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Screening for and Management of Obesity and Overweight in Adults

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Structured Abstract

Background: Overweight and obesity in adults are common and associated with cardiovascular risk and other adverse health effects.

Purpose: To review benefits and harms of screening for and treatment of overweight and obesity in adults to assist the U.S. Preventive Services Task Force (USPSTF) in updating its 2003 recommendation.

Data Sources: We searched MEDLINE, the Cochrane Central Registry of Controlled Trials, and PsycINFO from January 1, 2005 through September 9, 2010. Relevant trials published prior to 2005 were identified through good-quality systematic reviews.

Study Selection: Two investigators independently reviewed 6,499 abstracts and 649 articles against a set of a priori inclusion criteria. Two investigators rated the quality of each study based on USPSTF methods. We included trials that involved behavioral-based treatment (38 trials, n=13,495) or the use of orlistat (18 trials, n=11,256) or metformin (3 trials, n=2,652) for weight loss or weight maintenance in adults in settings that are generalizable to U.S. primary care. Additional studies were included for the evaluation of weight loss treatment harms (4 additional behavioral trials, 6 additional orlistat trials, and 1 additional metformin trial).

Data Extraction: Selected elements were abstracted into standardized tables from each study by one investigator and checked by another investigator.

Data Synthesis: Data were qualitatively and quantitatively (using meta-analysis) synthesized separately for each type of intervention. Behavioral treatment resulted in an average weight loss of 3.0 kg more in intervention participants compared with control, with greater weight loss in trials with more treatment sessions (generally 4–7 kg lost in the intervention group in trials with 11–26 treatment sessions in the first year). Orlistat was additive to behavioral counseling, resulting in even greater weight loss (generally 6–9 kg total). Metformin trials were heterogeneous, but one large, good-quality trial showed a weight loss of 2.3 kg more in the intervention group. Weight loss treatments did not improve health outcomes, but they were sparsely reported and most trials were not powered for outcomes such as death and cardiovascular events. Weight loss treatment resulted in a reduction in diabetes incidence in two large, good-quality behavioral-based trials of diabetes prevention. Behavioral-based treatment showed small positive effects on blood pressure. Orlistat improved blood pressure and lowered low-density lipoprotein cholesterol (by 7–16 mg/dL) and plasma glucose (by 12 mg/dL in patients with diabetes) compared with placebo. Metformin did not improve lipid levels or blood pressure, but reduced the incidence of diabetes. Withdrawals due to adverse effects were more common among medication users than placebo users and were primarily related to gastrointestinal complaints.

Limitations: There were minimal data on the distal health outcomes of death and cardiovascular disease. Many intermediate outcomes were sparsely reported, especially in the behavioral treatment literature. There were minimal data on behavioral-based treatment in people with class III obesity (body mass index >40 kg/m^2). Behavioral-based treatments were heterogeneous and specific elements were not always well reported. Many medication trials had high attrition and

most were conducted outside of the United States. There was one good-quality trial of orlistat and one of metformin but no data on maintenance of weight loss after medications were discontinued. Medication trials were not powered to identify group differences in rare but serious adverse effects.

Conclusions: Behavioral-based treatments are safe and effective for weight loss, although they have not been studied in persons with class III obesity. Medication may increase weight loss beyond behavioral approaches alone, although side effects are common.

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Chapter 1. Introduction

Scope and Purpose

This systematic evidence review examines the benefits and harms of screening adults for obesity and overweight. The U.S. Preventive Services Task Force (USPSTF) will use this review to update its previous 2003 recommendation on screening adults for obesity and overweight. This targeted systematic review addresses the benefits and harms of programs that screen for overweight and obesity in adults in primary care settings, and articulates the benefits and harms of primary care–feasible or –referable weight loss interventions (behavioral-based interventions and/or pharmacotherapy) for obese or overweight adults. Because the previous evidence report found good-quality evidence for using body mass index (BMI) to identify adults with increased risk of future morbidity and mortality, we did not systematically address reliable and valid clinical screening tests for obesity and overweight. As part of the "Screening Strategies" section, we briefly discuss whether waist-to-hip ratio (WHR), waist circumference, or other related measures of central adiposity have independent predictive value for future mortality and health risks compared with BMI measures only.

This review focuses primarily on cardiovascular health effects in addition to weight loss. Although we do report on health outcomes beyond cardiovascular events and mortality, the intermediate health outcomes are limited to those related to cardiovascular disease or its precursors—blood lipid levels, blood pressure, diabetes risk, and glucose tolerance.

The weight loss interventions covered in this review include behavioral-based interventions, pharmacological (orlistat and metformin) interventions, or a combination of both. Behavioral intervention programs had to include a primary focus on weight reduction through a decrease in caloric intake, increase in physical activity, or both. We did not review studies focused only on changes in dietary content without a decrease in calories or stated goal of causing weight loss. Physical activity had to include aerobic- and/or strength-related activity that resulted in increased energy expenditure. The USPSTF determined that surgical treatment for weight loss was not within the scope of this report, as surgical treatment is not considered to be in the purview of preventive primary care.

Background

Condition Definition

Obesity and overweight are most commonly defined by BMI, which is calculated as weight in kilograms divided by height in meters squared. Overweight is defined as a BMI of 25 to 29.9 kg/m^2. Obese is defined as a BMI of $\geq$30 kg/m^2. The category of "obese" is further divided into subcategories of class I (BMI 30.0–34.9 kg/m^2), class II (BMI 35.0–39.9 kg/m^2), and class III (BMI $\geq$40 kg/m^2).[1]

Prevalence and Burden of Disease/Illness

According to the most recent National Health and Nutrition Exam Survey data, the prevalence of obesity in the United States is high, exceeding 30 percent in most age- and sex-specific groups. In 2007–2008, 32 percent of U.S. men and 36 percent of U.S. women were obese and an additional 40 percent of men and 28 percent of women were overweight.[2] About 1 in 20 Americans has a BMI of >40 kg/m^2 (class III obesity).[2] The prevalence of obesity and overweight has increased by 134 percent and 48 percent, respectively, since 1976–1980.[3] Between 1999 and 2008, while overweight/obesity trends stabilized for women, overweight/obesity rates continued to rise for men.[2] In the Framingham cohort, the long-term risk for becoming overweight or obese was more than 50 and 25 percent, respectively.[4]

Using standard BMI definitions across ethnic groups, nonwhite adults have a higher prevalence of overweight and obesity than white adults. Among women, for example, the age-adjusted prevalence of obesity (BMI ≥30 kg/m^2) is higher among nonHispanic black (49.6 percent) and Hispanic women (43 percent) than among nonHispanic white women (33 percent). The difference in obesity prevalence is less marked among men (37.3 percent in nonHispanic black men, 34.3 percent in Hispanic men, and 31.9 percent in nonHispanic white men).[2] Rates of obesity among Asian Americans (8.9 percent) are much lower compared with other racial groups. Given that the relationship between BMI and disease risk appears to vary among ethnic groups (as discussed below), differences in the prevalence of obesity cannot be directly translated into comparable differences in disease risk.

Obesity is associated with an increased risk of death, particularly in adults younger than age 65 years.[5-9] Obesity has been shown to reduce life expectancy by 6 to 20 years depending on age and race.[7,10] Ischemic heart disease, diabetes, cancer (especially liver, kidney, breast, endometrial, prostate, and colon), and respiratory diseases are the leading causes of death in persons who are obese.[8]

Whether being overweight is associated with an increased mortality risk is less clear. Some,[5,8-11] but not all,[5,6,12,13] studies have found an increased risk of death in those who are overweight. The association between overweight/obesity and mortality risk, however, varies by sex, ethnicity, and age, which may be why data are mixed. The BMI value that is associated with the lowest mortality risk varies among different ethnic subgroups. For some groups, the lowest mortality risk is a BMI that falls in the normal range, but for other ethnic groups, the lowest mortality is associated with a BMI in the overweight range. Black populations, for example, appear to have lowest mortality rates at a BMI of 26.2 to 28.5 kg/m^2 in women and 27.1 to 30.2 kg/m^2 in men.[12,14] In comparison, white women and men experience lowest mortality at a BMI of 24.5 to 25.6 kg/m^2 and 24.8 kg/m^2, respectively.[12,14] On the other hand, certain Asian populations may experience lowest mortality rates at a BMI of 23 to 24.9 kg/m^2.[15-18]

The relationship between BMI and mortality is different in adults older than age 65 years.[19,20] In this population, waist circumference appears to have an association with mortality, but BMI does not. It is hypothesized that in the older adult population, a high BMI may be a marker of more lean mass (and thus decreased mortality risk), whereas waist circumference is a better marker of adiposity and thus more correlated with cardiovascular risk.

Being overweight or obese is associated with an increased risk of coronary heart disease (CHD),[21-23] even after adjustment for established risk factors.[21,24] In a meta-analysis of 21 cohort studies including more than 300,000 predominantly white persons, overweight increased the risk of CHD events by 17 percent and obesity increased it by 49 percent after adjustment for age, sex, physical activity, smoking, blood pressure, and cholesterol levels.[21] Recent adjusted estimates of CHD and hypertension health risks among nonHispanic white, nonHispanic black, East Asian, and Hispanic Americans suggest that all groups have increased cardiovascular disease risk with increasing BMI, but there are significant group-specific differences in absolute risk and the level of BMI at which increased risk occurs.[25] In black populations, increasing BMI is less associated with increasing cardiovascular disease risk compared with whites.[26-28] Data for Latino populations suggest a lesser association of cardiovascular disease and BMI compared with whites and other higher risk subgroups.[25] However, increasing BMI is associated with increased cardiovascular disease risk in many Asian populations, and cardiovascular disease risk seems to begin to rise at a lower BMI level in Asian compared with white populations.[29-31]

Type 2 diabetes is strongly associated with obesity or overweight. According to a systematic review and meta-analysis of prospective cohort studies, overweight and obese men had a respective 2.4- and 6.7-fold increased risk of type 2 diabetes compared with normal weight men.[32] Overweight and obese women had a respective 3.9- and 12.4–fold greater risk of type 2 diabetes compared with normal weight women.[32] A BMI of >25 kg/m^2 was associated with a 2.2-fold greater risk of death from diabetes, a greater association than with any other cause of death.[8]

Evidence suggests that the relationship between BMI and diabetes risk also varies by ethnicity. As with cardiovascular disease, there are significant group-specific differences in absolute risk and the level of BMI at which increased type 2 diabetes risk occurs.[25] For example, many nonwhite populations appear to have a higher diabetes risk at similar BMI levels than white populations, and diabetes risk can begin to increase at lower BMI levels in some ethnic groups. This has been best studied in East Asians (Chinese, Japanese, and Korean populations), and is also being increasingly recognized among South Asians and Latinos (two large subpopulations that also have a higher overall prevalence of diabetes relative to other groups).[33-36] Reacting to this trend, the World Health Organization (WHO) recently adjusted screening guidelines for Asia to recommend country-specific BMI cut-off points that may start as low as 23 kg/m^2 for some populations.[37-39]

The incidence of many types of cancer increases with increasing BMI. In particular, endometrial, gallbladder, esophageal, and renal cancer incidence is increased in obese women and esophageal, thyroid, colon, rectal, and renal cancer incidence is increased in obese men.[40-42] The risk of dying from several types of cancer (i.e., liver, pancreas, and stomach cancer in men and uterine, kidney, and cervical cancer in women) is increased with increasing BMI.[42,43]

Other diseases that have been associated with obesity include ischemic stroke,[31,44,45] heart failure,[24] atrial fibrillation/flutter,[46,47] dementia,[48] venous thrombosis,[49] gallstones,[50,51] gastroesophageal reflux disease,[52] renal disease,[53,54] and sleep apnea.[55] Obesity also increases the risk of developing osteoarthritis[56,57] and is associated with functional disability.[58] In addition,

maternal obesity is associated with pregnancy complications and adverse pregnancy outcomes and adversely influences fetal and neonatal health.[59-62]

Some observational studies suggest that obese individuals, even those without comorbid diseases, can have a decreased quality of life compared with normal weight individuals.[63] Among normal weight and overweight women, quality of life (especially physical function) decreased with weight gain. In contrast, quality of life improved in overweight women who lost weight.[64] A recent meta-analysis suggests a reciprocal link between obesity and depression.[65] As a result of the increased morbidity, there is increased use of health care services and costs among the obese.[66,67] Compared with adults with a BMI of 20 to 24.9 kg/m^2, those with a BMI of 30 to 34.9 kg/m^2 and ≥35 kg/m^2 had 25 and 44 percent higher mean annual total (inpatient and outpatient) health service costs, respectively. There was no increase in health service costs in overweight adults (BMI 25 to 29.9 kg/m^2).[67]

Etiology and Natural History

Overweight and obesity ultimately result from an imbalance between energy intake and energy output. Energy balance appears to have both environmental and genetic influences.[68,69] Environmental factors that play an important role in the growing obesity epidemic include an increasingly sedentary lifestyle,[70] television watching,[71] fast food consumption,[72] and sleep deprivation.[73] Exposures in early development may influence the risk of developing obesity later in life. For example, maternal smoking,[74] maternal gestational diabetes,[75] and short or no exposure to breastfeeding are associated with an increased risk of childhood obesity.[76] Childhood obesity increases the risk of adult obesity.[77,78]

In terms of the natural history of obesity, weight gain occurs until about the sixth decade of life, when weight appears to stabilize and then decline with age.[79-81] Having an elevated BMI in early adulthood (ages 20 to 22 years) appears to increase the risk of developing obesity within 15 years. For example, in a study of the natural history of the development of obesity in young U.S. adults, 41 percent of white, 47 percent of Hispanic, and 66 percent of black women who had a BMI of 24 to 25 kg/m^2 at ages 20 to 22 years became obese by ages 35 to 37 years.[82]

Rationale for Screening

Screening for overweight/obesity would be beneficial if persons with increased weight have an elevated disease risk and if interventions to reduce weight successfully decrease that disease risk. However, the harms of screening must also be considered. The act of obtaining BMI, as noted in a previous USPSTF statement, is ~~n~~ot associated with any direct physical harm."[83] Other methods of measuring obesity, such as waist circumference, WHR, or percent body fat, are still quite inexpensive and similarly not associated with any direct physical harm.[83]

Possible secondary harms might include labeling stigma, as well as potential financial cost to patients in the form of higher insurance premiums, or reinforcement of poor self-esteem. However, there are no data about how often these potential secondary harms actually result from screening for obesity.

Screening Strategies

Measurements that can be used to estimate body fat and quantify health risks include BMI, waist circumference, WHR, bioimpedance, and dual-energy x-ray absorptiometry (DXA).[3] Measuring height and weight to calculate BMI in a clinical setting is a low-cost, relatively quick, and reasonably reliable way to screen for obesity. Reference charts and BMI calculators are available to allow clinicians to look up a patient's BMI from his/her height and weight without manual calculation. The previous evidence report found good-quality evidence that BMI identifies adults with increased risk of future morbidity and mortality. As such, we did not systematically address the question of the relative value of different measures to screen for excess body fat.[84] Since that last evidence report, however, data from large (more than 10,000 persons) prospective studies have been published suggesting that WHR offers independent predictive value for mortality in addition to BMI.[85-93] WHR has an added benefit in that its cut-off points are similar even in different populations, simplifying interpretation.[94-96]

Of the central adiposity measures, waist circumference is probably the most reproducible and the simplest to measure, and is independently associated with risk. As such, waist circumference is emerging as the most useful measure to add to screening recommendations.[86,94,95,97-99] The bulk of the recent identified literature supports waist circumference as having an independent association with morbidity and mortality, especially in many higher-risk populations, such as South Asians or Mexicans, who might have a higher prevalence of obesity-associated morbidity such as diabetes.[36,98] It also appears to be more sensitive in detecting persons who are at increased cardiometabolic risk, even in the normal BMI categories.[86,97,99-105]

For waist circumference, the National Heart, Lung, and Blood Institute (NHLBI) has defined cut-off points for abdominal obesity as >88 cm in women and >102 cm in men.[106] However, WHO has recommended lower cut-off points for Asian populations of >80 cm in women and >90 cm in men, meant to correspond to the lower cut-off points defined by NHLBI.[107,108] A review and meta-analysis of waist circumference and WHR variation in cut-off points among different ethnic groups supports a lower waist circumference cut-off point for East Asian populations, consistent with WHO's guidelines, and that South Asian populations in particular may need similar or possibly even slightly lower cut-off points (>80 cm in women and >85 cm in men).[98] In Latino populations, data are mixed, likely in part due to cultural practices as well as genetics and body type variation within the overall categorization of "Latino" or "Hispanic." Black populations may have similar cut-off points to whites, but data in that population are not sufficient and require further study, as different components of risk exist in that population. Pacific Islander and Middle Eastern populations are not adequately studied to identify different cut-off points.[98] There are also increasing populations of adults in the United States of mixed ethnicity, and disease risk for them is complex and largely unstudied.

