain and obesity and improve function, quality of life (e.g., sleep, energy), and health outcomes?
   b. How does effectiveness of interventions to prevent obesity vary across population sub-groups (age, social-demographic and cultural groups, parity, menopausal status, comorbidities, other)?

2. a. What are the potential harms of interventions to prevent obesity in women without obesity, age 40 to 60 years?

b. How do harms of interventions to prevent obesity vary across population sub-groups (age, social-demographic and cultural groups, parity, menopausal status, comorbidities, other)?

Literature Searches

A research librarian conducted electronic database searches in Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews from 1946 to October 26, 2021. Search strategies are provided in **Appendix 1**. Investigators also manually reviewed reference lists of relevant articles and systematic reviews.

Study Selection

Investigators reviewed all titles and abstracts and determined inclusion based on pre-specified criteria (**Appendix 2**). Studies meeting eligibility criteria for inclusion at the abstract level subsequently underwent full-text dual review by two independent investigators. Disagreements regarding inclusion of studies were resolved by discussion and consensus. All results were tracked in an EndNote® database (Clarivate) including reasons for exclusion after full text review.

Investigators applied a best evidence approach when reviewing abstracts and selecting studies to include for this review that involved prioritizing the most relevant studies with the strongest methodology.[29-31] Randomized controlled trials (RCTs), large (>100) prospective cohort studies with comparison groups, and systematic reviews meeting eligibility criteria and applicable to clinical practice in the United States were included. Other study designs, such as case-control and modeling studies, were considered when evidence from other study designs was lacking. Included studies enrolled predominantly adult women (>60% female participants) ages 40 to 60 (>50% of participants or average age >40 years) with normal or overweight BMI (average BMI <30 kg/m^2). Women with low BMI (<18.5 kg/m^2) were outside the scope of this review.

This review focused on interventions conducted in, or referred from, primary care settings. Broader, community-based interventions and pharmacologic interventions were excluded. Interventions were classified as either *counseling-only* or *active* behavioral interventions. Counseling-only interventions consisted of recommendations or advice about exercise, weight monitoring, or specific dietary information provided during the course of an intervention without an active component. Active interventions consisted of a structured, physical element and could also include a counseling component. Active interventions often included supervised exercise programs, prescribed exercise or dietary programs, or intensive weight management.

The intensity of interventions depended on the number of sessions or contacts, the duration and frequency of sessions, and the length of the intervention period. For this review, intervention intensity was defined by the number of participant contacts beyond usual care or the comparison group, and was categorized as *low* (fewer than 2 contacts during the intervention period), *moderate* (3 to 11 contacts), or *high* intensity (12 or more contacts). Interventions were compared with an alternate control (i.e., usual care, attention control, minimal intervention). Minimal interventions (e.g., generic print materials) and attention controls (i.e., similar format as the intervention but different content) commonly consisted of initial sessions with a clinician regarding general education on healthy behavior, group education on general health topics, or

access to websites promoting healthy behaviors. In some trials, usual care included nutrition or physical activity materials based on national guidelines.

Outcomes were classified as weight-related intermediate outcomes (maintaining current weight, losing weight, or gaining weight) or health outcomes. Health outcomes include morbidity, mortality, function, or quality of life. Potential harms of interventions included psychosocial harms (e.g., anxiety, depression), distress, and other adverse events affecting quality of life or as reported by studies. Findings related to specific populations were included when available.

Data Extraction and Synthesis

For studies meeting inclusion criteria, data were abstracted into tables including characteristics of study populations, interventions, comparators, outcomes, study designs, settings, methods, and results. All data abstractions were reviewed for completeness and accuracy by a second investigator.

Each study was independently rated for quality by two investigators and disagreements were resolved by discussion and consensus with a third reviewer. Predefined criteria were used to assess the quality of individual studies rating them as *good*, *fair*, or *poor* (**Appendix 3**).[32] To summarize evidence on the effects of interventions, data were synthesized qualitatively for each key question by outcome, including weight-related outcomes and health outcomes. No statistical meta-analyses were conducted because of methodological and clinical heterogeneity.

Assessing Applicability

Applicability is defined as the extent to which the effects observed in published studies are likely to reflect the expected results when a specific intervention is applied to the population of interest under real-world conditions.[29] It is an indicator of the extent to which research included in a systematic review might be useful for informing clinical decisions. Factors important for understanding applicability were considered for each study including differences in the interventions, comparators, populations, and settings. Based on these factors, applicability was rated *high, moderate, low, or insufficient* (**Appendix 4**).

Establishing the Strength of Recommendations

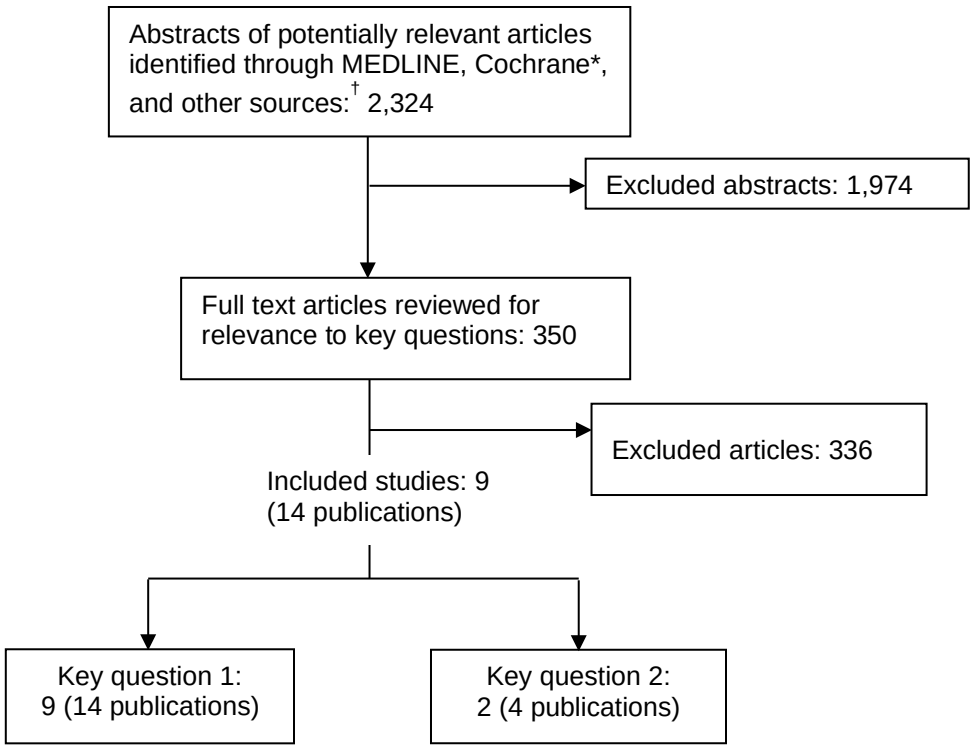
The strength of evidence for each key question was assessed by using the approach described in the AHRQ Methods Guide.[29] Grades were based on study limitations, consistency, directness, precision, and reporting bias (**Appendix 4**).