Interventions/Treatment

Clinical interventions to achieve and maintain weight reduction include behavioral-based interventions to induce lifestyle change (dietary restriction, increased physical activity, or both), pharmacotherapy, and surgery. Behavioral-based clinical interventions optimally will combine information on safe physical activity and healthy eating for weight loss with cognitive and

behavioral management techniques to help participants make and maintain lifestyle changes.[1] Several medications are currently approved in the United States for the management of obesity, including weight loss and maintenance of weight loss, in conjunction with a reduced calorie diet: orlistat, phentermine, and diethylpropion. These medications are recommended for obese patients with an initial BMI of ≥30 kg/m^2 or ≥27 kg/m^2 in the presence of other risk factors (e.g., diabetes, dyslipidemia, or controlled hypertension).

Orlistat decreases fat digestion by inhibiting pancreatic lipases. Ingested fat is not completely hydrolyzed, resulting in increased fecal fat excretion. The recommended prescription dose is 120 mg three times a day (tid) with each main meal containing fat. The patient should be on a nutritionally balanced, reduced-calorie diet that contains approximately 30 percent of calories from fat. A lower dose of 60 mg is available as an over-the-counter medication. Per the U.S. Food and Drug Administration (FDA), the safety and effectiveness of orlistat beyond 4 years have not been determined at this time. Orlistat is contraindicated in patients with chronic malabsorption syndrome or cholestasis and in patients with known hypersensitivity to orlistat or to any component of this product.

Sympathomimetic drugs block the reuptake of norepinephrine and serotonin into nerve terminals, thereby leading to early satiety and reduced food intake. The only currently approved sympathomimetic drugs, phentermine and diethylpropion, are for short-term use (usually interpreted as up to 12 weeks). The use of these short-term drugs in the treatment of obesity was not included in this systematic evidence review.

Sibutramine is a sympathomimetic weight loss drug that was previously approved for longer-term use. However, it was voluntarily removed from the market by Abbott Laboratories at the request of the FDA on October 8, 2010. The FDA recommended against continued prescribing and use of sibutramine because it concluded that the drug may pose unnecessary cardiovascular risks to patients. The FDA's recommendation was based on new data from the Sibutramine Cardiovascular Outcomes trial, a trial of persons older than age 55 years with cardiovascular disease. The FDA concluded that the risk for adverse cardiovascular events from sibutramine outweighed any benefit from the modest weight loss observed with the drug.

Metformin is primarily a medication used to treat diabetes, but has been used off label to promote weight loss and prevent diabetes in high-risk persons. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and increases peripheral glucose uptake and utilization. The mechanism by which metformin reduces weight is not clear. Metformin might enhance glucagon-like peptide (GLP-1) secretion.[109-111] GLP-1 has been shown to slow gastric emptying and reduce food intake.[112,113] There is no fixed dosage regimen for the management of hyperglycemia in patients with type 2 diabetes. Dosage must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose. The maximum recommended daily dose of metformin is 2,550 mg in adults. It should be taken in divided doses with meals. Metformin is contraindicated in patients with renal disease or renal dysfunction, known hypersensitivity to metformin, or acute or chronic metabolic acidosis.

Another medication that is used off label for weight loss is zonisamide, an antiepileptic agent.[114]

We did not include this medication in our systematic evidence review. There are also several novel antiobesity drugs in development. Lorcaserin, a selective 5-hydroxytryptamine receptor agonist, was voted against by an FDA advisory panel on September 16, 2010 because of concerns over both safety and efficacy. Qnexa, a combination of phentermine and topiramate, an antiepilepsy and migraine drug, was rejected by the FDA on October 28, 2010 because of safety concerns. Contrave, a combination of naltrexone (an opioid receptor antagonist) and bupropion (a dopamine and norepinephrine reuptake inhibitor), was rejected by the FDA on January 31, 2011, who cited the need for a large-scale study of the cardiovascular effects of the drug before it could be approved.[115] A combination of bupropion and zonisamide is currently being studied in phase III trials.[114]

Current Clinical Practice

Despite the ease of determining BMI, surveys have indicated that only 38 to 66 percent of overweight or obese patients have received diagnoses of overweight or obesity, and less than half of obese patients report that their physicians have advised them to lose weight and/or provided specific information about how to lose weight.[116,117] According to the most recent data from the U.S. National Ambulatory Medical Care Survey, almost 50 percent of clinic visits lack complete height and weight data needed to screen for obesity using BMI.[118] Of those visits where BMI was determined to be ≥30 kg/m^2, 70 percent of patients were not given a diagnosis of obesity and 63 percent did not receive any counseling for weight reduction.[118] Even among those who suffer from obesity-related comorbidities, only 52 percent were screened for obesity, 34 percent were diagnosed with obesity, and 46 percent were counseled about their obesity.[118] When overweight American adults were surveyed, only 24.4 percent of obese Americans were referred by their physician to a dietician or nutritionist and 11 percent were recommended to a formal diet program; less than 10 percent of those who were overweight were referred for these nutritional services.[119] Close to 10 percent of obese adults were prescribed a weight loss medication.[119] However, many who are prescribed weight loss medications may not meet approved indications and/or may have contraindications.[120] For example, a Swedish survey found that 6 percent of patients prescribed orlistat did not meet the BMI requirement (≥30 kg/m^2 with no cardiovascular risk factors or ≥27 kg/m^2 with cardiovascular risk factors).[120]

Recommendations of Other Groups

The National Institutes of Health (NIH) and the Canadian Task Force on Preventive Health Care recommend measuring BMI and waist circumference to screen adults for obesity.[1,121] The frequency of screening is not specified. The American Academy of Family Physicians (AAFP) advises physicians to evaluate patients for overweight and obesity during routine medical examinations.[122] In terms of interventions, NIH and the Canadian Task Force on Preventive Health Care recommend that weight loss and weight maintenance therapies should include the combination of a reduced-calorie diet, increased physical activity, and behavioral therapy.[1,121] Weight loss drugs could be used as part of a comprehensive program in patients who are obese or overweight (BMI >27 kg/m^2) with comorbidities.[1,121] AAFP recommends that providers discuss the health consequences of further weight gain with at-risk patients.[122]

Previous USPSTF Recommendation

In 2003, the USPSTF recommended that clinicians screen all adult patients for obesity and offer intensive counseling and behavioral interventions to promote sustained weight loss for obese adults (B recommendation). However, the USPSTF concluded that the evidence was insufficient to recommend for or against the use of moderate- or low-intensity counseling together with behavioral interventions to promote sustained weight loss in obese adults (I recommendation). Likewise, the USPSTF concluded that there was insufficient evidence to recommend for or against the use of counseling of any intensity together with behavioral interventions to promote sustained weight loss in overweight adults (I recommendation).

Chapter 2. Methods

Key Questions and Analytic Framework

Building on the methods and approach of the 2003 USPSTF evidence review, we developed an analytic framework (Figure 1) and formulated four key questions (KQs) to guide our literature search and targeted systematic review.[83] The KQs were designed to evaluate the benefits of programs to screen for and manage overweight and obesity in adults in primary care, and the benefits and harms of primary care–feasible or –referable weight loss interventions for obese or overweight adults.

KQ 1. Is there direct evidence that primary care screening programs for adult obesity or overweight improve health outcomes or result in short-term (12 months) or sustained (over 12 months) weight loss or improved physiological measures (e.g., glucose tolerance, blood pressure, and dyslipidemia)?

KQ 1a. How well is weight loss maintained after an intervention is completed?

KQ 2. Do primary care–relevant interventions (behavioral-based interventions and/or pharmacotherapy) in obese or overweight adults lead to improved health outcomes?

KQ 2a. What are common elements of efficacious interventions?
KQ 2b. Are there differences in efficacy between patient subgroups (e.g., ages 65 years or older, sex, race/ethnicity, degrees of obesity, baseline cardiovascular risk status)?

KQ 3. Do primary care–relevant interventions in obese or overweight adults lead to short-term or sustained weight loss, with or without improved physiological measures?

KQ 3a. How well is weight loss maintained after an intervention is completed?
KQ 3b. What are common elements of efficacious interventions?
KQ 3c. Are there differences in efficacy between patient subgroups (e.g., ages 65 years or older, sex, race/ethnicity, degrees of obesity, baseline cardiovascular risk status)?

KQ 4. What are the adverse effects of primary care–relevant interventions in obese or overweight adults (e.g., nutritional deficits, cardiovascular disease, bone mass loss, injuries, and death)?

KQ 4a. Are there differences in adverse effects between patient subgroups (e.g., ages 65 years or older, sex, race/ethnicity, degrees of obesity, baseline cardiovascular risk status)?

Literature Search Strategy

In addition to evaluating all trials included in the previous reviews for inclusion in the current review, we conducted a search (Appendix B) for relevant existing systematic reviews in databases (Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of

Effects, and MEDLINE), as well as Web sites (Institute of Medicine, NIH, and National Institute for Health and Clinical Excellence [NICE]). We identified a 2006 NICE systematic review with detailed reporting on behavioral weight loss interventions and orlistat which was current through November 2005. We used this review as the foundation for our literature search for KQs 1–4.[123] The NICE review, however, did not include metformin, so we identified an additional review to locate metformin trials published since the previous USPSTF review. This review focused specifically on metformin treatment for weight loss and searched into February 2008.[124] We then conducted a search for all four KQs (Appendix B) in MEDLINE, the Cochrane Central Registry of Controlled Trials, and PsycINFO beginning in January 1, 2005 through September 9, 2010. We supplemented our searches with suggestions from experts and reference lists from other relevant publications.

Study Selection

Two investigators independently reviewed all abstracts and articles against inclusion and exclusion criteria (Appendix B Table 2). Discrepancies were resolved by consensus. Articles excluded for not meeting inclusion criteria or for poor quality are listed in Appendix D Tables 1–4. Briefly, we included randomized or controlled clinical trials (additionally, cohort or case-control studies for KQ 4) conducted among adults (ages 18 years and older) in settings generalizable to or referable from primary care. Because we were examining the effects of weight loss programs versus usual care, we excluded trials with control groups receiving frequent weigh-ins, advice more frequently than annually, or at-home study materials; these studies were considered to be comparative effectiveness studies. Interventions were restricted to those focusing on weight loss and those not reporting weight outcomes were excluded. Only outcomes reported at 12 months or longer were included (with the exception of KQ 4).

Data Extraction and Quality Assessment

Two independent investigators dual-reviewed 6,498 abstracts and 648 articles (Appendix B Figure 1) for inclusion and critically appraised all included articles using design-specific criteria (Appendix B Table 2) and USPSTF methods.[125] The USPSTF has defined quality ratings of "good," "fair," and "poor" based on specific criteria. Discrepancies in quality ratings were resolved by consultation with a third investigator. All studies rated as poor quality were excluded from the review.

Briefly, for KQs 1–3, we assessed the validity of the randomization and measurement procedures, attrition, similarities between the groups in baseline characteristics and attrition, intervention fidelity, and statistical methods. Among other things, good-quality trials blinded researchers to participant randomization if they performed tasks related to assessment, had followup data on 90 percent or more of participants, reported group-specific followup with less than 10 percent difference between groups, and described important details related to the measurement of anthropomorphic measures. Trials were rated as "poor" if attrition in the treatment and control groups differed by more the 20 percent or if overall attrition was higher than 40 percent, or had other important flaws. All trials meeting quality criteria for KQs 1–3 were also examined for KQ 4 outcomes.

In addition, we developed separate quality assessment procedures for trials that were not included for KQs 1–3 (either due to quality issues or other inclusion criteria) but reported harms outcomes. The quality rating of KQ 4-only studies specifically focused on the assessment and analysis of harms. We did not have minimum attrition standards or duration of followup requirements because high attrition may be directly related to harms and a 12-month duration requirement would miss immediate harms. Because we had different standards for KQ 4 that focused only on factors specifically related to the assessment of harms, we simply rated them as ―acceptable" or ―poor." A poor-quality study was one that had a fatal flaw that made the harms data of questionable validity.

One investigator abstracted data from included studies into standardized evidence tables and a second investigator reviewed abstracted data for accuracy. We abstracted study design, setting, population characteristics, baseline health, intervention characteristics, outcomes, and adverse events (Appendix C Tables 1–3).

For KQ 1, no trials were included in this review. For KQs 2 and 3, 98 articles representing 58 unique trials were included, 30 of which were conducted in the United States. For KQ 4, we included an additional 12 articles representing 10 randomized, controlled trials (RCTs) and two cohort studies that were not included in KQs 2 and 3 for various reasons, including three trials for poor quality,[126-128] four for short duration (<12 months),[129-132] three for study design (not RCTs),[133-135] two for comparative effectiveness,[136,137] and one because the exercise intervention was not designed to promote weight loss.[138]

Data Synthesis and Analysis

We separately synthesized identified evidence for trials of behavioral-based interventions and each weight loss medication. Within each intervention type, trials were grouped according to the study population risk status (cardiovascular risk, subclinical risk, unselected/low risk) and then ordered by the intensity of the behavioral interventions within each risk status (number of sessions for behavioral trials, brief or intensive intensity for medication trials). Risk status and intensity are discussed in detail in Appendix A.

We conducted random effects meta-analyses to estimate the effect size of weight loss interventions on intermediate health outcomes (adiposity, systolic and diastolic blood pressure [SBP, DBP], total cholesterol, high-density and low-density lipoprotein [HDL, LDL] cholesterol, triglycerides, and glucose). For continuous outcomes, we analyzed change from baseline. Risk ratios were analyzed for dichotomous outcomes. Absolute risk difference was also estimated through meta-analysis in many cases so that the number needed to treat (NNT) could be calculated. We selected a single intervention arm for trials that included multiple active treatment arms and calculated change from baseline and standard deviations based on the information provided in the individual articles if they were not provided. We converted measurements into common units using standard conversion factors, which are provided in Appendix A. Additional details of the meta-analysis data management and calculations can also be found in Appendix A.

We assessed the presence of statistical heterogeneity among the studies using standard chi-square tests and estimated the magnitude of heterogeneity using the I^2 statistic.[139] We considered an I^2

statistic of <50 percent to represent low heterogeneity, 50–75 percent to represent moderate heterogeneity, and >75 percent to indicate high heterogeneity among the studies. Tests of publication bias on whether the distribution of the effect sizes was symmetrical with respect to the precision measure were performed using funnel plots and Egger's linear regression method[140] when the number of studies was about 10 or more.[141]

Meta-regressions were used to explore heterogeneity in effect sizes among the KQs 1–3 trials. Due to concerns about type I errors, we limited most exploration of heterogeneity to a single outcome—weight loss. Some factors were explored for the entire body of trials, combining behavioral interventions and all three medication types, while other factors were run separately for the medication trials only and the behavioral trials only. Continuous variables were left as continuous variables, and categorical variables were converted to one or more dummy variables.

Heterogeneity was explored with several factors. Prominent sources of heterogeneity were the risk status of the populations and the participant identification approach (see Appendix A for more details). Additional factors explored for the entire combined body of literature were: percent of participants retained at 12 to 18 months, whether the trial focused on weight maintenance as opposed to weight loss, whether primary care was the setting for either recruitment or the intervention, whether the trial was set in the United States, study quality rating, and selected patient-level characteristics.

For medication trials, we also examined the percent of participants that were retained after a run-in period, the specific type of medication, and whether the behavioral intervention was more intensive than would be delivered in primary care (see intensity definitions in Appendix A). The variables explored for the entire group of trials listed above were also examined separately in the medication trials. All meta-regression of the medication trials controlled for medication type and population risk status.

For behavioral trials, we also examined the number of sessions in the first year and, in separate models, the presence of each of the following intervention components: supervised physical activity sessions, group sessions, individual sessions, technology-based assessment or intervention, specific weight loss goals, spouse or family involvement, addressed barriers to weight loss, pros and cons of weight loss or similar motivational assessment, self monitoring, use of incentives for weight loss or intervention participation, and support for weight loss or lifestyle maintenance after active intervention phase. The variables examined in the combined medication and behavioral trials were also examined separately in the behavioral subgroup. Number of sessions in the first year and risk status of the patients were included in all models.

All analyses were performed using Stata 10.0 software (StataCorp, College Station, TX).

USPSTF Involvement

The authors worked with four USPSTF liaisons at key points throughout the review process to develop and refine the analytic framework and KQs, to address methodological decisions on applicable evidence, and to resolve issues regarding scope of the final evidence synthesis. This research was funded by the Agency for Healthcare Research and Quality (AHRQ) under a

contract to support the work of the USPSTF. AHRQ staff provided oversight for the project, reviewed the draft report, and assisted in external review of the draft evidence synthesis.

Chapter 3. Results

We identified 58 trials of benefits of weight loss interventions, reported in 98 publications. Of these, 38 trials examined the benefits of behavioral-based interventions[142-178] and 21 examined the benefits of medication (orlistat or metformin) for weight loss.[142,179-203] One of the trials included both medication and behavioral-based intervention arms and was counted in both groups.[142] Table 1 lists all included trials assessing benefits of weight loss or weight maintenance interventions, grouped by the risk status of the population. We also identified an additional 12 studies (in 14 publications) on harms of weight loss interventions; four of these targeted behavioral weight loss methods and eight addressed harms of orlistat and/or metformin.

The participants in the behavioral interventions had mean BMI values that ranged from 25 to 39 kg/m^2. Only three of the trials were limited to obese persons,[162,173,204] and the remaining included overweight as well as obese persons, usually requiring a BMI of at least 25 kg/m^2. Almost all of the medication trials required participants to have a BMI of at least 27 kg/m^2. The mean BMI values in the medication trials were all in the obese range (32 to 38 kg/m^2). For the purposes of this report, we use the term overweight and obese to refer to studies which had a minimum BMI criteria of 25 kg/m^2, even if the mean BMI of the participants in these studies was in the obese range. For studies with a minimum BMI of 30 kg/m^2, we refer to the subjects as obese.

KQ 1. Is There Direct Evidence That Primary Care Screening Programs for Adult Obesity or Overweight Improve Health Outcomes or Result in Short-Term or Sustained Weight Loss or Improved Physiological Measures?

We identified no trials of adult obesity screening programs (i.e., randomizing participants to either be screened or not and then providing appropriate management for those screening positive for obesity).

KQs 2–2b. Do Primary Care–Relevant Interventions (Behavioral-Based Interventions and/or Pharmacotherapy) in Obese or Overweight Adults Lead to Improved Health Outcomes? What Are Common Elements of Efficacious Interventions? Are There Differences in Efficacy Between Patient Subgroups?

Health outcomes (see methods for a full list of outcomes eligible for systematic review) were minimally reported in the included trials, and almost all showed no effect on the health outcomes that were examined. The Diabetes Prevention Project (DPP) provided the most complete examination of health outcomes for behavioral treatment and metformin, covering cardiovascular disease events and deaths, deaths from any cause, hospitalizations, and depressive symptomatology.[142,205-207] DPP was a large (n=3,234), good-quality randomized trial of persons with prediabetes (impaired fasting glucose [IFG] or impaired glucose tolerance [IGT]) with up to

3.2 years of followup. In addition to DPP, six behavioral-based trials (three fair-quality[156,177,208] and three good-quality[170,172,175]) and eight fair-quality pharmacotherapy trials[181,185,189,198,199,201,202,209] reported health outcomes.

Death

DPP reported deaths, but there were too few deaths to be able to draw conclusions about the effect of the program in the approximately 3 years of followup.[206] In the oldest age group (60 to 85 years), where deaths were most common, the death rates were 0.31 and 0.48 per 100 person-years in the lifestyle and metformin groups, respectively, compared with 0.86 per 100 person-years in the control group; neither active intervention group was statistically significantly different from the controls.[210] All of the remaining behavioral,[170] metformin,[185] and orlistat[181,189,202,209] trials that reported deaths had no more than one death in each treatment group.

Cardiovascular Disease

DPP also reported that metformin and lifestyle participants showed no differences from control groups in nonfatal cardiovascular disease events or in cardiovascular disease-related deaths at 3 years postrandomization,[207] and data were very similar in another large good-quality behavioral trial in persons with prediabetes.[172] Another good-quality behavioral trial of weight loss in older adults with hypertension[175] reported no differences in cardiovascular events (stroke, transient ischemic attack, myocardial infarction, angina, congestive heart failure, arrhythmia, and other) over 30 months of followup. The proportion with cardiovascular events was 14.3 percent in the weight loss group compared with 16.7 in the usual care group. Smaller trials also found no effect of behavioral treatment on use of medication for cardiovascular disease after 1 year,[165] and no effect of metformin treatment on the development of ischemic cardiovascular disease.[185]

Hospitalization

There were no differences in hospitalizations between the active treatment groups and control groups in DPP.[206] Among adults ages 60 to 85 years, the rate of hospitalizations per 100 person-years was 12.3 in the lifestyle intervention group, 13.3 in the metformin group, and 10.6 in the control group.[210]

Quality of Life and Depression

Of the few trials that examined depressive symptomatology or quality of life, almost none found positive effects of behavioral or medication treatment for weight loss. DPP,[156] two additional behavioral trials,[177,205] and two orlistat trials[199,201] reported depression or quality of life outcomes using validated screening instruments, including one that was specifically designed for obese adults.[199] None found group differences for depression, but DPP did report improvement in health-related quality of life (HRQL). The researchers characterized the HRQL effects as small and correlated with weight loss but not treatment assignment when weight loss was controlled for.[211] One orlistat trial did find less overweight distress after 1 and 2 years in those taking orlistat.[199] Another orlistat trial found greater improvement in the vitality subscale of the 36-item Short-form Health Survey (SF-36) in those taking orlistat compared with placebo (mean increase

of 5.42 vs. decrease of 1.5 in placebo; p=0.006). However, there were no statistically significant differences on the seven other SF-36 subscales in this trial.[201]

Common Elements of Efficacious Interventions

Too little data were provided to allow conclusions regarding components of efficacious interventions.

Results in Different Subgroups

Only very minimal data were found to shed light on whether some subpopulations benefit more from treatment than others. DPP found no treatment-by-age interaction effects in hospitalizations or deaths for either treatment group, although it reported inadequate power to assess the significance of effects within the subgroups.[206] Two behavioral trials that examined differential response to treatment on depression found no sex differences in response to treatment.[177,205]

KQs 3–3c. Do Primary Care–Relevant Interventions in Obese or Overweight Adults Lead to Short-Term or Sustained Weight Loss, With or Without Improved Physiological Measures? How Well is Weight Loss Maintained After an Intervention is Completed? What Are Common Elements of Efficacious Interventions? Are There Differences in Efficacy Between Patient Subgroups?

Behavioral-Based Interventions

General characteristics of the trials. All 38 trials of behavioral-based interventions reported some measure of weight loss (n=13,495 randomized to behavioral-based or control treatment arms), although other intermediate outcomes were more sparsely reported.[142-149,151-178,204,208] Three of these trials focused exclusively on maintenance of weight after weight loss had already been achieved.[148,164,170] One trial did not report 12- to 18-month outcomes, but did report 36-month outcomes.[143] The body of included behavioral treatment trials was a fairly high-quality, recent body of literature, overall. Twenty-six percent of the trials were rated as good quality,[142, 143,152,167-170,172,174,175] and 34 percent were published in 2008 or later. Among those rated as fair quality, randomization procedures (including generation of a random numbers table and blinding of allocation) were frequently not reported. In addition, a substantial number failed to report blinding of outcomes assessment. It was possible for a trial without evidence of outcomes blinding to be rated as good if assessment of anthropometric measures appeared to be highly standardized and involved training and/or quality assurance measures, although this was uncommon. Another common threat to internal validity in trials rated as fair was followup of less than 90 percent. Only approximately one fifth of the fair-quality trials had followup of 90 percent or more.[144,147,156,161,163,171] Average followup for the entire group of trials, weighted by study sample size, was 88.2 percent.

Almost two thirds of the trials were conducted in the United States,[142,143,146-149,152-154,157-159,163,164,167-170,173,175-177,204,208] but only four of the trials were conducted in primary care settings.[146,147,158,159,204,208] Five more trials were conducted in primary care settings in other countries, primarily Europe[155,162,171] and Australia.[165,178] Just over one third of the trials identified potentially eligible patients prior to recruitment and used individual outreach and screening for study recruitment (referred to as "study-identified" in this review).[144,146,147,157-160,162,163,165,171, 172,174,178] The remaining trials either failed to report how they recruited patients (13 percent)[154-156,168,208] or used broadbased media approaches that required potential participants to contact study staff in order to be screened for study eligibility (referred to as "self-identified" in this review).[142,143,143,145,148,149,151-153,161,164,166,167,169,170,173,175-177,204]

Thirteen of the trials were limited to overweight and obese persons with diabetes, hypertension, or dyslipidemia.[144-147,149,154,155,157,159,170,171,175,178] Nine additional trials included only overweight and obese persons who had prediabetes,[142,156,160,172,208] prehypertension,[143,168,169] or increased waist circumference.[161] One trial was limited to overweight or obese patients ages 60 years or older who also had some evidence of functional limitation or poor physical fitness.[173] The remaining trials (n=15 [39 percent]) either had no limitations related to cardiovascular risk factors or accepted only those without cardiovascular risk factors.[148,151-153,158,162-167,174,176,177, 204]

On average, the participants in the behavioral treatment trials were not extremely obese. The weighted average baseline BMI for participants across all trials was 31.9 kg/m^2. Two trials, however, did have substantially higher average BMI values: one in black women in Chicago[204] and one in frail obese older adults.[173] All but two trials included both overweight and obese participants.[162,173] Ethnicity was only reported in 18 of the 24 U.S.-based trials.[142,143,146,149,152-154,157-159,163,168-170,175,177,204,208] Eight trials included more than 25 percent black participants,[149,154,157-159,170,175,204] one reported 45 percent of participants were nonwhite,[142] and there were additionally trials comprised of exclusively or predominantly Hispanic/Latino[146,208] and exclusively Pima Indian participants.[163] Overall, the weighted average percent of nonwhite participants was 41.5 percent among the trials reporting ethnicity.

Six trials included only women[148,152,158,166,167,204] and two included only men.[174,176] The overall weighted average percent of female participants in all trials was 59.3 percent. Age ranges varied substantially across the trials. Two were limited to younger adults (ages 25 to 44 or 45 years)[151,153] and two to older adults.[173,175] Five trials focused on middle-aged adults (ages 30–44 to 50–55 years).[144,148,167-169] The remaining trials covered a broader range of ages. The overall weighted average age of the entire group was 51.4 years (range, 38 to 70 years).

Weight loss. Participants in behavioral-based interventions generally lost more weight than those in control groups. A meta-analysis combining the 21 weight loss trials reporting kilograms or pounds lost at 12 to 18 months estimated an average effect of 3.0 kg more lost in the intervention than control groups (95% CI, -4.0 to -2.0; I^2=94.9%; k=21; n=7,343) (Figure 2). Differences in the amount of weight change were highly variable, ranging from 1.7 kg greater weight gain[163] to 8.3 kg greater weight loss[177] in the intervention groups compared with placebo for all trials that reported these data (including those not included in the meta-analysis). The vast majority of weight loss trials did show a statistically significant effect on weight loss at 12 to 18 months (2 to 7 kg), including 16 of the 21 trials included in the meta-analysis and 10 of the 13 trials not

included (Table 2). Three additional trials examining weight maintenance interventions[148,164,170] and one that reported only long-term outcomes[143] are discussed in the section titled "Weight maintenance and longer-term results."

In addition to reporting amount of weight loss, six trials also reported the proportion of participants losing at least 5 percent of their baseline weight (Figure 3).[146,158,166,172,204,208] Intervention groups had an almost 2.5 times greater probability of losing 5 percent of their initial weight compared with control groups (relative risk [RR], 2.39 [95% CI, 1.72 to 3.31]; n=1,387). Absolute risk reduction was 19 percentage points, which translates into a NNT benefit of 5 (risk difference [RD], 0.19 [95% CI, 0.06 to 0.32]). Only one trial reported the proportion who lost 10 percent or more of their baseline weight, and found an almost fivefold increase in the intervention group compared with the control group (Figure 4).[166] Taking all trials into account, participants in behavioral-based interventions lost an average of 4 percent of their baseline weight, based on average baseline and followup weights.

Interventions with more sessions generally showed greater amounts of weight loss. Meta-regression indicates that number of sessions was a predictor of variability in effect size (coefficient, -0.01; $p<0.02$), after controlling for the risk status of the population. The effect remained statistically significant even after including each of the following factors: study quality, specific outcome reported (weight vs. BMI/other), year of publication, followup rate, method of participant identification (self vs. study identified), presence of physical activity sessions, use of group sessions, type of control group used, role of primary care, US vs. nonUS setting, and baseline BMI. Trials with interventions that involved 12 to 26 sessions generally reported 4 to 7 kg of total weight loss (weighted average, 5.3 kg [6 percent of baseline weight]) in intervention group participants. Weight loss in less intensive interventions was more on the order of 1.5 to 4 kg (weighted average, 2.3 kg [2.8 percent of baseline weight]) compared with less than 1 percent average weight loss in the control groups.

One trial, although being coded as low intensity because it had no face-to-face or phone contact sessions, had an average of 269 text messages or Web site contacts with participants over 1 year. The intervention group lost 3 kg more compared with the control group.[151]

A meta-analysis limited to primary care-based trials showed a statistically significant but smaller effect size than seen in all trials (weighted mean difference [WMD], -1.1 kg [95% CI, -1.7 to -0.6]; I^2=0.0; k=5; n=957) (figure not shown).[146,147,158,171,178] Examined individually, only one of the five trials showed a benefit of treatment.[171] Three of four additional primary care-based trials (one U.S.-based[159] and three nonU.S.-based[155,162,165]) that were not included in the meta-analysis showed a benefit of treatment. Of the four U.S.-based trials, three focused on training primary care clinicians to deliver weight loss interventions,[146,147,158] and two[146,158] of these offered training in motivational techniques. The fourth trial had two treatment arms, one of which was designed for implementation in primary care and involved one individual and three 1-hour group visits with a study interventionist.[159]

Six trials either screened consecutive patients in primary care practice[158,162,165] or identified potentially eligible participants through medical records or disease registries.[146,159,178] Only two of these reported greater weight loss in intervention participants,[159,165] although all but one[159]

involved interventions with fewer than 10 sessions.

Weight maintenance and longer-term results. Data from 12 trials (36 percent) demonstrated that weight loss can be maintained in the longer term (Table 3).[142,143,149,153,155,160,166,167,169,172,174,175] Six of these trials reported outcomes immediately after a long-running (24 to 54 months) intervention was completed and all found greater weight loss at the end of the trials, with participants generally showing 2 to 4 kg greater weight loss than controls.[143,160,167,169,172,175]

The other six trials reported long-term outcomes 4 to 18 months after an intervention had ended.[142,149,153,155,166,174] Weight loss was greater in the intervention group in four of these six trials.[142,149,155,166] The trials showing a treatment benefit varied in intensity from five to 30 intervention contacts. Of the two that showed no benefit, one had an online-only intervention[174] and the other was a high-intensity (27 contacts over 12 months) behavioral program in which some treatment arms received meal provisions and/or cash incentives.[153]

Three trials targeted maintenance after weight loss in seven different active treatment arms (Table 4).[148,164,170] The intervention arms with 26 or more sessions over 18 to 24 months had better weight maintenance.[164,170] These intensive intervention groups generally had weight regain of 2 to 4 kg compared with 5 to 7 kg in the control groups over the 1- to 2-year maintenance sessions. In lower-intensity interventions (two added maintenance sessions or Web only), there were no group differences.[148,170]

Decrease in waist circumference. Waist circumference was reported in only 14 of the 38 trials, 12 of which were included in the meta-analysis (Figure 5).[142,145,146,151,152,156,160,161,171,172,174,208] Waist circumference declined by an average of 2.7 cm more for participants in weight loss interventions than those in control conditions (WMD, -2.7 [95% CI, -4.1 to -1.4]; I^2=93.8%; n=4,427). Statistical heterogeneity was very high, but most trials did show statistically significant group differences. Statistical heterogeneity was reduced slightly (to 78 percent) when DPP was dropped from the analysis. In DPP, a good-quality study of adults with prediabetes, the estimated 23 intervention sessions resulted in an almost 6.4 cm reduction in waist circumference in the lifestyle intervention group, almost 6 cm more than the control group.[212] Because DPP was a very large trial, the confidence interval was very small, so it did not overlap estimates from many of the other trials. While generalizability to primary care may be somewhat questionable in the self-identified sample, internal validity was good and its generalizability was improved by the use of a large number of interventionists at many different sites. The two trials not included in the meta-analysis were contradictory.[155,163] Three additional trials reported only WHR.[167,177,178] Two of these trials found a greater improvement in the intervention group than in the control group.

Improvement in lipid levels. Only 16 of the 38 weight loss or weight maintenance trials reported lipid outcomes.[144-146,152,155,156,160,161,163,167,171,172,176-178,208] According to meta-analysis, weight loss intervention groups showed an average 5.8 mg/dL greater decline in total cholesterol (95% CI, -8.6 to -2.9; I^2=26.1%; k=10; n=2,414) (Figure 6), 4.9 mg/dL greater decline in LDL cholesterol (95% CI, -7.3 to -2.6; I^2=0.0%,;k=8; n=1,755) (Figure 7), and 11.1 mg/dL greater decline in triglycerides (95% CI, -15.6 to -6.5; I^2=25.0%; k=8; n=1,955) (Figure 9) compared with control groups at 12 to 18 months. The pooled average showed no group differences in

HDL cholesterol (Figure 8). Five additional trials could not be included in the meta-analysis, and most showed no statistically significant group differences in lipid level changes (Table 5).[144,145,155,163,178] Because outcomes were sparsely reported (and therefore subject to reporting bias) and more likely to have null findings if not included in the meta-analysis, the meta-analysis likely overestimated the true effect size. The three good-quality trials reporting lipid levels had either null findings or small group differences in only some lipids outcomes.[152, 167,172] No trials were limited to patients with dyslipidemia. Results were mixed in the three trials limited to patients with hypertension or dyslipidemia.[144,170,171]

Improvement in blood pressure. Twenty-two of 38 trials reported blood pressure.[143-147,149,154-157,161,163,167-169,171,172,174,175,177,207,208] In the 14 trials combined by meta-analysis,[144-146,156,161,167-169,171,172,174,177,207,208] intervention groups showed an average 2 mm Hg greater reduction in both SBP and DBP compared with control groups (SBP: WMD, -2.5 [95% CI, -3.2 to -1.7]; I^2=32.8%; DBP: WMD, -1.9 [95% CI, -2.6 to -1.2]; I^2=64.0%; n=6,427) (Figures 10 and 11). Although blood pressure was not frequently reported in the behavioral trials, the pooled effect sizes are less likely to be biased than the pooled effect sizes for lipid outcomes. Most of the good-quality trials reported blood pressure, and the nine trials that could not be included in the meta-analysis were mixed, but generally supported the meta-analysis results of a small treatment benefit (Table 6).[143,144,147,149,154,155,157,163,175] In addition, 12 of the 13 trials that recruited participants with hypertension,[145,147,149,154,155,157,175] prehypertension,[143,168,169] or hypertension or another cardiovascular risk factor[144,171,178] provided blood pressure outcomes, and effect sizes were very similar in these trials.