RESULTS

Included Studies

The literature search resulted in 2,324 unique citations. Following dual review of titles and abstracts and dual evaluation of 350 full-text articles, nine trials of interventions to prevent obesity (reported in 14 publications) were included for Key Question 1; and two of these trials (reported in 4 publications) were included for Key Question 2 (**Figure 2**).

Figure 2. Literature Flow Diagram



*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.

†Identified from reference lists, hand searching, and other sources.

Characteristics of Included Trials

Nine trials in 14 publications evaluated the effectiveness of behavioral or counseling interventions to prevent obesity (**Appendix Table 1**).[33-46] Study designs included RCTs,[34-39,41-46] cluster RCTs,[40] or crossover RCTs.[33] All trials reported weight-related outcomes. Two trials reported quality of life outcomes,[35,39,45,46] but no studies reported other health outcomes such as morbidity or mortality. Two trials in four publications reported potential harms of interventions.[37-39,44]

Across all trials, sample sizes ranged from 54 to 18,003 participants (N=21,337). Trials enrolled women aged 18 years or older; had more than 50% of participants older than 40 years; and reported mean ages ranging from 40 to 62 years. The majority of participants had normal or overweight BMI (average BMI <30 kg/m^2). Seven trials enrolled women only including two trials with exclusively postmenopausal women[33,36,43] and 4 trials with women aged 40 to 60 years.[33,37,42,44,46] In the 2 trials that also enrolled men, women constituted the majority of participants (71% and 79%).[34,41] Six trials were conducted in the U.S.,[33,34,36-38,41-44] two in Australia,[35,40,45,46] and one in New Zealand.[39] Trials did not report outcomes by age, race, ethnicity, socioeconomic status, parity, smoking status, or other factors, precluding analysis based on specific populations.

Trials included women from different combinations of BMI categories: normal weight only, overweight and obese only, and mixed (all BMI categories). Four trials recruited participants from community settings,[34,40-42] three from university settings,[33,35,37,38,44-46] and two from primary care clinics.[36,39,43] Seven trials evaluated counseling only interventions, where clinicians offered advice or specific recommendations on behavior change (e.g., weight monitoring, dietary changes, physical activity),[34-38,40-46] while one trial evaluated an active intervention, where clinicians implemented a structured, physical element, such as medically supervised exercise.[33]

Interventions were highly variable in intensity (number of sessions or contacts) and modes of delivery. One trial included a low-intensity intervention (fewer than 2 contacts during the intervention period);[41] three evaluated moderate-intensity interventions (3 to 11 contacts);[34,35,39,45,46] and five evaluated high-intensity interventions (12 or more contacts).[33,36-38,40,42-44] The mode of delivery for the interventions included face-to-face in seven trials,[33,35-39,41-46] face-to-face plus print materials in one trial,[40] and print materials only in one trial.[34] The comparison, or control intervention, consisted of no intervention in four trials,[33,34,37,38,42,44] general information (such as information on women's health and dietary guidelines) in three trials,[36,40,41,43] and a self-directed motivational interviewing technique in one trial.[35,45,46] The timing of initiation and study duration varied across trials, ranging from two weeks[41] to 9 years.[36]

Two trials met criteria for good quality[37-39,44] and seven for fair quality[33-36,40,42,43,45,46] (**Appendix Table 2**). Limitations for fair quality studies included unclear randomization methods,[33,34,42] inadequate allocation concealment,[33,34,36,43] limited reporting of analytic methods, unclear intention to treat analysis,[34-36,43,45,46] or baseline differences between groups.[34]

Key Question 1. Effectiveness of interventions to prevent weight gain in midlife women

Health Outcomes

Two trials evaluated the effect of counseling interventions on measures of patient reported quality of life using the short-form-36 (SF-36) (**Appendix Table 1**).[35,39,45,46] One trial demonstrated statistically significant improvements in physical and mental health subscores for the intervention compared with comparison group,[39] while the other smaller trial showed no differences between groups.[35,45,46]

A good quality, moderate intensity counseling RCT evaluated the effect of an exercise prescription compared with no prescription in 1,089 inactive, women with overweight (mean BMI 29) BMI, age 40 to 74 years (mean age 59).[39] Participants in the intervention group were initially given an exercise prescription with brief counseling to increase physical activity, followed by telephone support for 3 months (5 calls) to assist with choice of activity, goal setting, and ways to overcome personal barriers to physical activity. An additional 30-minute counseling visit occurred at 6 months. At both 12-month and 24-month follow-ups, SF-36 sub-scores were better for the intervention compared with comparison group for physical functioning (2.17 vs. 0.07, p=0.03 and -0.09 vs. -0.91, p=0.03, respectively) and mental health (1.73 vs. 0.51, p<0.05 and 1.49 vs. 0.39, respectively).

Another fair quality trial evaluated a moderate-intensity counseling intervention to modify diet and physical activity for obesity prevention compared with a self-directed intervention in 54 premenopausal women without obesity age 44 to 50 years old.[35,45,46] The SF-36 subscale was also used to evaluate physical and mental health as indicators of quality of life. This trial showed no differences between intervention groups at any time point and no changes in scores over time, however, fewer participants were enrolled compared with the exercise prescription trial.