Five out of six long-term (24 to 54 month) intervention trials reported blood pressure outcomes at the end of the intervention phase (Table 3). All five interventions found group differences.[143,167,169,172,175] A good-quality trial, the Finnish Diabetes Prevention Study, reported the largest intervention effect: an average reduction of 5 mm Hg in both SBP and DBP (compared with 0 and 3 mm Hg in the control group, respectively) after 24 months.[172]

Maintenance of blood pressure improvements after intervention completion varied. After two long-term (30 to 34 months) intensive interventions (≥10 sessions), blood pressure improvements were maintained for 4 to 18 months.[142,149,207] Two less intensive trials (0 to 5 sessions) showed no group differences 12 to 18 months later.[155,174]

Behavioral treatment was successful in reducing the risk of a hypertension diagnosis in participants with prehypertension. Trials of Hypertension (TOHP) I and II, both good-quality trials, reported reduced risk of incident hypertension at 12 and 18 months of 34 and 22 percent, respectively.[168,169] By 3 years in TOHP II, fewer participants in the intervention group (32 percent) met criteria for hypertension compared with the control group (39 percent) (absolute RD, 7.3 [NNT=14]).[169] The effect was no longer statistically significant at 4 years.

Development of diabetes. Two large, good-quality behavioral trials of diabetes prevention in overweight and obese patients with elevated plasma glucose showed reduced onset of diabetes in the intervention group compared with control, with similar effect sizes (Table 7).[172,206] In DPP, twice as many people in the control group than the lifestyle management group had developed diabetes by 3 years (absolute RR, 14.5 [28.9 vs.14.4%]; NNT=7).[206] Ten-year followup from

DPP reported long-term diabetes onset, but did not meet inclusion criteria (see discussion section).[213] Similarly, the Finnish Diabetes Prevention Study intervention resulted in incidence rates that were less than half of the control group rates at 2- and 6-year followup (2 years: 5.7 vs. 14.4%; 6 years: 10.2 vs. 23.0% in intervention and control groups, respectively).[172] There was no reduction in diabetes onset at 12-month followup in a third, smaller (n=90) fair-quality trial of persons with prediabetes who were primarily Hispanic residents of the East Harlem neighborhood in New York City. This population had very high rates of elevated fasting glucose levels; only 29 percent of those screened had normal glucose levels.[208]

Glucose tolerance. Twelve of 38 trials reported glucose tolerance.[145,146,152,156,161-163,167,171,172,208,212] When eight were pooled, behavioral interventions reduced fasting glucose levels by an average of 3.4 mg/dL more than control conditions (WMD, -3.4 [95% CI, -5.5 to -1.4]; I^2=82.8%; k=8; n=3,849) (Figure 12), although with high statistical heterogeneity.[156,160,161,167,171,172,208,212] These outcomes were rarely reported, and the four trials that could not be included in the meta-analysis[145,146,152,163] were uniformly lacking in group differences (Table 8), suggesting that the pooled result overestimated the true effect.

Six of the seven weight loss trials targeting adults with type 2 diabetes or type 2 prediabetes measured change in glucose control at 12–18 months.[142,146,156,159,160,172,208] Five trials measuring change in fasting glucose levels that could be pooled showed similar treatment effects, ranging from a 1.0 to 6.1 mg/dL greater decline in fasting glucose level in the intervention group compared with the control group (WMD, -5.3 [95% CI, -6.2 to -4.5]; I^2=0.0%; k=5; n=2,901) (figure not shown). The sixth trial, which was not in the meta-analysis, showed no differences in hemoglobin A_{1C} levels between treatment groups.[146] Pooled results from this subset of trials were less subject to bias since most trials limited to populations with diabetes or prediabetes reported glucose outcomes, which was presumably identified a priori as a major outcome.

Common elements of efficacious interventions. We present a number of intervention components in Table 9. However, it was difficult to qualitatively and quantitatively determine important components of efficacious interventions in this body of literature. First, some trials provided much greater detail about their interventions, so the reliability of coding was limited. Second, because most interventions were successful, there were very few nonefficacious trials for comparison. Finally, with so many outcomes of potential interest, there was a risk of over-interpreting spurious results. To address these concerns, we limited our analysis to a single outcome—weight loss. And, instead of comparing efficacious with nonefficacious trials, we used meta-regression to examine whether any components were predictive of effect size. The components examined were chosen based on expert advice and our ability to robustly identify that component in the published trials.

As described previously, meta-regression suggests that the number of sessions provided in the first 12 months was predictive of weight loss; a greater number of sessions correlated with greater effect size. After controlling for number of sessions in the first year, none of the following components demonstrated a relationship with effect size: physical activity sessions, group sessions, individual sessions, technology-based intervention, specific weight loss goals, spouse or family involvement, addressed barriers to weight loss, motivational assessment (i.e., pros and cons of weight loss), self monitoring, incentives for weight loss or participation, or

support after active intervention phase. However, our confidence in these results is limited because these components were not always explicitly reported, especially not in primary care settings and trials with less intensive interventions.

Differences in patient subgroups. Data on subgroup differences should be viewed as exploratory due to incomplete reporting of these data across all included trials.

Age. Data on age effects were mixed, but suggest that older adults may benefit even more than younger adults. Of five trials examining the effect of age on treatment effect,[152,169-171,210] two good-quality studies found increasing treatment benefits with increasing age.[169,210] In DPP, increasing age was associated with more weight loss, greater decrease in waist circumference, and lower diabetes incidence with treatment.[210] In DPP, diabetes incidence decreased more in the oldest age group compared with the youngest in the behavioral intervention group, although the effect disappeared after controlling for weight loss and behavior change.[210] However, the older DPP participants were likely healthier than the general population, so the results may not be representative.[142] In a trial of hypertension prevention in adults ages 30 to 54 years, increasing age was associated with greater weight loss at 36 months (but not 18 months).[169]

Sex. Five trials examined sex differences in the impact of treatment on weight loss[168-171,214] and four found that men showed greater weight loss than women.[168,169,171,214] However, in one study (DPP), the difference was primarily seen in black women, as black women in the intervention group lost little weight; five other sex-by-race groups showed comparable differences between intervention and control group participants.[214] In another trial (TOHP I), the sex-by-treatment interaction disappeared after controlling for baseline BMI.[168]

Six of the included trials were limited to women.[148,152,158,166,167,204] One focused on weight maintenance[148] and had comparable findings to a similar intensity weight maintenance trial of men and women.[170] Four[152,166,167,204] of the five[152,158,166,167,204] weight loss trials demonstrated a treatment effect, with 1.4 to 3.3 kg greater weight loss in the intervention groups than in control groups, which was slightly less than the overall pooled effect of 3.3 kg. Four studies examined sex differences for additional intermediate health outcomes.[145,157,168,177] Sex differences were absent for blood pressure outcomes.[145,157,168] In one trial, men had improvements in HDL cholesterol, while women showed no group differences. In contrast, women had improvements in LDL and total cholesterol while men did not, but the sex-by-treatment interactions were not directly tested.[177] In DPP, diabetes incidence did not differ significantly according to sex. However, DPP was not powered to assess the significance of effects within the subgroups.[206]

Race. Four trials[169,170,175,214] examined the effect of race on response to behavioral weight loss or weight maintenance treatment. Three[169,175,214] found that black participants lost a smaller amount of weight than nonblack participants. In one of these trials, the effect was limited to black women.[214] However, in another trial, the effect of race remained after controlling for sex and multiple other covariates.[175] Two trials examined the effect of race on hypertension,[157,168] with mixed results: one trial found no race-by-treatment interaction,[168] but another reported that black participants were twice as likely to resume taking hypertension medications compared with white participants.[157] In DPP, diabetes incidence did not differ significantly according to ethnicity. However, DPP was not powered to assess the significance of effects within the subgroups.[206]

Baseline obesity. Four trials examined whether weight loss was modified by baseline BMI[152,168,169,171] and three found no relationship.[152,169,171] One trial's finding that greater weight loss was associated with a higher BMI[168] was not replicated in a similar, larger followup trial by the same author, in which the effect of baseline obesity that had been present at 6 months disappeared by 18- and 36-month followup.[169] In meta-regression, baseline BMI did not predict effect size in the behavioral trials (p=0.70).

Pharmacotherapy

All 21 pharmacotherapy trials reported a measure of weight loss, and most also reported one or more other physiologic intermediate health outcomes.[142,179-203] Eighteen of the included trials tested the effects of orlistat (n=11,256 randomized to orlistat or placebo treatment arms)[180-184,187,189-191,193,194,197-202] and three examined metformin (n=2,652 randomized to orlistat or placebo treatment arms).[142,185,186]

Orlistat.

General characteristics of trials. Eighteen trials examined the effect of 120 mg tid of orlistat on some measure of weight over at least 12 to 18 months. One was rated as good quality[215] and 17 were rated as fair quality.[180-184,187,189-191,193,194,197-202,215] Three of the trials were conducted in primary care settings.[181,189,209] Three additional studies were possibly conducted in primary care.[180,187,215] The role of the primary care provider was not described in any study. Five trials were conducted in the United States,[182,189-191,197] but only one study was conducted in a U.S. primary care setting.[189] This fair-quality study suffered from higher attrition in the control group (43 percent) compared with the orlistat group (28 percent) at 12 months.[189]

The orlistat data were limited in that there was only one good-quality trial.[215] All of the remaining trials were rated as fair quality. The most common defect was a high attrition rate. Only five studies had greater than 80 percent followup at 12 to 18 months (followup ranged from 61 to 96 percent among all orlistat trials).[189,191,199,202,215] Followup in the control group was often more than 10 percent lower than in the orlistat group.[189,191,199,202] In addition, randomization procedures (including allocation concealment) and medication adherence rates were rarely reported.

Participants in the orlistat studies were required to have a BMI of at least 28 to 30 kg/m^2. Participants with at least one established or subclinical risk factor were allowed to have a minimum BMI in the overweight (27 to 28 kg/m^2)[180,181,187,191,197,209] to obese range (at least 30 kg/m^2).[183,201,202,215] In studies of unselected or low-risk populations, a minority of trials required a BMI of at least 30 kg/m^2.[182,184,189] The remaining trials required a BMI of at least 28 kg/m^2.[190,193,199,200] Participants overall were moderately obese, with a weighted average baseline BMI of 36.1 kg/m^2 (range, 32 to 38 kg/m^2) across all trials.

Nonwhite Americans were not highly represented in the included trials. Only eight of 18 trials (including all of the U.S. trials) reported the percentage of nonwhite participants.[180,182,184,189-191,197,215] The weighted average percent of nonwhite participants was 12.3 percent among the eight trials reporting ethnicity (range, 0 to 19.2 percent). All studies included both men and women.

The weighted average percent of female participants in all trials was 65.9 percent (range, 45 to 88 percent). The age ranges were wide in most of the trials. Thirteen trials included participants ages 18 to at least 60 years.[181,182,184,187,189-191,193,194,198-200,215] The remaining five trials included participants ages 30 to 40 years to at least 60 years.[180,183,197,201,202] The average age of participants ranged from 41 to 59 years and the overall weighted average age of the entire group was 46.2 years.

The trials were conducted in a range of participants, from those who were healthy to those with multiple risk factors. Seven of the trials were conducted in overweight and obese participants who did not necessarily have a cardiovascular risk factor.[182,184,189,190,193,199,200] Six trials were conducted in overweight and obese subjects with diabetes[180,187,191,197,215] or prediabetes (IGT or IFG).[202] One included only obese participants with dyslipidemia.[183] Four additional trials were conducted in overweight and obese participants who had at least one cardiovascular risk factor.[181,194,198,201]

One trial implemented a 6-month, very low calorie diet (VLCD) with the requirement that overweight and obese participants lose at least 6 percent of their body weight prior to entry in the orlistat phase of the trial.[190] This study was considered a weight maintenance trial. Only 55 percent of the participants from the weight loss phase of the trial were entered into the randomized weight maintenance phase of the trial.

The majority (64.7 percent) of the weight loss studies (not counting the weight maintenance trial) used a pretrial run-in period prior to randomization to orlistat or placebo. The duration of the run-in period ranged from 2 to 5 weeks. To be randomized, participants often needed to meet a certain level of compliance with the medication and/or behavioral component and/or a prespecified degree of weight loss during the run-in period. Seventy-five to 98 percent of the participants successfully fulfilled the run-in requirements.

All of the studies applied some dietary education and/or behavioral therapy to both the orlistat and placebo groups. Almost all trials prescribed a low-calorie diet, and 10 of 18 trials reported that a physical activity recommendation was given to participants.[180,182,183,189,194,197,198,201,202,215] Fourteen trials provided enough detail to ascertain the intensity of their behavioral intervention, and they were all rated as having an ~~"in~~tense" behavioral intervention (i.e., monthly to quarterly dietary reinforcement, with or without behavioral modification, combined with monthly to quarterly weigh-ins). While all 18 studies prescribed 120 mg tid of orlistat, three trials (two weight loss trials and one maintenance trial) randomized additional intervention groups to smaller doses of orlistat (30 or 60 mg tid).[189,190,199]

No trials examined whether treatment effects were maintained after medication was discontinued; however, two trials provided data on the effects of longer-term (beyond 12 to 18 months) orlistat treatment on intermediate health outcomes.[198,199] One trial examined the effects of orlistat over 24 months in an unselected overweight and obese population in Europe.[199] The other examined 36 months of orlistat treatment in obese Scandinavians following a pretrial 8-week VLCD.[198] We did not include long-term data from two additional trials[189,202] because there was high attrition at 2 to 4 years (41 to 43 percent followup at 2 to 4 years); however, 12-month data from these studies were included.

Weight loss. Treatment with orlistat resulted in more weight loss than treatment with placebo. All 18 trials of orlistat reported some measure of weight loss over 12–18 months (N=11,256). Of these, 17 addressed weight loss,[180-184,187,189,191,193,194,197-202,215] and one addressed weight maintenance.[190] Twelve of the 17 weight loss trials could be combined into a meta-analysis (n=5,190).[181-183,187,189,191,193,194,197,199,201,215] Overweight and obese participants who were randomized to orlistat lost an average of 3 kg more than those randomized to placebo after 12 months (WMD, -3.0 [95% CI, -3.9 to -2.0]; I^2=84.9%; k=12) (Figure 2). With one exception,[215] the studies were not highly variable, with 1.0 to 3.8 kg more lost in the orlistat group compared with the placebo group. The outlier study was the only good-quality study. In this study, obese participants with uncontrolled diabetes who were randomized to orlistat lost nearly 7 kg more than those given placebo.[215] In terms of overall weight loss, most trials reported a weight loss of 6 to 9 kg among those taking orlistat compared with 3 to 6 kg in those taking placebo. Five orlistat weight loss trials could not be included in the meta-analysis (Table 10),[180,184,198,200,202] including one of the largest and better conducted studies,[202] but these studies generally confirmed the meta-analysis results. The only trial conducted in a U.S. primary care setting had very similar results to the other trials, showing a weight loss of 7 kg in those taking orlistat and 4 kg in those taking placebo.[189]

Visual inspection of the forest plots suggests that weight loss did not vary by risk status. This impression was confirmed by a meta-regression of all medication trials, controlling for medication type (samples with cardiovascular risk factors vs. unselected or low-risk samples; p=0.75).

In 13 of 18 studies, the probability of losing 5 percent of one's initial weight was evaluated.[180-182,184,187,189,191,193,194,197,198,200,202] Overweight and obese participants who were randomized to orlistat had a 1.6-fold greater chance of losing 5 percent of their initial weight than those who were randomized to placebo (RR, 1.57 [95% CI, 1.40 to 1.75]; I^2= 76.2%; k=13; n=8,579) (Figure 3). This is an absolute risk difference of 19 percentage points, which translates into a NNT benefit of 5 (RD, 0.19 [95% CI, -0.05 to 0.43]). The relatively high statistical heterogeneity is likely due to one trial with a substantially larger risk reduction than the other trials.[180] The reason for the higher risk reduction in this trial is not clear, although there was a particularly low rate of 5 percent weight loss in the placebo group. The probability of losing 10 percent of one's initial weight was about 2 times greater in overweight and obese patients receiving orlistat compared with placebo (RR, 1.99 [95% CI, 1.69 to 2.35]; I^2=49.2%; k=11; n=7,500) (Figure 4). The absolute risk difference was 12 percentage points, which translates into a NNT benefit of 8 (RD, 0.12 [95% CI, -0.05 to 0.29]). Based on average baseline and posttreatment weight, the orlistat trials reported an average weight loss of 5 percent in the placebo groups and 8 percent in the orlistat groups.

No trials screened consecutive patients in primary care practices. Three studies identified potentially eligible participants through medical records or disease registries, and then invited them for further screening. Two found that orlistat was associated with more weight loss than placebo,[200,215] but the other did not.[183]

Dose effects. Different dosages were compared in two weight loss trials and in the maintenance trial. In the two weight loss trials, weight loss in both the 60 mg and 120 mg tid dosage groups

was greater than in the placebo groups.[189,199] Neither trial tested for group differences between the 60 mg and 120 mg groups, but absolute weight loss appeared very similar; those in the 60 mg tid groups lost 7.1[189] and 6.6 kg[199] compared with 7.9 and 7.4 kg in the 120 mg tid groups. In the maintenance trial of orlistat after a VLCD, only overweight and obese participants who took orlistat 120 mg tid (not 30 or 60 mg tid) had a statistically significant smaller weight regain than placebo over 12 months.[190]

Long-term weight loss. According to two trials, weight loss was maintained in the longer term (24 to 36 months) with continued treatment (Table 11).[198,199] Overweight and obese participants who were randomized to orlistat lost 2 to 3 kg more than those receiving placebo in both trials.[198,199] The amount of weight loss at 24 to 36 months was not greater, and perhaps a bit less, than at 12 months, although statistical testing of weight loss between the time points was not conducted. No trials reported long-term outcomes after an intervention had ended.

Maintenance of weight loss. One trial found that orlistat was helpful in maintaining the weight loss that occurred during a 6-month VLCD combined with an intensive behavioral intervention, which led to an average weight loss of 10 kg.[190] By 12 months followup, those who were randomized to 120 mg tid of orlistat regained 2.7 kg compared with 4.4 kg in those taking placebo, which was statistically significant.[190] Only 55.5 percent of participants who started the VLCD were ultimately randomized to orlistat or placebo.

Effect of orlistat on other measures of adiposity. Orlistat was generally associated with a decrease in waist circumference, although data were somewhat mixed. Twelve trials reported the effects of orlistat on waist circumference.[180,181,183,187,191,193,194,198,199,201,202,215] Seven studies could be combined by meta-analysis.[180,183,187,191,193,201,215] Waist circumference declined 2.3 cm more in participants taking orlistat compared with placebo over 12 to 18 months (WMD, -2.3 [95% CI, -3.6 to -0.9]; k=7; I^2=87.7%; n=2,227) (Figure 5).

The pooled data on waist circumference were quite heterogeneous (I^2=87.7%), as were the results from studies that could not be pooled (Table 12). The main outlier was a good-quality trial that reported a decrease in waist circumference of 5 cm more in participants with diabetes taking orlistat compared with those taking placebo.[215] Among the 12 trials, there was an absolute 5 to 7 cm decline in waist circumference in those taking orlistat compared with a 2 to 6.5 cm decline in the placebo groups. No trials reported WHR.

Effect of orlistat on lipid levels. Orlistat was associated with a greater decrease in total and LDL cholesterol than placebo, but also a decrease in HDL cholesterol. Triglycerides were not affected. All 18 trials examined the effect of orlistat on at one least lipid measure. Twelve of the weight loss trials had data that could be combined in meta-analyses.[180,183,184,187,189,191,194,197,199-201,215] Overweight and obese participants in the orlistat group had a 12.6 mg/dL greater decline in total cholesterol (95% CI, -17.0 to -8.2; I^2=84.1%; k=12; n=4,213) (Figure 6), 11.4 mg/dL greater decline in LDL cholesterol (95% CI, -15.8 to -7.0; I^2=86.3%,;k=12; n=4,213) (Figure 7), and 0.9 mg/dL greater decline in HDL cholesterol (95% CI, -1.7 to -0.1; I^2=58.0%; k=12; n=4,213) (Figure 8) compared with placebo over 12 to 18 months. Triglycerides did not change differently between groups (WMD, -4.8 [95% CI, -10.4 to 0.7]; I^2=80.1%,;k=10; N=3,626) (Figure 9). The five weight loss trials that measured lipid levels but could not be included in the meta-analyses

reported similar results (Table 13).[181,182,193,198,202] Additionally, the trial of weight maintenance showed greater improvement in total and LDL cholesterol in participants taking any dose of orlistat, but minimal effect on HDL cholesterol and triglycerides.[190] Two studies examined the effects of orlistat on the use of lipid-lowering medications and did not find any differences between groups.[198,201]

Only one trial recruited participants with dyslipidemia.[183] Obese participants in this study who received orlistat showed greater declines in LDL and total cholesterol, but did not have a greater change in triglycerides or HDL cholesterol compared with placebo.[183] In the intervention group, LDL cholesterol declined by 37 mg/dL (vs. 24 mg/dL in placebo group) and total cholesterol declined by 39 mg/dL (vs. 32 mg/dL in placebo group). In the one study that examined the subgroup of participants with dyslipidemia, overweight and obese participants who received orlistat had a significant decrease in total and LDL cholesterol but experienced no change in HDL cholesterol compared with the placebo group.[181] This result was similar to the study's findings for the entire population.[181]

Only two trials reported long-term effect of orlistat treatment (>12 to 18 months) on lipid levels (Table 11).[198,199] One trial found group differences in the longer term (LDL and total cholesterol)[199] and one did not (LDL cholesterol).[198] The latter trial also reported no differences at 12 months.

Effect of orlistat on blood pressure. Orlistat treatment was associated with a decrease in blood pressure compared with placebo. Fourteen of 18 RCTs of orlistat evaluated blood pressure.[180-183, 187,189,190,197-202,209] Seven of the weight loss trials could be included in a meta-analysis.[182,189,197,199-201, 209] Participants who were randomized to orlistat had a 2.0 mm Hg greater decline in SBP (WMD, -2.0 [95% CI, -3.1 to -1.0]; I^2=0.0%, k=7; n=3,683) (Figure 10) and a 1.3 mm Hg greater decline in DBP (WMD, -1.3 [95% CI, -2.5 to -0.2]; I^2=52.2%; k=6; n=3,179) (Figure 11) after 12 to 18 months compared with those given placebo.

Five trials, including one of the largest and better conducted trials,[202] measured blood pressure but could not be included in the meta-analysis (Table 14).[180,181,187,198,202] They supported the meta-analysis results in that they all reported no or small changes in blood pressure.

There were little data about the effect of orlistat on persons with hypertension. No trials evaluated only participants with hypertension. One trial examined separately the 43 percent of participants with hypertension at baseline and found no treatment effect.[181] Two studies examined the effects of orlistat on the use of blood pressure medications with conflicting results.[198,201]

There was also very little data on the long-term effect of orlistat on blood pressure. Two studies had longer-term followup (Table 11).[198,199] Neither study found that long-term orlistat use was associated with a greater decrease in blood pressure compared with placebo. However, neither study had found a difference in blood pressure in the treatment groups at 12 months.[198,199] No study evaluated whether the decrease in blood pressure associated with orlistat was maintained after stopping the medication.

Development of diabetes. Limited data suggest that orlistat may be associated with a decreased risk of type 2 diabetes in both low- and high-risk obese individuals. Two of 18 orlistat trials reported the risk of developing new-onset type 2 diabetes.[198,202] Both studies were rated as fair quality for attrition issues; one study had 35.3 percent attrition at 36 months[198] and the other had somewhat differential attrition (90 percent followup in the orlistat group compared with 77 percent in the placebo group) at 12 months (Table 7).[202]

The first orlistat trial examined type 2 diabetes risk in obese individuals with an elevated waist circumference and IFG and/or dyslipidemia. To enter into the trial, participants had to lose at least 5 percent of their weight during an 8-week VLCD (600–800 kcal); 80.7 percent of participants were retained after the run-in period. Eight percent of participants who were randomized to orlistat compared with 17 percent of those who were randomized to placebo were newly diagnosed with type 2 diabetes by the final visit at 36 months (p=0.04).[198]

In the largest trial of orlistat, cumulative incidence of diabetes was reported over 4 years of study followup. Although the study's attrition by 4 years was high (48 and 68 percent in orlistat and placebo groups, respectively), we present these data because they are cumulative (see methods for a full description of quality rating and data abstraction) and because the data on the association between orlistat and diabetes risk are limited. Both high-risk (IGT) and low-risk (normal glucose tolerance) obese populations who received orlistat had a lower incidence of type 2 diabetes compared with those given placebo. In the high-risk population, the cumulative incidence of type 2 diabetes was 19 percent in the orlistat group compared with 29 percent in the placebo group over 4 years. The respective cumulative incidence in the low-risk population was 6 percent versus 17 percent.[202] In both studies, participants in the orlistat group lost more weight than those in the control group. However, the relationship between the degree of weight loss with orlistat and the subsequent risk of type 2 diabetes was not evaluated.

Effect of orlistat on glucose tolerance. Orlistat was generally associated with a decrease in fasting glucose level, but with mixed results. Fourteen trials examined the effect of orlistat on fasting glucose in individuals with diabetes and prediabetes and in unselected/low-risk overweight and obese populations.[180,181,187,189-191,194,197-202,215] Nine weight loss trials could be combined in a meta-analysis.[187,189,191,194,197,199-201,215] Those participants who were randomized to orlistat experienced a 5.7 mg/dL greater reduction in fasting glucose over 12 months compared with those given placebo (95% CI, -8.3 to -3.0; I^2=79.6%; k=9; n=3,727) (Figure 12). These results were heterogeneous due to different degrees of glucose reduction in participants with diabetes versus those without. When only the four RCTs that recruited individuals with type 2 diabetes were combined,[187,191,197,215] overweight and obese individuals with diabetes who were randomized to orlistat had a 12 mg/dL greater decline in fasting glucose level compared with those given placebo (WMD, -12.1 [95% CI, -21.9 to -2.4]; I^2=86.6%; k=4; n=1,428) (figure not shown), with absolute reductions of up to 36 mg/dL.[197]

A greater effect of orlistat on glucose reduction in individuals with diabetes compared with those without it was supported by a subgroup analysis in a study of overweight and obese participants with multiple cardiovascular risk factors. The 26 percent of the population with diabetes had a greater decrease in fasting glucose (-29.4 vs. +5.0 mg/dL for orlistat compared with placebo) compared with the entire population (-9.9 vs. -1.6 mg/dL for orlistat compared with placebo),

although this interaction was not statistically tested.[209] A second study suggested that these effects do not extend to individuals with prediabetes. The small subgroup with IGT (17 percent [n=125]) did not have a greater improvement in fasting glucose compared with the whole population.[181]

The five orlistat trials that were not included in the meta-analysis were heterogeneous, but generally showed that orlistat improved fasting glucose levels with a similar effect size as the meta-analysis, with the largest effect seen in the trial of patients with diabetes (Table 15).[180,181,190,198,202]

Orlistat appeared to have a favorable impact on diabetes medication use. Three trials found that orlistat resulted in either a greater discontinuation rate (12 percent) or greater dose reduction than placebo.[191,197,201] However, a fourth trial found that orlistat did not affect the use of diabetes medications.[187] Neither of the two trials reporting longer-term effects found group differences at 24 to 36 months.[198,199]

Results in different subgroups. Differences in efficacy between ethnic, sex, or age subgroups could not be determined. No study examined weight loss by ethnicity and the percentage of minorities included in the trials was very small (5.1 to 19.2 percent of the study population in the few studies that reported ethnicity).[182,184,189-191,197] No study examined results by sex, age, or baseline BMI. Weight loss with orlistat did not vary by the cardiovascular risk status of the population.

Metformin.

General characteristics of studies. We included three trials examining the effect of metformin (850 mg twice daily) on weight loss over 12 to 18 months in 2,652 overweight and obese participants selected for prediabetes,[142] polycystic ovary syndrome,[186] or an elevated WHR.[185] None of the studies recruited exclusively from primary care or were conducted in the primary care setting. Only one study, DPP, was conducted in the United States.[142] The largest trial (n=2,155 in the metformin and placebo arms), DPP was rated as good quality and was conducted in overweight and obese participants with prediabetes (IFG or IGT).[142] The other two trials were rated as fair quality. Neither trial described how treatment allocation was concealed[185,186] and one trial also suffered from high attrition: only 70.9 percent had followup at 12 months.[185] Although the other fair-quality study had adequate followup, the number of participants was quite small (N=40).[186] This small study was also not double blind—the providers were aware of the participants' treatment allocation and the blinding of the outcome assessors was not described.[186]

All of the studies applied some dietary education and/or behavioral therapy to both the metformin and placebo groups. Only one study specifically prescribed a hypocaloric diet.[186] In the other trials, participants were told to follow the NHLBI National Cholesterol Education Program step 1 diet (DPP) or were given dietary advice to reduce insulin resistance.[185] Two studies recommended an increase in physical activity,[142,185] while the other encouraged participants to continue their usual activities.[186] The trials provided enough detail to ascertain the intensity of their behavioral intervention (see methods for definition). One was rated as having an intensive behavioral intervention.[186] Participants had monthly meetings and weigh-ins with

the dietician.[186] In DPP, there was a yearly 20- to 30-minute meeting with a case manager addressing the importance of a healthy lifestyle, so we considered this trial to have a brief behavioral component. We also considered the third study as brief, as there were quarterly weigh-ins with dietary and exercise advice of unclear frequency.[185] All three studies prescribed a dose of metformin of 850 mg twice daily.

The second largest trial examined overweight and obese participants with an elevated WHR.[185] The two larger trials included both men and women (67 percent female) and the mean age of the population was 50 years.[185,212] The final trial was a small study of relatively young (average age, 27 years) overweight and obese women with polycystic ovary syndrome.[186] Participants in the studies were required to have a BMI of at least 24[142] or 28 kg/m^2 [186] or an elevated WHR (≥0.95 for men; ≥0.80 for women).[185] Participants overall were moderately obese, with baseline mean BMI values ranging from 33 to 37 kg/m^2.

Only one trial, DPP, reported the ethnicity of participants: 54.7 percent were white, 19.9 percent black, 15.7 percent Hispanic, 5.3 percent American Indian, and 4.4 percent Asian/Pacific Islanders.[206]

No study examined weight loss after stopping metformin or the use of metformin for weight maintenance.

The validity of the meta-analyses were limited by the marked differences in study populations. None of the studies used the same adiposity or risk factor criteria for study entry and had varying baseline demographics. Therefore, we include the metformin trials in Figures 2–12 for comparison purposes, but do not discuss meta-analysis results.

Effect of metformin on weight loss. Metformin treatment generally led to more weight loss than placebo. All three RCTs of metformin reported some measure of weight loss over 12 months.[185, 186,212] In DPP, participants who were randomized to metformin lost 2.7 kg after 12 months, 2.3 kg more than those who were randomized to placebo.[212] After 3 years, weight loss was greatest in the older (ages 60 to 85 years) participants, who lost an average of 2.7 kg compared with 1.5 to 1.7 kg in younger age groups. Effect size did not appear to vary by sex, race, or ethnicity, but DPP reported inadequate power to assess subgroup effects.[206] A second study examined the effects of metformin in overweight and obese individuals with a high WHR.[185] Approximately 22 percent had abnormal glucose tolerance. The metformin group lost 2 kg over 12 months, which was 1.2 kg more than in the placebo group, a nonsignificant difference.[185] The final study involved younger overweight and obese women with polycystic ovary syndrome.[186] There was no differential weight change between the metformin and placebo groups: both lost 4 to 5 kg. None of the studies examined weight loss of 5 and 10 percent of baseline weight.

Long-term weight loss with metformin. Longer-term metformin treatment (>12 to 18 months) was associated with greater weight loss than placebo (Table 11). In DPP, overweight and obese participants who were randomized to metformin lost 2.0 kg more after 2.8 years than those in the placebo group. This was similar to the 1-year results of 2.3 kg more than the placebo group.[206] Ten-year followup from DPP is reviewed in the discussion section (this 10-year outcomes study did not meet criteria for inclusion in this evidence review).

Effect of metformin on other measures of adiposity. Metformin decreased waist circumference by 1.5 cm compared with placebo in DPP.[212] Waist circumference declined more in the oldest age group (-2.8 cm in ages 60 to 85 years vs. -1.2 in ages 25 to 44 years; $p<0.001$).[210] However, there were no group differences in the small trial of patients with polycystic ovary syndrome, in which both groups had 4 to 5 cm declines in waist circumference.[186] No trials reported WHR.

Effect of metformin on lipid levels. Twelve months of metformin treatment did not have favorable effects on total, HDL, or LDL cholesterol or triglycerides compared with placebo in the two fair-quality trials.[185,186] In DPP, long-term (36 months) metformin treatment led to favorable effects on HDL cholesterol compared with placebo, but the changes in both groups were less than 1 mg/dL (Table 11).[207] No trial recruited participants with dyslipidemia at baseline.

Effect of metformin on blood pressure. Metformin treatment did not improve blood pressure outcomes compared with placebo in DPP.[207] In DPP and a second trial, blood pressure changes between metformin and placebo groups did not differ by more than 1 mm Hg after 12 to 36 months.[185,207] No study recruited participants with elevated blood pressure.