Weight Outcomes

Nine trials in 14 publications evaluated the effectiveness of exercise or counseling interventions to prevent obesity (**Table 2**).[33-46] Results indicated statistically significant reductions in weight for intervention versus comparison groups in five trials,[35-38,40,41,44-46] but no differences in four trials (**Table 3**).[33,34,39,42]

High Intensity Interventions

Five trials evaluated the effectiveness of high-intensity interventions including one trial of an active, exercise-based intervention,[33] and four trials of counseling interventions.[34,36-38,40,42-44]

A high-intensity, active intervention was evaluated in a fair quality crossover trial of 122 postmenopausal women ages 40 to 65 years with BMI ranging from 19.0 to 33.0 kg/m^2.[33] The intervention included a high-intensity exercise program of 60 to 75 minute sessions, 3-days per week for 1 year compared with no exercise intervention. All women maintained their usual dietary practices and those in the intervention group also received comprehensive social support to optimize adherence. A limited group of controls crossed over to the exercise group at 1 year. At the 6-year follow-up, overall weight gain was highest among the no exercise control group, although differences between exercise, crossover, and control groups were not statistically significantly different (0.43 kg [standard deviation, SD 6.16] vs. 0.70 kg [SD 4.38] vs. 2.08 kg [SD 4.25] respectively; p=0.44).

Four high-intensity trials evaluated the effect of counseling interventions. The Women's Health Initiative Dietary Modification Trial, a fair quality trial of 48,835 postmenopausal women ages 50 to 79 years with a range of BMI, evaluated a high-intensity counseling intervention promoting a low-fat diet without encouraging weight loss or caloric restriction.[36,43] Among 18,003 women age 50 to 59 years weight was reduced for the intervention versus control group during the first year (mean difference -2.2 vs. 0.6, p<0.001) and maintained during the average 7.5 years of

follow-up. However, by the 9-year follow-up, the difference between groups was not statistically significant.

A good quality trial enrolled 535 premenopausal women 44 to 50 years old with a range of BMI to evaluate the effect of a 5-year, high-intensity counseling intervention that also included an activity prescription.[37,38,44] Results indicated weight loss for the intervention vs. control groups overall (mean weight change -0.2 kg [SD 4.3] vs. 2.8 kg [SD 3.6], $p<0.001$), and at all follow-up times (6, 18, 30, 42, and 54 months) for women with normal weight BMI specifically. Women with overweight BMI at baseline also experienced weight loss at all follow-up times during the first 4 years of the study, but not at 54-months follow-up.[44]

A fair quality cluster RCT included 649 rural Australian women ages 18 to 50 years with a range of BMI including two-thirds with normal or overweight BMI.[40] The intervention involved a 60-minute interactive group session, followed by a 20-minute counseling phone call, and subsequent text messages every 4 weeks. Weight loss at 1-year follow-up was greater for the intervention versus control group overall (adjusted mean difference in weight change from baseline, -0.87 kg; 95% CI -1.62 to -0.13), but not when stratified by BMI groups.

A fair quality trial of 354 women ages 40 to 60 years with a range of BMI[42] evaluated the effect of individualized 1-hour counseling sessions every 2 weeks for 6 months compared with no counseling. The intervention had no effect on weight (mean difference -0.31 kg; 95% CI -1.09 to 0.46) or BMI (mean difference, -0.09 kg/m^2; 95% CI -0.39 to 0.21) at 24-month follow-up.

Moderate Intensity Interventions

Three moderate-intensity trials evaluated counseling interventions. A fair quality parallel RCT from Australia included 54, premenopausal women without obesity, ages 44 to 50 years.[45] The intervention group received counseling about obesity prevention from a multidisciplinary team that included a dietician and exercise physiologist while the control group received written materials only. Overall weight loss was greater for the intervention versus control group at the 24-month follow-up (-2.3 kg vs. -0.3 kg, adjusted $p=0.02$). When analyzed according to baseline BMI, women with normal BMI demonstrated lower weight compared with controls at 24 months (-1.9 vs. 0.1 kg, adjusted $p=0.03$), while no there were no statistically significant differences between groups for women with overweight BMI (-2.5 vs. -0.8 kg, adjusted $p=0.20$).

A good quality RCT, also included for quality of life outcomes, evaluated the effect of an exercise prescription in 1089 inactive, women with overweight BMI, ages 40 to 74 years.[39] Participants in the intervention group were initially given an exercise prescription with brief counseling to increase physical activity; followed by telephone support for 3 months (5 calls) to assist with choice of activity, goal setting, and ways to overcome personal barriers to physical activity; and then an additional 30-minute counseling visit at 6 months. Results indicated no differences in weight between groups at 12 and 24-month follow-up.

A fair quality RCT evaluated a weight gain prevention intervention in 219 normal weight adults (71% women).[34] Participants in the intervention group received monthly newsletters with self-reported weight recording, a financial incentive, and optional counseling. Results indicated no

difference in overall weight change from baseline for the intervention group compared with controls over a 12-month period.

Low Intensity Interventions

A fair quality trial of 272 participants with a range of BMI (median 28.8 kg/m^2) evaluated a brief, low-intensity, counseling intervention to prevent weight gain over the winter holidays.[41] The 45-day follow-up demonstrated a statistically significant weight reduction with the intervention, adjusted for baseline weight and attendance at a weight loss program (mean difference, -0.49 kg; 95% CI, -0.85 to -0.13, p=0.008).

Table 2. Characteristics of Trials of Interventions to Prevent Weight Gain in Midlife Women