Effect of metformin on diabetes incidence. Data reported in two trials suggest that metformin reduced the risk of developing diabetes (Table 7).[185,206] In DPP, overweight and obese participants with IFG or IGT who were randomized to metformin had a reduced cumulative incidence of diabetes after 3 years compared with those given placebo (21.7 vs. 28.9 percent, respectively).[206] This absolute risk reduction of 7.2 percentage points translates into a NNT of 14. Ten-year followup from DPP is reviewed in the discussion section (it did not meet inclusion criteria for this evidence review). In DPP, diabetes incidence was marginally lower in the youngest age group in the metformin intervention group compared with the oldest, but this effect disappeared after controlling for baseline glucose levels. There was no difference in diabetes incidence by age in the placebo group.[210] Metformin had greater effects in those with lower fasting glucose levels and higher BMI compared with those with higher values for those variables. Treatment effects did not differ significantly according to either sex or ethnicity. However, DPP was not powered to assess the significance of effects within these subgroups.[206]

A smaller, fair-quality study examined overweight and obese participants with a high WHR, 22 percent of whom also had IGT.[185] Five (2.2 percent) overweight and obese participants with prediabetes who were given placebo were diagnosed with diabetes during the study compared with none of those with prediabetes in the metformin group.[185] However, diabetes diagnosis was done at the local investigator level, with unclear adjudication.

Effect of metformin on glucose tolerance. Data suggest that metformin may reduce fasting glucose levels. All three trials examined the effect of metformin on fasting glucose. In DPP, participants taking metformin had average reductions of 4.2 mg/dL in fasting glucose level compared with an average 0.6 mg/dL increase in those taking placebo at 12 months.[212] Neither of the other two fair-quality trials showed group differences.[185,186]

Heterogeneity of medication studies (meta-regression analysis). To examine how study characteristics may have influenced the treatment effects of the medications, we performed a meta-regression analysis on the main outcome of weight loss. We examined multiple trial factors, including how many participants returned for followup, the percentage of participants that were retained after a run-in period, whether subjects were self- or study-identified, the intensity of the behavioral component, the role of primary care in the study, whether the study was conducted in the United States, and study quality. Study quality was associated with treatment effect sizes; however, the results should be interpreted with great caution because of the truncated range of study quality—only two of the medication trials were rated as good-quality trials,[142,215] both of which had very large effect sizes. Meta-regression also showed that trials which relied on participants to contact the researchers to enroll in the trial (self-identified) had smaller effect sizes than trials which identified potentially eligible participants through medical records or registries (study-identified). However, again, this result should be interpreted very cautiously because this effect was driven primarily by a single trial with a very large effect size;[215] the participant identification approach was not statistically significant when this trial was dropped from the analysis. None of the other factors influenced treatment effect size. The characteristics of the participants, including the presence of cardiovascular risk factors, sex, age, and ethnicity, also did not predict effect size for weight loss with medications. The type of medication also did not influence treatment effect size.

KQs 4 and 4a. What Are the Adverse Effects of Primary Care–Relevant Interventions in Obese or Overweight Adults? Are There Differences in Adverse Effects Between Patient Subgroups?

In addition to evaluating all 58 studies from KQs 2 and 3 for harms, we abstracted an additional 12 weight loss studies for harms data (Appendix A).

Behavioral-Based Interventions

General characteristics of studies. Ten studies reported on possible harms of behavioral weight loss interventions. Six were RCTs from KQs 2 and 3,[142,152,160,167,173,175] three were additional published RCTs,[128,137,138] and one was a prospective cohort study.[135] The three additional trials did not meet inclusion criteria for KQ 3 due to high or differential attrition.

Adverse events. Four fair- to good-quality trials of adults ages 40 to 80 years examined bone density.[135,167,173,175] In three studies, weight loss reduced total[175]or hip bone mineral density (BMD).[167,173] In one trial, a small subset of participants (67/975) were studied, and those who lost weight had a greater decrease in total bone density (0.05 percent decrease in BMD per pound of weight lost) at 12 months, although there was not a statistically significant difference between the intervention and control groups. The other two studies noted a decrease in hip (0.9 to 2.4 percent) BMD with 12 months of intervention that was greater than the control condition.[167,173] Changes in body weight were correlated with changes in BMD.[167,173] A more recent trial reported no change in bone mineral content at any site after a 12-month weight loss program, even among those in the highest tertile of weight loss.[135] No study noted a significant decrease in

spine BMD.

Four trials reported no serious adverse effects or serious injuries with increased physical activity over 1 to 2 years.[128,138,152,160] One trial of only female participants ages 25 to 44 years reported an increase in physical activity- and strength training-related injuries in the intervention group compared with the control group (odds ratio [OR], 4.0 [95% CI, 1.8 to 9.0] and OR, 10.1 [95% CI, 3.0 to 34.2], respectively).[138] The cumulative incidence of physical activity- and strength training-related injuries was 46.9 and 33.3 per 100 women, respectively, although the number of participants who lost work time or had to make major changes in daily activities was low (7 percent) and not different from the control group.[138]

One trial found that participants in the intervention group either showed no difference or greater improvement in eating disorder measures.[137]

Pharmacotherapy

Orlistat.

General characteristics of studies. We included a total of 24 placebo-controlled studies on the harms of orlistat (120 mg tid) and one comparing orlistat with metformin (Table 16).[136] Eighteen were RCTs from KQs 2 and 3,[180-184,187,189-191,193,194,197-202,215] five were additional published RCTs,[126,127,129,130,132] and one was an event monitoring study from the United Kingdom.[133] The event monitoring study relied on doctors' retrospective reports of adverse events and had low response rates. We chose to include the study because we wanted to capture rare adverse events that might not be picked up in relatively small RCTs. Of the placebo-controlled RCTs, eight recruited unselected populations[129,182,184,189,190,193,199,200] and 15 recruited participants with at least one clinical or subclinical cardiovascular risk factor.[126,127,130,132,180,181, 183,187,191,194,197,198,201,202,215]

Seven of the 23 placebo-controlled trials (30 percent) were conducted in the United States.[126,127, 182,189-191,197] All trials included both men and women (overall weighted average percent of female participants, 66 percent). The overall weighted average age of the entire group was 47.1 years (range, 41 to 59 years). Only 10 of 23 trials reported ethnicity of the participants, and in these trials the weighted average percent of nonwhite participants was 14.7 percent (range, 0 to 28 percent). The median trial duration was 52 weeks (range, 24 to 208 weeks), but five trials provided data beyond 52 weeks.

Adverse events. Participants who were randomized to orlistat were more likely to experience adverse effects (Figure 13) and withdrawals due to adverse effects (Figure 14) compared with those who were randomized to placebo. However, a similar number of participants reported serious adverse effects in the orlistat group compared with the placebo group (Figure 15). Data were limited and contradictory regarding whether orlistat led to hypoglycemia in drug-treated participants with type 2 diabetes.[127,187,197] Data were insufficient to determine whether orlistat had detrimental effects on bone density.[216]

Gastrointestinal-related adverse effects were more common in the orlistat group compared with the placebo group and were the main cause of excess adverse effects in the orlistat group (Figure

16). Gastrointestinal side effects included loose stools, increased defecation, uncontrolled oily discharge/oily evacuation, oily spotting, fatty/oily stool, fecal urgency, discolored feces, flatus with discharge, fecal incontinence, and abdominal pain. Most gastrointestinal adverse effects were mild to moderate in intensity, occurred early in treatment, and resolved spontaneously. Orlistat treatment appeared to be associated with a decrease in some fat-soluble vitamin levels compared with placebo.[129,190,191,199,202] Data were strongest for vitamin E and beta-carotene, but there were also several reports for vitamin D. There were insufficient data to evaluate orlistat's effects on the liver.

In the trial comparing orlistat and metformin, there were no differences in withdrawals due to adverse effects, but more people reported abdominal discomfort using orlistat (44 percent) than metformin (28 percent). These percentages were not tested for statistical significance. Table 17 and Appendix F provide more details on adverse events.

Dosage effects. All 24 trials prescribed orlistat 120 mg tid.[126,127,129,130,132,136,180-184,187,189-191,193,194,197-202,215] Four trials included additional dosage regimens (30 to 240 mg tid), but did not present statistical comparisons between dosage groups.[129,189,190,199] Data do not suggest that higher dosages were associated with elevated adverse effect rates, although the results were somewhat mixed.

Subgroup analysis. Withdrawals due to adverse effects and serious adverse events were more likely in trials of unselected participants taking orlistat[129,182,184,189,190,193,199,200] than in participants with cardiovascular risk factors,[126,127,130,132,180,181,183,187,191,194,197,198,201,202] regardless of age.

Metformin.

General characteristics of studies. We included a total of four trials on the harms of metformin (850 mg twice daily) (Table 16). Three trials were RCTs from KQs 2 and 3[142,185,186] and one was an additional published RCT.[131] Recruitment criteria included IFG or IGT,[142] high WHR,[185] or polycystic ovary syndrome.[131,186] One trial additionally compared metformin with orlistat, and was described previously.[136] Only one of the four trials was conducted in the United States.[142] The overall weighted average percent of female participants in all trials was 68.7 percent (range, 67 to 100 percent); two small trials included only women. The overall weighted average age of participants was 49.7 years (range, 27 to 50 years), and 45.3 percent of the participants in the largest trial of metformin were nonwhite.[142] The other trials did not describe ethnicity. Two trials had a duration of 1 year (range, 26 to 208 weeks).

Withdrawals and adverse effects. Participants who were randomized to metformin were more likely to have any adverse event and to withdraw due to adverse effects (Table 17) compared with those who were randomized to placebo.[131,185,186] No studies reported the proportion of participants with serious adverse effects, although one listed all adverse effects and none fit our criteria for serious.[186] There were no data about the effects of metformin on bone density or hypoglycemia. Gastrointestinal adverse effects (abdominal swelling, diarrhea, flatulence, nausea, vomiting) were more likely to occur in those who were randomized to metformin compared with placebo and were the main reason for excess adverse effects (Table 17).[131,185,186,210] Table 17 and Appendix F provide more details on adverse events.

Dosage effects. We were unable to examine the relationship between metformin dose and adverse effects, as all studies prescribed the same dose of 850 mg twice daily.

Subgroup analysis. In DPP, the relative increase in gastrointestinal adverse events in the metformin group did not appear to differ by age.[210]

Heterogeneity of medication studies (meta-regression analysis). We performed meta-regression to examine whether study characteristics influenced the association between medication and the proportion of participants who withdrew due to adverse effects or reported any adverse effects, any serious adverse effects, or gastrointestinal-related adverse effects, in all cases controlling for risk status of the participants and medication type. We examined multiple trial factors, including how many participants returned for followup, whether the study was conducted in the United States, and the duration of the study. None of these trial factors influenced the harms effect size of the medications. Sex and age did not predict effect size for any adverse event associated with medications. We were unable to examine ethnicity because of the paucity of reporting and low percentage of nonwhite participants in the medication studies.

The type of medication did not influence withdrawals due to adverse effects, total adverse effects, or serious adverse effects in any of the meta-regression models, although the number of metformin trials was fairly small. We had limited ability to detect differences in harms between medications since we did not include trials that did not have placebo comparison groups. Only one trial of obese women included a head-to-head comparison of orlistat and metformin.[136] Two participants withdrew due to side effects (none serious) from the orlistat group and none withdrew from the metformin group.

Chapter 4. Discussion

Benefits of Screening for Adult Obesity

We found no trials directly examining the benefit of screening for adult obesity. Six behavioral-based trials either screened consecutive patients in primary care practices[158,162,165] or identified potentially eligible participants through medical records or disease registries and then invited them for further screening.[146,159,178] All of these trials included fewer than 10 treatment sessions. Two of the five trials (both fair-quality) showed greater weight loss in intervention participants.[159,165] No medication trials screened consecutive patients in primary care practices; however, three orlistat studies (one good- and two fair-quality) identified potentially eligible participants through medical records or disease registries and then invited them for screening.[183, 200,215] These trials showed mixed but generally positive results. These trials suggest that weight loss programs can be effective in screen-detected patients, although it cannot be determined if screening affects the likelihood of success in weight loss (Table 18).

Benefits of Weight Loss Treatment

Weight Loss

Participants of behavioral interventions lost an average of 3.0 kg more than control groups. Participants in control groups generally lost little or no weight, while the average weight loss in intervention groups ranged from 0 to 7 kg, with most falling in the 1.5 to 5 kg range, losing 4 percent of baseline weight on average (Table 19). These results are consistent with the previous review, despite the fact that only five of the trials in the current review were included in the 2002 review (Appendix B Table 3). Also consistent with the previous review, we found that intervention intensity influenced the amount of weight loss. Trials that provided 12 to 26 intervention sessions during the first year had a weighted average weight loss of 5.3 kg (generally 4 to 7 kg), or 6 percent of baseline weight, at 12 to 18 months compared with 0.3 kg weight loss (<1 percent of baseline weight) in control groups. The 2002 review reported an average weight loss of 2.7 to 5.5 kg in trials that involved more than monthly face-to-face contact for the first 3 months.

Weight loss could be maintained for an additional year or more after completion of an active weight loss phase, particularly with additional support after completion. No other factors were clearly related to effect size in the included trials, but high variability in the intervention approaches, trial design, and populations may have obscured important relationships.

Taking a weight loss medication generally increased the amount of weight loss over and above that of the accompanying behavioral-based intervention (Table 19). These results are generally similar to the previous evidence review, despite the fact that only two of the 13 medication trials from the previous review were included in the current review (Appendix B Table 4). The absolute amount of weight loss varied substantially between trials, as did the extent of the treatment's behavioral component. Orlistat resulted in 5 to 10 kg of weight loss (8 percent of baseline weight). Metformin was associated with a smaller degree of weight loss (2 to 4 kg). The

previous evidence review did not conclude that metformin led to significant weight loss, but it included only one study of metformin[217] and that study was not included in our review.

Although the medication trials were conducted in more obese samples than the behavioral trials, the placebo groups that received an intensive behavioral intervention typically experienced 3 to 6 kg of weight loss, which is roughly comparable with that seen in behavioral weight loss trials with 12 or more intervention sessions (Table 19). Weight loss in placebo groups that received no or minimal behavioral treatment was minimal to nonexistent, consistent with the control groups of behavioral trials.

Weight loss of 5 and 10 percent of baseline weight was frequently reported in orlistat trials but not for metformin. This outcome was only rarely reported and varied substantially in the behavioral-based trials. Five percent weight loss is considered to be clinically meaningful by the FDA, where it is considered a primary weight loss outcome.[218] Most orlistat trials reported that between one third and three fourths of intervention participants lost 5 percent or more of their initial weight after 1 year (compared with one tenth to one half in placebo participants). About half as many participants lost 10 percent of their initial weight as those who lost 5 percent.

Behavioral-based weight loss interventions consistently showed 2 to 5 cm greater reductions in waist circumference than placebo. The absolute reduction in waist circumference with orlistat was generally 5 to 9 cm compared with 2 to 7 cm in the placebo groups. Metformin led to a smaller, but still significant, reduction in waist circumference (2 to 5 cm).

Weight Loss Results in Different Patient Subgroups

Data on the effects of weight loss or maintenance programs in subgroups were sparsely reported and somewhat mixed. Behavioral interventions appeared, on average, to lead to less weight loss in blacks and women than nonblacks and men.[28,145,152,157,168,170,171,175,177,214] The only trial of medication examining subgroup effects was the metformin arm of DPP, which found that ethnicity and sex were not related to amount of weight lost.[214] Older participants showed greater weight loss than younger participants in both the lifestyle and metformin arms of DPP.[142] Although another good-quality behavioral trial[169] also found increased weight loss with increasing age, three other behavioral trials showed no age-by-treatment interactions.[152,170,171] Baseline BMI generally did not have an impact on treatment effect size at 12 months or beyond.

Clinical Health Outcomes

The amount of weight loss apparent in the included trials did not demonstrate an effect on mortality, cardiovascular disease events, hospitalizations, or depression, although data were sparse for all outcomes. The two good-quality trials reporting one or more of these outcomes were not powered to detect group differences in these outcomes, other than depressive symptoms.[142,172]

Epidemiologic data about whether the degree of weight loss seen in the behavioral and medication trials is associated with reduced mortality were mixed. The relationship is likely confounded by a number of factors, particularly health status. Most,[219-222] but not all,[223] data

suggest that intentional weight loss of less than 9 kg was not associated with reduced mortality. However, these studies generally assessed the intentionality of weight loss at only one time point and several relied on retrospective assessment of weight loss. Prospective cohort studies of obese adults undergoing bariatric surgery show substantial improvements in health; however, weight loss in these patients is generally on the order of 25 to 50 kg.[224,225]

Lipids

The pooled estimates for lipid changes with behavioral interventions were at high risk of reporting bias because lipid outcomes were rarely reported. We concluded that there were either no or very small effects of weight loss interventions on lipid outcomes in the included trials. In the few studies that did report lipid changes with behavioral weight loss interventions, the reduction in LDL cholesterol (generally 2 to 11 mg/dL) was substantially smaller than that seen with statin medications, which can cause LDL reduction on the order of 70 mg/dL.[226] These negative results for total cholesterol are not unexpected, based on data from the Swedish Obesity Subjects Study. This observational study of surgically and conventionally treated obese persons found that a weight loss of 20 to 30 kg was required to detect improvements in total cholesterol. Triglycerides and HDL cholesterol demonstrated marked improvements in response to large amounts of weight loss in this study.[227]

Orlistat had favorable effects on lipid outcomes compared with placebo. Reductions in LDL cholesterol ranged from 3 to 27 mg/dL. Patients with dyslipidemia, however, had LDL reduction of more than 37 mg/dL with orlistat.[183] Orlistat may cause a decrease in lipid levels by a mechanism independent of weight loss;[228] it may decrease lipids as a result of decreased absorption and increased fecal fat loss. Although still substantially smaller than statins' effects, an LDL reduction of 38 mg/dL has been associated with a 50 percent or more reduction in ischemic heart disease-related mortality in persons ages 45 to 59 years.[9] In contrast, metformin did not improve lipid profiles compared with placebo.