Author, year	Study design	Country; setting	Sample size; population (% women)	Age, mean, *years*	BMI, mean *kg/m²*	Intervention	Comparison	Duration, *weeks*	Study quality
Bea et al., 2010[33]	Cross-over RCT	United States; university	122 menopausal women ages 40-65 (100)	56.2	NR*	Supervised exercise sessions 60-75 minutes, 3-days/week for 1 year; followed by self-directed program	Crossover (n=32) no intervention in the first year then exercise vs. no exercise (n=25)	312	Fair
Forster et al., 1988[34]	RCT	United States; health department	219 normal weight adults (71)	45.9	23.1	Four education sessions, newsletter, self-monitoring, financial incentive	No counseling, newsletters, or incentive	52	Fair
Howard et al., 2006; Ritenbaugh et al., 2003[36,43]	RCT	United States; WHI clinics	18,003 postmenopausal women (100)	62.3	29.1	Group counseling about low fat diet	No counseling	390	Fair
Klem et al., 1997; Kuller et al., 2000; Simkin-Silverman et al., 2003[37,38,44]	RCT	United States; university	535 women ages 44-50 years (100)	47	25.1	Group counseling program followed by individual or group sessions	No counseling	216	Good
Lawton et al., 2008[39]	RCT	New Zealand; primary care practices	1,089 women ages 40-74 years (100)	59.2	29	Individual counseling with exercise prescription; 5 follow-up telephone calls, one individual, 30-minute counseling session	No intervention	36	Good
Lombard et al., 2016[40]	Cluster RCT	Australia; community clinics	649 women ages 18-50 years (100)	39.6	NR†	Small group counseling, phone coaching, text messaging	45-minute group education session on general women's health topics	52	Fair
Mason et al., 2018[41]	RCT	United States; community	272 adults (79)	43.9	28.8	Brief counseling session	No counseling	2	Fair
Perry et al., 2016[42]	RCT	United States; community	354 women ages 40-60 years (100)	50.1	NR‡	Individualized counseling	No counseling	104	Fair
Williams et al., 2014; Williams et al., 2019; Hollis et al., 2014[35,45,46]	Parallel RCT	Australia, university hospital	54 non-obese premenopausal women 44-50 years (100)	47.3	25.1	Motivational interviewing with dietician and exercise physiologist	Self-directed intervention	48	Fair

Abbreviations: BMI=body mass index; kg=kilogram; NR=not reported; RCT=randomized controlled trial; vs.= versus; WHI= Women's Health Initiative

*Range provided only (19.0-33.0 kg/m^2).

†35.2% normal; 31.9% overweight; 33.9% obese.

‡39.9% normal; 32.3% overweight; 27.1% obese.

Table 3. Summary of Weight Loss Outcomes in Trials of Interventions to Prevent Weight Gain in Midlife Women

Author, year	Intervention intensity*	Intervention; focus	Participants, *n*	Duration of follow-up, *months*; adherence, *%*	Weight change from baseline, *mean kg* (SD) or difference in weight change, *kg* (95% CI); intervention vs. controls	Difference in mean weight change between groups, *kg* (lbs)
Trials reporting differences in weight change						
Howard et al., 2006; Ritenbaugh et al., 2003[36,43]	High	Counseling; low-fat diet, changing diet patterns	18,003	108; 81%	-2.2 vs. 0.6; p<0.001[†]	2.8 (6.18)
Klem et al., 1997; Kuller et al., 2000; Simkin-Silverman et al., 2003[37,38,44]	High	Counseling; preventing increased cholesterol, preventing weight gain, increasing physical activity	535	54; 51-59%	-0.09 vs. 2.36; p<0.01[‡]	2.45 (5.40)
Lombard et al., 2016[40]	High	Counseling; preventing weight gain, healthy diet, physical activity, self-monitoring	649	12; 74%	-0.22 vs. 0.20; p=0.02[‡]	0.42 (1.93)
Williams et al., 2014; Williams et al., 2019; Hollis et al, 2014[35,45,46]	Moderate	Counseling; healthy weight, weight maintenance, healthy diet, exercise	54	24; 56%	-2.3 vs -0.3, p=0.02	2.0 (4.41)
Mason et al., 2018[41]	Low	Counseling; self-weighing, weight management, food restraint, physical activity	272	2; 98%	-0.49 (-0.85 to -0.13), p=0.008	0.49 (1.08)
Trials reporting no differences in weight or weight change						
Bea et al., 2010[33]	High	Active; physical activity	122	72; 48%	0.43 (6.16) vs. 0.70 (4.38) vs. 2.08 (4.25); p=0.44[§]	
Forster et al., 1988[34]	Moderate	Counseling; weight control, diet, exercise, weight management	219	12; 28%	-1.0 (0.8) vs. -0.1 (0.7)[‖]	
Lawton et al., 2008[39]	Moderate	Counseling; exercise prescription	1,089	24; 89%	72.6 (0.6) vs 72.5 (0.6)[¶]	
Perry et al., 2016[42]	High	Counseling; dietary changes, eating behaviors	354	24; 95%	-0.31 (-1.09 to 0.46), p=0.43	

Abbreviations: BMI=body mass index; kg=kilograms; SD=standard deviation; vs.=versus

*Low intervention intensity indicates <2 contacts; moderate intensity 2-11 contacts; high intensity >12 contacts.

[†]Results at 1-year; statistically significant weight loss during years 1 to 7, but not at 9 years for age group 50 to 59 years.

[‡]Reported as pounds, calculated in kilograms.

[§]Compares two intervention groups with no intervention.

[‖]Reported as not statistically significant by the study; *p*-value not provided.

[¶]Weight not weight change reported.

Key Question 2. Harms of interventions

Two good quality trials (in 4 publications) included for Key Question 1 also reported potential harms of exercise or counseling interventions.[37-39,44] A moderate intensity RCT evaluated the effect of an exercise prescription on 1,089 inactive, women with overweight BMI, ages 40 to 74 years.[39] While this trial indicated no differences in weight change, participants in the intervention group reported more falls (37% vs. 29%; $p<0.001$) and injuries (19% vs. 14%; $p=0.03$) over the 24-month follow-up period.

Symptoms of depression were evaluated for potential harm in a RCT of high-intensity counseling involving 15 group meetings over 20 weeks in 535 premenopausal women age 44 to 50 years.[37] However, rather than harm, results showed improvement in symptoms for the intervention versus control group reflected by reduction in depression scores from baseline to 6-month follow-up (Beck Depression Inventory score 4.95 to 3.91 vs. 4.30 to 4.46, respectively, $p<0.05$).[37] In addition, perceived stress was unchanged during 6-month follow-up for the intervention versus control group which showed increased stress measures (Perceived Stress Scale score, 5.10 to 5.11 vs. 4.58 to 5.30, respectively, $p<0.03$). The clinical significance of these changes in mean scores is not clear.

Table 4. Trials Reporting Potential Harms of Interventions to Prevent Weight Gain in Midlife Women

Author, year	Design, Study	Participants	Intervention	Outcome Measures	Results (Intervention vs. Control)*	Study Quality
Klem et al., 1997; Kuller et al., 2000; Simkin-Sliverman et al., 2003[37,38,44]	RCT	535 women age 44-50 years; mean BMI 25.1 kg/m^2	High-intensity counseling with a 5-year cognitive-behavioral program including 15 group meetings over 20 weeks (n=260) vs. no meetings (n=275)	Beck Depression Inventory (BDI); Perceived Stress Scale (PSS)	BDI at 6 months, mean (SD): 4.95 to 3.91 (4.48) vs. 4.30 to 4.46 (4.76), p<0.05 PSS at 6 months, mean (SD): 55.10 to 5.11 (2.85) vs. 4.58 to 5.30 (4.90), p<0.03	Good
Lawton et al., 2008[39]	RCT	1089 women age 40-74 years (mean 59); mean BMI 29 kg/m^2	Counseling intervention that included an exercise prescription (n=544) vs. no intervention (n=545)	Patient recall of falls and injuries at 12 and 24 months	Falls, number (%): • Baseline, 138 (25) vs. 155 (29) • 12 months, 158 (32) vs. 127 (25) • 24 months, 179 (37) vs. 143 (29); p<0.001 Injuries, number (%): • Baseline, 77 (14) vs. 103 (19) • 12 months, 91 (18) vs. 86 (17) • 24 months, 92 (19) vs. 66 (14); p=0.03	Good

Abbreviations: BDI=Beck Depression Inventory; BMI=body mass index; kg=kilograms; m=meters; PSS=Perceived Stress Scale; RCT=randomized controlled trial; SD=standard deviation; vs.=versus.
*p-values listed when reported by study

CONCLUSIONS

A summary of evidence of the nine trials of interventions to prevent obesity in midlife women included in this systematic review is described in **Table 5.** Five trials demonstrated statistically significant differences in weight change for intervention compared with control groups including the three largest trials.[35-38,41,44-46] All were counseling based trials of either low-,[41] moderate-,[35,45,46] or high-intensity.[36-38,40,44] Results indicated modest weight loss ranging from 0.49 kg (1.08 lbs) in a trial of a low-intensity counseling intervention[41] to 2.8 kg (6.18 lbs) in the Women's Health Initiative trial of a high-intensity intervention.[36,43] The other four trials demonstrated no statistically significant effects of interventions on weight change, although the benefit of weight maintenance or stabilization was not consistently addressed.[33,34,39,42]

Trials varied in several ways that limit comparisons across trials. Interventions differed in their type, intensity, duration, and content. Only one trial evaluated the effectiveness of an active, exercise-based intervention,[33] while the remainder employed counseling interventions to change diet, physical activity, or weight management. Weight change from baseline was the primary outcome reported by most trials; however, trials varied by follow-up and study duration. Although study populations enrolled midlife women with normal or overweight BMI, additional characteristics of participants were not reported and subgroup analysis was limited.

The larger of two trials evaluating changes in SF-36 quality of life scores reported higher physical functioning and mental health for the intervention group,[39] while the smaller trial reported no differences.[35,45,46] Two trials described potential harms of interventions. One trial reported no adverse psychological effects of the intervention as measured by standardized scales of depression and stress.[37,38,44] Another trial reported increased self-reported falls and injuries related to a counseling prescription to increase physical activity in a previously inactive population of overweight women.[39] These findings suggest that it may be prudent to include fall prevention guidelines when initiating an exercise program for previously inactive participants. Based on a limited number of studies, these interventions seem to pose very little harm and may have a positive effect on psychological outcomes,[37,38,44] although the clinical significance of a mean decrease of 1-point on the Beck Depression Inventory is not clear.

Limitations of trials included unclear randomization methods,[33,34,42] inadequate allocation concealment,[33,34,36,43] limited reporting of analytic methods, unclear intention to treat analysis,[34-36,43,45,46] and baseline differences between groups,[34] all of which could impact the accuracy of results. Furthermore, the applicability of these findings may be limited by small trials[33,35,45,46] and trials enrolling homogenous populations.[35,40,45,46] Although trials evaluated interventions with a range of components with varying intensity, they did not provide sufficient data to determine whether particular approaches to obesity prevention or weight maintenance are more effective than others.

Other potential effects of active interventions, not reflected in the reported data, may include changes in body composition that occur with exercise or resistance training.[33] Known benefits of regular exercise include improvements in sleep, quality of life, and executive function, in addition to disease prevention.[47] Current physical activity recommendations for adults have been established by advisory groups and are publically available;[47] and dietary guidelines continue to

be updated.[48,49] While individuals may not be able to achieve the recommended levels of physical activity (at least 150 to 300 minutes of moderate-intensity aerobic activity each week, and muscle-strengthening activity at least 2 days each week), an increase in any amount of physical activity may reduce the burden of chronic disease.[50]

In women with normal weight, the long-term benefits of maintaining a healthy BMI include reduced risk of conditions associated with obesity including cardiovascular disease, diabetes, and some types of cancer.[51-53] Opportunities for counseling women to encourage maintenance of a normal BMI is important because most women will experience weight gain as they age and transition through menopause. In this review, three trials that demonstrated statistically significant differences in weight change in the overall analysis also conducted subgroup analyses by BMI categories. Of these, two trials demonstrated statistically significant differences in weight change for women with normal BMI, but no effect for those with overweight BMI.[35,37,38,44-46] The remaining study did not demonstrate subgroup differences for the normal or overweight BMI subgroups.[40]

While women with overweight BMI may be unable to lose weight to achieve a normal BMI in trials, weight maintenance or prevention of weight gain could also prove beneficial in staving off the transition to obesity and its related health consequences. In one trial, persistent weight gain was prevented among overweight women receiving a counseling intervention,[40] while another trial demonstrated how a low-intensity counseling intervention that encouraged self-monitoring, with regular advice for weight management, prevented weight gain.[41]

No studies reported outcomes for specific populations based on age, social-demographic and cultural groups, parity, menopausal status, comorbidities, or other factors or evaluated how effects of interventions on health outcomes or weight related outcomes varied in these populations. Importantly, more studies are needed to evaluate the effect of interventions in these populations. Future trials could evaluate more intensive behavioral interventions, which may be more effective, and whether components should be tailored to specific populations of women. Research would be helpful to determine the optimal frequency, length of sessions, and number of sessions needed for an intervention to provide additional evidence on effectiveness.