Blood Pressure

Behavioral weight loss interventions led to a greater reduction in blood pressure compared with placebo. SBP and DBP decreased by 2.5 and 1.9 mm Hg more, respectively, in behavioral intervention groups than in control conditions. Our findings are consistent with the findings of a previous meta-analysis of behavioral weight loss RCTs,[229] which estimated that each kilogram of weight loss led to a 1.0 and 0.9 mm Hg decrease in SBP and DBP, respectively.[229] Translated to our trials, we would expect a decrease of roughly 5 mm Hg in SBP and 4.8 mm Hg in DBP in the high-intensity intervention groups, which is what we observed.

Participants taking orlistat showed a 2.0 mm Hg greater reduction in SBP and a 1.3 mm Hg greater reduction in DBP than those taking placebo medications. However, the absolute reduction in blood pressure (SBP: 2 to 6 mm Hg; DBP: 2 to 5 mm Hg) with orlistat was about the same as in the behavioral trials, despite the greater weight loss achieved with orlistat. The reduction was highest in studies of participants with any cardiovascular risk factor, including hypertension. Metformin did not have favorable effects on blood pressure compared with placebo.

Reductions of 5 to 6 mm Hg in DBP over 5 to 10 years have been associated with 33 percent or more reduction in stroke incidence and 16 percent reduction in CHD events in persons with and without hypertension.[230] Reductions of this magnitude were reported in some orlistat and behavioral-based trials in this review over 12 to 36 months, although none reported outcomes beyond 3 years.

Diabetes

Diabetes outcomes were rarely reported in behavioral trials. We therefore focused on two large, good-quality behavioral trials of diabetes prevention.[142,172] Behavioral interventions (7 to 23 sessions in first year) led to weight loss of 4 to 7 kg and decreased the incidence of diabetes by approximately half or more over 2 to 3 years. One of these trials, DPP, also examined metformin and noted a 31 percent reduction in diabetes incidence.[213] The authors continued to follow participants after unblinding them and offering all participants the lifestyle treatment program, as well as additional booster sessions. Ten years after the original randomization, lifestyle and metformin participants still had a median delay of diabetes onset of 4 and 2 years, respectively, compared with controls.[213] In two studies of persons with and without IGT, orlistat was associated with a reduced incidence of diabetes, although we had concerns about the reliability and generalizability of the data.

Glucose Tolerance

Because trials of low-risk populations inconsistently reported fasting glucose outcomes, we focused on studies of individuals with prediabetes or diabetes, which more consistently reported fasting glucose changes. Behavioral-based interventions, orlistat, and metformin all led to a greater decline in fasting glucose than controls. Glucose reduction was greatest with orlistat (12 mg/dL greater reduction than placebo), possibly because those studies were all conducted in persons with diabetes. In behavioral and metformin studies of persons with prediabetes and diabetes, the decrease in fasting glucose was more modest (group differences of 5.3 and 4.8 mg/dL with behavioral intervention and metformin, respectively).

We did not find recent epidemiologic data that would allow us to gauge whether the effects of weight loss on diabetes risk or glucose tolerance in the included trials was consistent with the effects in real-world settings.

Harms of Screening for Adult Obesity

No trials directly examined the harms of screening for adult obesity. The methods of measuring obesity in common practice (BMI, waist circumference, WHR) are low cost and have no direct physical harms. Possible secondary harms include labeling stigma, higher insurance premiums, or reinforcement of poor self-esteem. Misclassification is possible if BMI is used for screening because of differences in BMI's ability to predict future health risk, especially in different ethnic groups. Evidence is still being obtained on how we should adjust guidelines for more accurate identification of those at risk in order to better target management once screening positive.

Harms of Weight Loss Treatment

Possible harms that could accrue from weight loss interventions include bone loss and increased fracture risk, injuries from increased physical activity, decreased self-esteem from being labeled as obese or failure to lose weight, use of extreme or unhealthy dietary approaches, and weight cycling. Limited data suggest that weight loss may be associated with decreased bone density at the hip. However, whether it is valid to measure bone density changes during weight changes is unclear; changes in fat distribution may alter bone measurements despite no real change in bone density.[231-233] Also, the clinical significance of the bone loss is unclear, given the lack of data on changes in bone density after weight loss has stopped and subsequent fracture risk. Risk of minor, but not serious, injuries increased with a supervised exercise component. However, the mild injuries did not result in lost work time or a major change in daily activities. The included trials found no evidence that weight loss interventions are associated with an increased risk of eating disorders or depression, but these data were limited. No studies evaluated whether weight loss interventions increase the risk of weight cycling. However, whether weight cycling even leads to increased morbidity or mortality is unclear.[234-237]

Medications can lead to additional harms due to side effects. Orlistat and metformin caused mild to moderate gastrointestinal side effects that resulted in medication discontinuation.

Although orlistat did not cause more serious side effects than placebo in the included trials, the FDA recently (May 2010) approved a revised label for orlistat 120 mg (prescription strength) and 60 mg (over-the-counter strength). The revised label includes ~~"n~~ew safety information about cases of severe liver injury that have been reported rarely with the use of this medication."[238] The FDA noted the possibility of severe liver injury during routine monitoring of submitted postmarketing adverse events. In the FDA's review, 13 cases of severe liver injury were identified. Two persons died and three required liver transplantation. Twelve of the identified persons had taken 120 mg tid and one had taken 60 mg tid. The FDA could not establish if there was a cause and effect relationship because other factors or drugs may have contributed in some of the cases.[238]

As described in Appendix G, surgery is another treatment option for obesity. There are short-term risks associated with surgery, including perioperative mortality, infection, bleeding, deep venous thrombosis, pulmonary embolism, and gastrointestinal leaks.[239,240] Long-term harms include symptomatic ulcers, gastroesophageal reflux disease, diarrhea, cholelithiasis,[241] and nutritional deficiencies.[242] Surgical reoperations (excluding reoperation in the perioperative period for complications) range from 17–31 percent depending on the type of surgery.[239,243,244]

Effectiveness of Specific Weight Loss Strategies

Greater treatment intensity was associated with greater weight loss. The association with treatment intensity was apparent despite the fact that our measure of treatment intensity (number of sessions in the first year) was imperfect, and particularly broke down at the extremes (e.g., one trial with ~~0~~" sessions involved extensive electronic contact, and one trial with 128 sessions was targeted toward physical activity and provided little counseling for dietary change). We also defined treatment intensity slightly differently in the behavioral and medication trials, but found

similar weight loss in medication trials labeled as "intense" and behavioral trials involving 12 or more intervention sessions. Most of the higher-intensity behavioral-based interventions included coverage of behavioral management activities, such as self-monitoring, setting weight loss goals, addressing barriers to change, and strategizing how to maintain long-term behavioral changes. However, we found no association between effect size and any of these components or any other specific intervention characteristics.

We examined reviews and comparative effectiveness trials (which were excluded from this evidence review) to provide more information on the effectiveness of specific weight loss approaches. In two systematic reviews, all diets—if adhered to—resulted in weight loss, and the difference in weight loss between the various diets was negligible.[123,245] Some reviews have found slight benefits to protein sparing modified fasts (e.g., Optifast and Modifast products),[246] the Atkins diet (low carbohydrate),[247] or a low carbohydrate/high protein diet.[248]

Weight loss may be sustained better over time when diet and exercise are combined.[249-252] Higher-intensity exercise led to greater improvement in cardiovascular disease risk factors.[251] In the National Weight Control Registry, a database of over 4,000 persons who successfully maintained their weight after a weight loss, those who successfully maintained weight loss had a high level of physical activity, consumed low-calorie, low-fat diets, consumed a regular breakfast, self-monitored weight and food intake (e.g., kept food diaries), maintained consistent eating patterns across weekdays and weekends, and recovered from small weight regains quickly. The most common weight loss trigger for this population was a medical event (23 percent), which included diagnosis of diabetes, a family member having a heart attack, or a doctor telling them they must lose weight.[253]

Applicability to Primary Care

Only four trials of behavioral-based interventions were conducted in primary care settings in the United States.[146,147,158,159] All reported small amounts of weight loss in the intervention groups (0.1 to 2.2 kg), and only one showed greater weight loss compared with the control group (by 1.7 kg) after 1 year.[159] This trial had the most intensive intervention arm of all four trials, including 22 group sessions with a nutritionist in the first year. The same trial had a lower-intensity intervention arm (only four sessions over the course of the first year) that was not effective in helping participants lose weight. Aside from this trial, most of the successful behavioral-based interventions in the United States were not highly applicable to primary care. The participants had to be motivated to respond to advertisements or other media announcements. The interventions usually involved 12 or more sessions in 1 year, a high burden for a primary care clinic to undertake.

One fair-quality orlistat trial was conducted in a U.S. primary care setting.[189] Only study physicians (not dietitians) were involved, along with video presentations. Weight loss was 3 kg greater in the intervention group (7 kg vs. 4 kg). None of the metformin studies recruited exclusively from primary care or were conducted in the primary care setting.

Cost/Cost Effectiveness

The only included study that had accompanying cost effectiveness data was DPP.[254] Compared with placebo, cost per quality-adjusted life year (QALY) gained was estimated at approximately $1,100 for the DPP lifestyle intervention and $31,300 for the metformin intervention in year 2000 dollars.[254] (The standard threshold of cost effectiveness in the United States is $35,000 to $50,000 per QALY gained.) Because the weight loss effect was greater in DPP compared with other trials, this cost effectiveness evaluation may be a best care scenario. Over 3 years, implementing the lifestyle or metformin arms of DPP was estimated to cost a health care plan $2,250 per participant and reduce health care utilization and direct medical costs by $423 and $272 in the lifestyle and metformin intervention groups, respectively.[254]

Simulation studies are the main source of data on the cost effectiveness of behavioral interventions. For example, a recent Monte Carlo simulation study[255] estimated that a weight loss intervention that included dietary counseling, physical activity, and behavioral modification training in otherwise healthy overweight or obese women ages 35 years would cost $12,600 per QALY gained over their lifetime.

A systematic review modeled the cost effectiveness or cost utility of orlistat treatment for obesity.[256] The median incremental cost effectiveness ratio for orlistat was $36,400 per QALY, with a median modeled time horizon of 7.5 years.

Limitations of the Review

Although we included 58 unique trials of weight loss efficacy, they were variable in the specific outcomes reported, and about one third of the trials could not be included in the meta-analysis of our primary outcome—weight loss. Intermediate physiologic outcomes (blood pressure, lipid levels, and fasting glucose) were sparsely reported, and also could not often be included in meta-analyses.

The applicability of our findings to primary care patients is unclear. Few of the studies were conducted in primary care settings and the interventions were often intensive and difficult to implement within a primary care setting (although overweight and obese patients could be referred into such programs by primary care providers). Participants in the behavioral-based weight loss trials generally fell into the overweight or class I obesity range, and the generalizability of these results to extremely obese persons is unknown. Most of the medication trials had run-in periods before randomization and usually required a certain degree of weight loss and/or compliance for inclusion in the main trial. Therefore, trial participants were likely more highly motivated, compliant, and responsive than primary care patient populations. The medication trials were almost exclusively financed by pharmaceutical companies; however, the one orlistat trial not financed by a pharmaceutical company had the largest effect size of all the trials.[215]

Our results, especially our medication findings, could also have been biased by high attrition. We chose to include studies with up to 40 percent attrition and/or 20 percent differential attrition. We made this decision because we believed it might be challenging for overweight and obese

populations to continue participating in a trial for a full year or longer. We felt that early discontinuation might be common regardless of trial design and not necessarily due to a design flaw. The majority of medication trials included all randomized participants using the last-observation-carried-forward method of imputing intention-to-treat results. Epidemiological studies have shown that most weight loss occurs early in the intervention and that weight is often regained toward baseline or even higher levels.[257] Therefore, using the last-observation-carried-forward approach to impute such large amounts of data (up to 40 percent) might have led to biased comparisons in unknown directions. We did examine the effect of attrition on effect size using meta-regression, but did not find that attrition had significant effects. The last-observation-carried-forward method was less common in the behavioral trials (in which attrition was generally lower than in medication trials). Behavioral trials were more likely to impute missing data through multilevel repeated measures modeling than carrying the last observation forward. However, behavioral trials were also more likely to drop participants from an analysis if they had missing data.

We reviewed several topics of high relevance to this topic as contextual questions only and not systematically. We did not include comparative effectiveness trials, as included studies had to have a control group with only a minimal intervention (Appendix A). Comparative effectiveness trials would shed more light on the components of an effective intervention. We also did not systematically examine the best screening approach. A growing body of evidence suggests that WHR or waist circumference may be better predictors of future health effects than BMI, especially for some subgroups. Finally, we only included one off-label medication, metformin. Other medications that are used off label for weight loss include zonisamide, an antiepileptic agent.[114] We also did not include antiobesity drugs in development, including Lorcaserin, Qnexa (a combination of phentermine and topiramate), or Contrave (a combination of naltrexone and bupropion).

We excluded studies with control groups that had more than a minimal intervention. A total of 143 studies were excluded because the control intervention was considered too intensive. One such study, Look AHEAD (Action for Health in Diabetes), is an important study of a behavioral weight loss intervention in persons with diabetes. The controls in this study had three group sessions on diet, physical activity, and social support each year. Look AHEAD had similar, if not slightly more positive, findings than the findings of our systematic evidence report. In Look AHEAD, 4 years of an intensive lifestyle intervention (42 sessions in the first year) led to 6 percent weight loss (compared with <1 percent in controls), decreased SBP and DBP, and improvement in HDL cholesterol and triglycerides.[258] The lifestyle intervention also led to significant and clinically relevant improvements in obstructive sleep apnea, especially in those participants who lost at least 10 kg.[259]

Future Research

A study examining the effect of screening for adult obesity on long-term weight and health outcomes should be of high priority. We found little or no data on whether weight loss interventions (both behavioral and pharmacological) can lead to lasting weight loss and improvements in health outcomes. The benefits and harms of weight loss in the elderly are of particular interest given the potentially greater harms (e.g., decreased bone density and injuries

from increased physical activity). There is also a need to examine patterns of how weight gain and loss across the lifetime might affect long-term health outcomes.

Future research should clarify the degree to which the benefits seen from weight loss are derived specifically from the weight loss itself or from the effects of behavioral factors, such as increased physical activity or changes in diet. We also believe that the next systematic review of the evidence on adult obesity should re-review the question of the best screening tool for adult obesity; BMI may not be the best screening tool in general, and particularly so in specific subgroups such as the elderly and some nonwhite populations. The cost effectiveness of behavioral and medication interventions also deserves more careful study.