Efforts to prevent obesity in the general population, especially among women, are important considering the ongoing burden and health consequences of this condition, including increased rates of chronic disease and reduced life expectancy.[54] Continued debates about the “healthiest” diet[55] pose challenges to this effort as do fad diets[56] and conflicting data,[57] which can be confusing to both health professionals and the public. However, combating an obesogenic environment of decreased physical activity, sedentary lifestyle, sweetened beverages, processed foods, and increased portion sizes could be an opportunity for prevention given that many of these factors can be modified or avoided. Careful consideration of the impacts of weight stigma and bias is important when providing counseling for women in any weight category. In addition to assessing diet and exercise, a review of other contributors to weight gain (e.g., medications, sleep deprivation, mood disorders, disordered eating) is appropriate. Irrespective of whether weight gain in midlife is the result of changes in body composition, hormones, or is age-related, consideration of methods to modify risk factors could prevent or minimize weight gain.

Table 5. Summary of Evidence

Key Question	Number of studies; design; participants, *n*	Summary of Findings	Limitations	Consistency; precision	Strength of evidence*	Overall applicability†
KQ 1. Effectiveness of interventions to prevent obesity in midlife women	9 RCTs (*n*=21,337)	• The larger of 2 trials evaluating changes in SF-36 quality of life scores reported higher physical functioning and mental health for the intervention group, while the smaller trial reported no differences. • 5 trials reported statistically significant reductions in weight with intervention compared with control, including the 3 largest trials, while differences were not statistically significant in 4 trials. • Subgroup analysis in 2 trials demonstrated weight reduction for normal BMI subgroups, but no reduction for overweight BMI subgroups. There were no differences among subgroups in 1 trial.	Studies varied in size, duration, and type of intervention.	Inconsistent; imprecise for health outcomes Consistent; precise for weight outcomes Inconsistent, imprecise for weight outcomes by subgroups	Moderate	Moderate
KQ 2. Harms of interventions	2 trials (*n*=1,624)	One trial demonstrated increased self-reported falls and injuries in the intervention group. One trial demonstrated reduction in depressive symptoms from baseline to 6-month follow-up for the intervention group.	Studies varied in size, duration, and type of intervention; low event rates for harms.	Inconsistent; imprecise for harms	Low	Low

Abbreviations: BMI=body mass index; RCT=randomized controlled trial

*Overall ranking of evidence: high = high confidence that the evidence reflects the true effect. Further research is very unlikely to change confidence in the estimate of effect; moderate = moderate confidence that the evidence reflects the true effect. Further research may change confidence in the estimate of effect and may change the estimate; low = low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is likely to change the estimate; insufficient = evidence either is unavailable or does not permit a conclusion.

† Applicability describes how well the overall body of evidence would apply to the U.S. population based on settings, populations, and intervention characteristics (high, moderate, low, insufficient)

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APPENDIX 1

Search Strategies

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to October 26, 2021>

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1 Weight Gain/ (30211)
2 pc.fs. (1240428)
3 prevent*.ti,ab,kf. (1362873)
4 1 and (2 or 3) (5735)
5 (weight adj2 (gain or increas*)).ti,ab,kf. (81670)
6 5 and (2 or 3) (13934)
7 4 or 6 (15945)
8 Women's Health/ (26772)
9 Female/ (8377164)
10 (woman or women or female or menopaus* or premenopaus* or perimenopaus* or postmenopaus*).ti,ab,kf. (1682295)
11 7 and (8 or 9 or 10) (8183)
12 Middle Aged/ (4172659)
13 exp Menopause/ (55327)
14 ("middle age*" or "mid age*" or menopaus* or premenopaus* or perimenopaus* or postmenopaus*).ti,ab,kf. (144285)
15 12 or 13 or 14 (4238565)
16 11 and 15 (2177)
17 (canine or dog or dogs or mouse or mice or rat or rats).ti. (1455342)
18 16 not 17 (2066)
19 dt.fs. (2138172)

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to October 26, 2021Page **22** of **30**>

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1 Obesity/ (171888)
2 Weight Gain/ (30211)
3 (obese or obesity).ti,ab,kf. (284753)
4 (weight adj2 (gain or increas*)).ti,ab,kf. (81670)
5 or/1-4 (394876)
6 Women's Health/ (26772)
7 Female/ (8377164)
8 (woman or women or female or menopaus* or premenopaus* or perimenopaus* or postmenopaus*).ti,ab,kf. (1682295)
9 6 or 7 or 8 (8661187)
10 5 and 9 (213200)
11 Middle Aged/ (4172659)
12 exp Menopause/ (55327)

13 ("middle age*" or "mid age*" or menopaus* or premenopaus* or perimenopaus* or postmenopaus*).ti,ab,kf. (144285)
14 11 or 12 or 13 (4238565)
15 10 and 14 (91383)
16 limit 15 to (meta analysis or "systematic review" or systematic reviews as topic) (858)
17 limit 16 to yr="2014 -Current" (458)
18 limit 17 to english language (449)
19 dt.fs. (2138172)
20 18 not 19 (390)
21 su.fs. (1921806)
22 20 not 21 (333)

APPENDIX 2

Inclusion and Exclusion Criteria

Category	Inclusion	Exclusion
Populations	Women without obesity, age 40-60 years who are not pregnant or postpartum	Women with obesity (BMI ≥30 kg/m^2); pregnant and postpartum women; women <40 or >60 years; men
Interventions	Behavioral and counseling interventions to prevent obesity or maintain current BMI (counseling, diet, exercise, combined interventions). Interventions may be delivered via face-to-face contact, telephone, print materials, or technology (e.g., computer based, text messages) and can be delivered by numerous potential providers, including but not limited to physicians, nurses, exercise specialists, dietitians, nutritionists, and behavioral health specialists	Pharmacologic interventions; broader community-based programs (e.g., mass media, changes to the community-built environment)
Comparisons	Intervention vs. no treatment (e.g., wait-list control, usual care); attention control (e.g., similar format and intensity to intervention but different content area); minimal intervention (including the use of generic printed/electronic communications)	Active comparators without a control group (i.e., head-to-head studies, comparisons of two active interventions as defined above). Other types of comparisons.
Outcomes	KQ 1a: Changes in BMI, maintenance of BMI, function, quality of life (i.e., emotional functioning as measured by mental health subscales or instruments, physical subscales of quality of life measures); obesity-related health conditions and outcomes including mortality. KQ 2a: Adverse effects of interventions (i.e., psychological adverse events related to interventions) KQ 1b, 2b: Weight outcomes and adverse effects across population subgroups	Intermediate outcomes (lab results), behavioral changes (e.g., physical activity level), cardiometabolic measures (e.g., glucose level, blood pressure, lipid level); cost effectiveness.
Setting	Primary care settings; settings comparable to U.S. practice.	Practice settings dissimilar than those in the U.S.
Study Design	KQ 1, 2: RCTs for all questions; observational studies with comparison groups for all questions.	Ecological studies, case reports, case series, or other noncomparative reviews; letters to the editor; other study designs
Study Quality	Good- and fair-quality studies for meta-analyses	Studies rated poor-quality

Abbreviations: BMI=body mass index; kg=kilogram; KQ=key question; m=meters; RCT = randomized controlled trial

APPENDIX 3

U.S. Preventive Services Task Force Quality Rating Criteria

Randomized Controlled Trials (RCTs) and Cohort Studies

Criteria:

- Initial assembly of comparable groups:
  - For RCTs: Adequate randomization, including first concealment and whether potential confounders were distributed equally among groups
  - For cohort studies: Consideration of potential confounders, with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- All important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies or intention-to treat analysis for RCTs

Definition of ratings based on above criteria:

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (follow-up ≥80%); reliable and valid measurement instruments are used and applied equally to all groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, intention-to-treat analysis is used for RCTs.

Fair: Studies are graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially, but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention-to-treat analysis is used for RCTs.

Poor: Studies are graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. Intention-to-treat analysis is lacking for RCTs.

APPENDIX 4

Strength of Evidence

The strength of evidence for each key question is assessed by using the approach described in the AHRQ Methods Guide.[29] Grades are based on:

- Study limitations (low, medium, or high level of study limitations)
- Consistency (consistent, inconsistent, or unknown/not applicable)
- Directness (direct or indirect)
- Precision (precise or imprecise)
- Reporting bias (suspected or undetected)

An overall grade of high, moderate, low, or insufficient is assigned according to a four-level scale by evaluating and weighing the combined results of the above domains:

- High: Very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. The findings are stable, i.e., another study would not change the conclusions.
- Moderate: Moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. The findings are likely to be stable, but some doubt remains.
- Low: Limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). Additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
- Insufficient: No evidence, are unable to estimate an effect, or have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

Applicability

Applicability (external validity) is estimated by examining the characteristics of the patient populations; the sample size of the studies; clinical settings (e.g., primary care, community setting); and clinical relevance of the screening approach. Variability in the studies may limit the ability to generalize the results to other populations and settings. Applicability is rated high, moderate, or low.

Appendix Table 1. Trials of Interventions to Prevent Weight Gain in Midlife Women

Author, year	Study design	Participants	Baseline BMI, *kg/m²*	Interventions and comparisons	Outcome measures	Results (intervention vs. control)*
Bea et al., 2010[33]	Cross-over RCT	122 women age 40-65 years with surgical or natural menopause; <120 min low intensity low impact exercise per week	19.0-33.0	High-intensity exercise 60-75 min sessions, 3-days per week for 1 year (n=65) vs. crossover (n=32) no intervention in the first year then exercise vs. no exercise (n=25)	Change from baseline at 6 years	Weight change from baseline, mean kg (SD): 0.43 (6.16) intervention vs. 0.70 (4.38) cross-over vs. 2.08 (4.25) no intervention; p=0.44
Forster et al., 1988[34]	RCT	219 normal weight adults (71% women); mean age 45.9 years	Average 23.1	Moderate-intensity counseling (4 sessions, monthly newsletters, financial incentive) vs. no counseling, newsletters, or incentive	Weight change from baseline at 1 year	Weight change from baseline, mean kg (SD): • Women: -1.0 (0.8) vs. -0.1 (0.7), NS • All adults by age: 41-50 years, 0.0 (1.2) vs. -0.2 (1.0), NS; >51 years, -3.7 (0.9) vs. -0.8 (0.9), p<0.01
Howard et al., 2006; Ritenbaugh et al., 2003[36,43]	RCT	48,835 postmenopausal women age 50-79 years (mean 62.3 years); 81.2% white; baseline diet with fat intake >32% of daily total calories	Mean 29.1; 25.7% normal; 35.8% overweight; 38.2% obese	High-intensity counseling (n=19,517) vs. control (n=29,273)	Annual weight change from baseline at 1 and 9 years	Weight change from baseline, mean difference in kg, age 50-59 years (n=18,003): • 1-year follow-up: -2.2 vs 0.6, p<0.001 • 9-year follow-up: +1.0 vs. +1.2 kg, NS
Klem et al., 1997; Kuller et al., 2000; Simkin-Silverman et al., 2003[37,38,44]	RCT	535 women age 44-50 years	Mean 25.1	High-intensity counseling, 5-year cognitive-behavioral program including 15 group meetings over 20 weeks (n=260) vs. no meetings (n=275)	Change from baseline at various follow-up times	• Weight change from baseline, mean lbs at 54 months: -0.2 vs. +5.2, p<0.01 • BMI change from baseline, mean kg/m^2 (SD) at 54 months: 0.05 (2.0) vs. 0.96 (1.8), p<0.001

Author, year	Study design	Participants	Baseline BMI, *kg/m²*	Interventions and comparisons	Outcome measures	Results (intervention vs. control)*
Lawton et al., 2008[39]	RCT	1,089 women age 40-74 years (mean age 59)	Mean 29	Moderate-intensity counseling (n=544) vs. control (545)	Weight at 12 and 24 months; quality of life at 12 and 24 months measured by SF-36 subscore	Weight, kg (SD) • 12 months: 72.6 (0.6) vs 72.7 (0.6) • 24 months: 72.6 (0.6) vs 72.5 (0.6) SF-36 subscale, physical function • 12 months: 2.17 (1.12 to 3.21) vs 0.07 (-0.97 to 1.11), p=0.03 • 24 months: -0.09 (-1.13 to 0.94) vs -0.91(-1.94 to 0.12), p=0.03 SF-36 subscale, mental health • 12 months: 1.73 (0.82 to 2.63) vs 0.51 (-0.39 to 1.42), p<0.05 • 24 months: 1.49 (0.54 to 2.44) vs 0.39 (-0.56 to 1.34), p<0.05
Lombard et al., 2016[40]	Cluster RCT	649 women age 18-50 years (mean 39.6) living near 41 Australian towns	35.2% normal; 31.9% overweight; 33.9% obese	High-intensity counseling (n=348) including one 60-minute facilitator-led interactive small group session, program manual, and a 20-minute phone coaching and 1 text message every 4 weeks vs. 45-minute group education session on general women's health topics (n=301)	Change from baseline at 1-year follow-up	• Weight change, mean lbs (95% CI): -0.48 (95% CI -0.99 to 0.03) vs. 0.44 (95% CI -0.09 to 0.97); adjusted difference -0.87 (-1.62 to -0.13 95% CI), p=0.02 • BMI change (95% CI): for normal weight, 0.17 (95% CI -0.40 to 0.74) vs. 0.57 (95% CI -0.02 to 1.16); for overweight, -0.65 (95% CI -1.56 to 0.26) vs. 0.53 (95% CI -0.47 to 1.52), p=0.46 • BMI change (95% CI): for age 30-45 years, -0.22 (95% CI -0.84 to 0.39) vs. 0.27 (95% CI -0.43 to 0.97); for > 45 years, -0.85 (95% CI -1.87 to 0.17) vs. 0.54 (95% CI -0.40 to 1.48), p=0.20
Mason et al., 2018[41]	RCT	272 adults (213 women); mean age 43.9	Mean 28.8	Low-intensity counseling (n=136) vs. no counseling (n=136)	Change from baseline at 45 days follow-up	Adjusted mean difference in follow-up weight • Adjusted for baseline weight and attendance at a weight loss program): -0.49 kg (95% CI -0.85 to -0.13), p=0.008 • Further adjusted for baseline BMI and time in study: -0.48 kg (95% CI -0.84 to -0.12), p=0.01

Author, year	Study design	Participants	Baseline BMI, *kg/m²*	Interventions and comparisons	Outcome measures	Results (intervention vs. control)*
Perry et al., 2016[42]	RCT	354 women age 40-60 years	39.9% normal; 32.3% overweight; 27.1% obese	High-intensity counseling including 10 hours of counseling sessions (n=185) vs. no counseling (n=169)	Change from baseline at 2 years	• Weight change, mean kg: 76.8 (1.3) vs. 74.6 (1.4) • BMI change, mean kg/m^2: 28.1 (0.5) vs. 28.1 (0.5) • Adjusted mean difference (95% CI) weight, kg: -0.31 (-1.09 to 0.46), p=0.43 • Adjusted mean difference (95% CI) BMI, kg/m^2: -0.09 (-0.39 to 0.21), p=0.57
Williams et al., 2014; Williams et al., 2019; Hollis et al., 2014[35,45,46]	Parallel RCT	54 women age 44-50 years (mean 47.3); mean body fat 35.8%	18.5-29.9 (mean 25.1)	Moderate-intensity motivational interviewing including four 1-hour individual sessions with a dietitian and one 1-hour individual session with an exercise physiologist (n=28) vs. self-directed intervention (n=26)	Change from baseline at 12 and 24 months; quality of life measured by Short-Form 36-item (SF-36)	Weight change at 12 months, mean kg: • Overall: -2.2 vs. -3.1 kg, adjusted p=0.034 • Normal weight at baseline: -2.5 vs. -0.1 kg, adjusted p=0.002; • Overweight at baseline: interview -3.5 vs. self-directed -2.3 kg, adjusted p=0.47 Weight change at 24 months, mean kg: • Overall: -2.3 vs. -0.3 kg, adjusted p=0.02 • Normal weight at baseline: -1.9 vs. 0.1 kg, adjusted p=0.03 • Overweight at baseline: -2.5 vs. -0.8 kg, adjusted p=0.20 SF-36 subscale, physical function, mean (SD) • 12 months: 51.6(5.5) vs 49.4 (8.1), NS • 24 months: 51.5 (6.1) vs 47.9 (7.3), NS SF-36 subscale, mental health, mean (SD) • 12 months: 49.9 (11.0) vs 52.0 (9.7), NS • 24 months: 48.7 (12.0) vs 51.5 (9.1), NS

Abbreviations: BMI=body mass index; CI=confidence interval; kg=kilogram; lbs=pounds; NS= not significant; RCT=randomized controlled trial; SD=standard deviation; vs.= versus

*p-values listed when provided by the study.

Appendix Table 2. Quality Assessment of Trials

Author, Year	Randomiz-ation adequate	Allocation concealment adequate	Groups similar at baseline	Eligibility criteria specified	Outcome assessors masked	Care provider masked	Patient masked	Intention-to-treat analysis?	Important loss to follow-up	Funding source reported	Quality Rating
Bea et al., 2010[33]	Unclear	Unclear	Yes	Yes	No	No	No	Yes	No	Yes	Fair
Forster et al.,1988[34]	Unclear	Unclear	Unclear	Yes	No	No	No	Unclear	No	Yes	Fair
Howard et al., 2006; Ritenbaugh et al., 2003[36,43]	Yes	Unclear	Yes	Yes	Unclear	No	No	Unclear	No	Yes	Fair
Klem et al., 1997; Kuller et al., 2000; Simkin-Silverman et al., 2003[37,38,44]	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	No	Yes	Good
Lawton et al., 2008[39]	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Good
Lombard et al., 2016[40]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Fair
Mason et al., 2018[41]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Fair
Perry et al., 2016[42]	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	Yes	Fair
Williams et al., 2014; Williams et al., 2019; Hollis et al, 2014[35,45,46]	Yes	Unclear	Yes	Yes	No	No	No	Yes	No	Yes	Fair