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Table 1. Summary of Medication and Behavioral-Based Interventions

Medication Interventions						Behavioral-based Interventions					
Reference; Medication type; Quality rating	**# Randomized**	**Average age (yrs)**	**% Female**	**% Nonwhite**	**Mean baseline BMI (kg/m^2); Minimum BMI**	**Reference; # of sessions in 12 months; Quality rating**	**# Randomized**	**Average age (yrs)**	**% Female**	**% Nonwhite**	**Mean baseline BMI (kg/m^2); Minimum BMI**
With cardiovascular risk factors											
Diabetes											
Berne 2005[180] Orlistat; Fair	220	59.1	45.5	0	32.7 ≥28	Christian 2008[146] (US-PC) 4 sessions; Fair	310	53.2	66.1	100	35.1 ≥25
Hanefeld 2002[187] Orlistat; Fair	383	56.2	50.9	NR	34.1 ≥28	Mayer-Davis 2004[159] (US-PC) (POWER) 30 sessions; Fair	152	60.4	80.3	82.2	36.3 ≥25
Hollander 1998[191] Orlistat; Fair	322	55.1	48.9	12.5	34.3 ≥28						
Miles 2002[197] Orlistat; Fair	516	53.1	48	18	NR ≥28						
Derosa 2010[215] Orlistat; Good	254	52.5	49.6	NR	32.8 ≥30						
Hypertension											
						Burke 2005[145] (ADAPT) 20 sessions; Fair	241	56.2	55.6	NR	30.1 >25
						Cohen 1991[147] (US-PC) 12 sessions; Fair	30	59.5	NR	NR	34.1 ≥27.8 (men) ≥27.3 (women)
						Davis 1992[149] (TAIM) 16 sessions; Fair	200	47.7	50.0	34.0	194.2 lb (weight) NR
						Jones 1999[154] (HOT) 10 sessions; Fair	111	58.0	52.0	40.2	34.0 ≥27
						Kastarinen 2002[155] (LIHEF) 5 sessions; Fair	715	54.3	53.0	NR	28.7 NR
						Langford 1985[157] (DISH) 18 sessions; Fair	176	56.7	65.9	65.9	87.9 kg (weight) NR
						Whelton 1998[175] (TONE) 26 sessions; Good	585	66.0	52.6	28.2	86 kg (weight) NR
Dyslipidemia											
Derosa 2003[183] Orlistat; Fair	50	52.0	52.0	NR	31.9 >30						
Multiple risk factors											
Broom 2002[181] (UK Multimorbidity Study) Orlistat; Fair	531	46.0	78.4	NR	37.0 ≥28	Anderssen 1995[144] (ODES) 159 sessions; Fair	219	44.9	9.6	NR	28.4 >24
Lindgarde 2000[194] (Swedish Multimorbidity Study); Orlistat; Fair	376	53.5	63.6	NR	33.2 ≥28	Svetkey 2008[170] (WLM) 12 sessions; Good	1032	55.6	63.4	37.6	NR ≥25
Swinburn 2005[201] Orlistat; Fair	339	52.2	56.9	NR	37.8 ≥30	ter Bogt 2009[171] 5 sessions; Fair	457	56.1	51.9	NR	29.6 ≥25
						Woollard 2003[178] 12 sessions; Fair	212	60.2	50.7	NR	30.1 NR
Total trials (n) with cardiovascular risk factors											
9 (2991)						13 (4440)					

Table 1. Summary of Medication and Behavioral-Based Interventions

Medication Interventions						Behavioral-based Interventions					
Reference; Medication type; Quality rating	**# Randomized**	**Average age (yrs)**	**% Female**	**% Nonwhite**	**Mean baseline BMI (kg/m^2); Minimum BMI**	**Reference; # of sessions in 12 months; Quality rating**	**# Randomized**	**Average age (yrs)**	**% Female**	**% Nonwhite**	**Mean baseline BMI (kg/m^2); Minimum BMI**
With subclinical increase in cardiovascular risk or risk factors											
Prediabetes											
Torgerson 2004[202] (XENDOS); Orlistat; Fair	3305	43.3	55.2	NR	37.4 ≥30	DPP 2005[142] 23 sessions; Good	2161	50.6	67.7	45.3	34.1 ≥24 (≥22 in Asian Americans)
DPP 2005[142] Metformin; Good	2155	50.6	67.7	45.3	34.1 ≥24 (≥22 in Asian Americans)	Kulzer 2009[156] (PREDIAS) 12 sessions; Fair	182	56.3	43.0	NR	31.5 ≥26
						Mensink 2003[160] 4 sessions; Fair	114	56.7	43.9	0	29.5 ≥25
						Parikh 2010[204] (Project HEED); 8 sessions; Fair	99	48.0	85.0	98.0	31.5 ≥25
						Tuomilehto 2001[172] (FDPS) 7 sessions; Good	522	55.0	67.0	NR	31.2 >25
Prehypertension											
						HPT 1990[143] 16 sessions; Good	251	38.8	32.7	19.9	28.5 NR
						Stevens 1993[168] (TOHP I) 23 sessions; Good	564	43.0	29.9	17.8	NR ≥115% of ideal weight
						Stevens 2001[169] (TOHP II) 32 sessions; Good	1191	43.3	34.3	21.2	NR 26.1 (men) 24.4 (women)
Multiple risk factors											
Richelsen 2007[198] Orlistat; Fair	309	47.0	50.8	NR	37.5 ≥30						
Total trials (n) with subclinical increase in cardiovascular risk or risk factors											
3 (5769)						8 (5084)					
Without increase in cardiovascular risk factors											
Davidson 1999[182] Orlistat; Fair	892	43.5	84.2	19.2	36.3 ≥30	Cussler 2008[148] 2 sessions; Fair	135	48.2	100	NR	30.3 ≥25
Finer 2000[184] Orlistat; Fair	228	41.5	88.5	5.1	36.8 ≥30	Fitzgibbon 2010[200] (ORBIT) 116 sessions; Fair	213	46.0	100	100	39.3 ≥30
Hauptman 2000[189] (US-PC); Orlistat; Fair	635	42.5	78.3	9.1	36.1 ≥30	Haapala 2009[151] 0 sessions; Fair	125	38.1	77.4	NR	30.5 ≥25
Hill 1999[190] Orlistat; Fair	729	46.3	84.0	11.7	32.8 ≥28	Irwin 2003[152] (PATH) 128 sessions; Good	173	60.8	100	13.0	30.5 >25 (>24 if body fat >33%)
Krempf 2003[193] Orlistat; Fair	696	41.0	86.4	NR	36.1 ≥28	Jeffery 1993[153] (Trial of Food Provision and Monetary Incentives) 27 sessions; Fair	202	37.5	50.0	7.9	31.1 NR
Rossner 2000[199] Orlistat; Fair	783	44.2	82.3	NR	35.0 ≥28	Martin 2008[158] (US-PC) 6 sessions; Fair	137	41.8	100	100	39.1 ≥25

Table 1. Summary of Medication and Behavioral-Based Interventions

Medication Interventions						Behavioral-based Interventions					
Reference; Medication type; Quality rating	**# Randomized**	**Average age (yrs)**	**% Female**	**% Nonwhite**	**Mean baseline BMI (kg/m^2); Minimum BMI**	**Reference; # of sessions in 12 months; Quality rating**	**# Randomized**	**Average age (yrs)**	**% Female**	**% Nonwhite**	**Mean baseline BMI (kg/m^2); Minimum BMI**
Sjostrom 1998[200] Orlistat; Fair	688	44.8	83.0	NR	36.0 ≥28	Mitsui 2008[161] 24 sessions, Fair	46	63.3	54.3	100	25.2 NR
Fontbonne 1996[185] (BIGPRO) Metformin; Fair	457	49.5	66.7	NR	33.1 No min BMI (high WHR)	Moore 2003[162] sessions NR; Fair	843	48.6	73.9	NR	36.9 ≥30
Gambineri 2006[186] Metformin; Fair	40	27.0	100	NR	36.0 ≥28	Narayan 1998[163] 52 sessions; Fair	95	33.5	75.8	100	34.9 ≥27 (men) ≥25 (women)
						Perri 1988[164] 26 sessions; Fair	123	NR	78.9	NR	NR NR
						Pritchard 1999[165] 8 sessions; Fair	270	NR	72.5	NR	90.4 kg (weight) NR
Without increase in cardiovascular risk factors											
						Silva 2009[166] 30 sessions; Fair	239	37.6	100	NR	31.5 ≥25
						Simkin-Silverman 2003[167] (WHLP) 20 sessions; Good	535	47.0	100	NR	25.0 ≥20
						Villareal 2008[173] 208 sessions; Fair	27	70.0	66.7	NR	NR ≥30
						Werkman 2010[174] 0 sessions; Good	413	59.5	0	NR	27.0 NR
						Wood 1988[176] 23 sessions; Fair	131	44.5	0	NR	NR NR
						Wood 1991[177] 25 sessions; Fair	264	39.7	48.5	11.3	30.7 ≥28 (men) ≥24 (women)
Total trials (n) with low cardiovascular risk or unselected samples											
9 (5148)						17 (3971)					
Total trials (n)											
21 (13908)						38 (13495)					

Abbreviations: ADAPT= Activity, Diet, and Blood Pressure Trial; BIGPRO=Biguanides and Prevention of Risks in Obesity; BMI=body mass index; DISH=Dietary Intervention to Study Hypertension; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HOT=Hypertension Optimal Treatment; HPT=Hypertension Prevention Trial; LIHEF=Lifestyle Intervention Against Hypertension in Eastern Finland; min=minimum; NR=not reported; ODES=Oslo Diet and Exercise Study; ORBIT=Obesity Reduction Black Intervention Trial; PATH=Physical Activity for Total Health; POWER=Pounds Off With Empowerment; HEED=Help Educate to Eliminate Diabetes; PREDIAS=Prevention of Diabetes Self-Management Program; TAIM=Trial of Antihypertensive Interventions and Management; TOHP=Trials of Hypertension Prevention; TONE=Trial of Nonpharmacologic Interventions in the Elderly; UK=United Kingdom; US-PC=participants recruited from primary care and/or intervention conducted in U.S. primary care; WHLP=Women's Healthy Lifestyle Project; WHR=waist-to-hip ratio; WLM=Weight Loss Maintenance; XENDOS=Xenical in the Prevention of Diabetes in Obese Subjects.

Table 2. Trials Not Included in Meta-Analysis: Weight Loss in Behavioral Trials, 12- to 18-Month Outcomes

Study	Population risk status (risk group)	# Sessions in first 12 months	N	Weight (kg) or BMI change (kg/m^2)
Anderssen 1995[144]	Multiple risk factors	159	IG: 67 CG: 43	Mean (SD) change in BMI at 12 mo 12 mo IG **-1.8 (1.4)** CG **0.3 (0.8)**
Kastarinen 2002[155] (LIHEF)	Hypertension	5	IG: 360 CG: 355	Mean (SD) at baseline, mean change BL 12 mo IG 81.1 (15.7) **-1.5** CG 80.0 (14.8) **-0.2**
Mayer-Davis 2004[159] (POWER)	Diabetes	22	Total: 187	Mean (SD) at baseline, mean change at 12 mo BL 12 mo IG 99.5 (17.1) **-2.2** CG 93.0 (20.3) **-0.3**
Davis 1992[149]	Hypertension	16	IG: 100 CG: 100	**Figures show difference between weight loss and usual care groups through 2-2.5 years (p<0.05)**
Jones 1999[154] (HOT)	Hypertension	10	IG: 55 CG: 56	Mean (SD) at baseline, mean change at 12 mo BL 12 mo (estimated from figures) IG 97 (18) -0.7 CG 92 (18) -0.5
Whelton 1998[175] (TONE)	Hypertension	26	IG: 147 CG: 147	Mean at baseline, mean change at 12 +18 mo BL 12 mo 18 mo IG 86.5 **-4.7** **-4.4** CG 87 **-1.1** **-0.8**
Jeffery 1993[153]	Unselected/low risk	27	IG: 41 CG: 40	Mean BMI at 12 + 18 mo BL 12 mo 18 mo IG 31.3 **28.3** **29.0** CG 30.9 **30.4** **30.7**
Mitsui 2008[161]	Unselected/low risk	24	IG: 24 CG: 22	Mean (SD) BMI at 12 mo BL 12 mo IG 24.8 (2.2) 23.7 (2.4) CG 25.6 (2.5) 25.5 (2.6)
Moore 2003[162]	Unselected/low risk	12-24 (estimated)	IG: 415 CG: 428	Mean (SD) BL 12 mo 18 mo IG 100.8 (18.1) 100.3 (--) 100.8 (--) CG 100.2 (17.4) 99.3 (--) 99.5 (--)
Narayan 1998[163]	Unselected/low risk	52	IG: 48 CG: 47	Median (range) at baseline, median change at 12 mo BL 12 mo IG 96.4 (59.4-159.1) **2.5** CG 89.3 (59.2-184.8) **0.8**
Pritchard 1999[165]	Unselected/low risk	8	IG: 92 CG: 90	Mean at baseline, mean change at 12 mo BL 12 mo IG1 85.5 **-5.1** IG2 91.7 **-6.2** CG 89.1 **0.6**
Silva 2009[166]	Unselected/low risk	30	IG: 123 CG: 116	Mean (SD) BMI at baseline, mean change at 12 mo BL 12 mo IG 31.7 (4.24) **-2.3 (1.9)** CG 31.3 (4.00) **0.7 (1.9)**
Villareal 2008[173]	Unselected/low risk	208	IG: 17 CG: 10	Mean (SD) at baseline, % change (SD) in body weight at 12 mo BL 12 mo IG 99.7 (13.6) -10.1 (2.0) CG 103.2 (19.8) 1.2 (1.3)

Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; BMI=body mass index; CG=control group; HOT=Hypertension Optimal Treatment; IG=intervention group; LIHEF=Lifestyle Intervention Against Hypertension in Eastern Finland; Mo=month; POWER=Pounds Off With Empowerment; SD=standard deviation; TONE=Trial of Nonpharmacologic Interventions in the Elderly.

Table 3. Long-Term Weight Loss and Blood Pressure Outcomes in Behavioral-Based Interventions Beyond 18 Months

Study	Time to followup/ since intervention ended (mo)	Population risk status (risk group)	# Sessions in first 12 months	N	Weight (kg) or BMI (kg/m^2) change	Average greater reduction in SBP/DBP in intervention vs. control (mmHg)
Long-term interventions						
Mensink 2003[160]	24/0	Prediabetes	4	IG: 55 CG: 59	Mean (SE) at baseline, mean change (SE) at 24 mo BL 24 mo IG 86 (1.9) **-2.4 (0.7)** CG 83.7 (1.5) **-0.1 (0.5)**	NR
Tuomilento 2001[172] (FDPS)	24/0	Prediabetes	7	IG: 265 CG: 257	Mean (SD) at baseline, mean change (SD) at 24 mo BL 24 mo IG -- **-3.5 (5.5)** CG -- **-0.8 (4.4)**	**5 vs. 2**
HPT 1990[143]	36/0	Prehypertension	16	IG: 125 CG: 126	Mean at baseline, mean change (SE) at 36 mo BL 36 mo IG 87.4 **-1.63 (0.41)** CG 83.4 **1.86 (0.41)**	**2.4 vs. 1.8**
Simkin-Silverman 2003[167] (WHLP)	30, 42, 54/0, 0, 0	Unselected/low risk	20	IG: 260 CG: 275	Mean (SD) at baseline, mean change (SD) at 30, 42, 54 mo BL 30 mo 42 mo 54 mo IG 24.9 (3.2) **-0.67 (1.8) -0.34 (1.9) 0.05 (2.0)** CG 25.1 (3.3) **0.44 (1.6) 0.67 (1.7) 0.96 (1.8)**	**2.2 vs. 0.6**
Whelton 1998[175] (TONE)	30/0	Hypertension	26	IG: 147 CG: 147	Mean at baseline, mean change at 18, 30 mo BL 30 mo IG -- **-4.7** CG -- **-0.9**	**HR=0.70 for being free of hypertension, its medications, or cardiovascular events**
Stevens 2001[169] (TOHP II)	36/0	Prehypertension	32	IG: 595 CG: 596	Mean (SD) at baseline, mean change (95% CI) at 18 mo BL 36 mo IG 93.4 (14.1) **-0.2 (-0.7 to 0.3)** CG 93.6 (13.5) **1.8 (1.3 to 2.2)**	**0.2 vs. 0.8**
Time lag since intervention completed						
Davis 1992[149] (TAIM)	30/18 (duration=18)	Hypertension	10	IG: 100 CG: 100	**NR (figure shows differences through 30 mo)**	**NR (figure shows differences from 12-30 mo)**
DPP 2005[212]	34/4 (duration=30)	Prediabetes	23	IG: 1079 CG: 1082	Mean (SD) at baseline, mean change at 34 mo BL 34 mo IG 94.1 (20.8) **-5.6** CG 94.3 (20.2) **-0.1**	**2.7 vs. 1.9**
Jeffery 1993[153]	30/12 (duration=18)	Unselected/low risk	27	IG: 41 CG: 40	Mean at baseline, mean change (SD) at 30 mo BL 30 mo IG4* 91.1 -1.6 (6.3) CG 88.2 0.6 (5.3)	NR
Kastarinen 2002[155] (LIHEF)	24/6 (duration=18)	Hypertension	5	IG: 360 CG: 355	Mean (SD) at baseline, mean change at 24 mo BL 24 mo IG 81.1 (15.7) **-1.5** CG 80.0 (14.8) **-0.3**	2 vs. 0.9
Silva 2009[166]	24/12 (duration=12)	Unselected/low risk	30	IG: 123 CG: 116	**NR (% weight lost and % losing 5% and 10% >in IG vs. CG; p<0.05)**	NR
Werkman 2010[174]	24/12 (duration=12)	Unselected/low risk	0 (online only)	IG: 174 CG: 178	Mean (SD) at baseline, mean change (SD) at 24 mo BL 24 mo IG 85.1 (11.9) -0.37 (1.12) CG 86.1 (11.4) -0.40 (1.29)	0.4 increase vs. 0.4 decrease

* Other intervention groups showed similar results.

Table 3. Long-Term Weight Loss and Blood Pressure Outcomes in Behavioral-Based Interventions Beyond 18 Months

Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; BMI=body mass index; CG=control group; CI=confidence interval; DBP=diastolic blood pressure; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HPT=Hypertension Prevention Trial; HR=hazard ratio; IG=intervention group; LIHEF=Lifestyle Intervention Against Hypertension in Eastern Finland; Mo=month; NR=not reported; SBP=systolic blood pressure; SD=standard deviation; SE=standard error; TAIM=Trial of Antihypertensive Interventions and Management; TOHP=Trials of Hypertension Prevention; TONE=Trial of Nonpharmacologic Interventions in the Elderly; WHLP=Women's Healthy Lifestyle Project.

Table 4. Weight Change in Behavioral-Based Weight Maintenance Interventions

Reference	Time since baseline	Time since weight loss intervention ended	Time since maintenance intervention ended	# of maintenance sessions	Baseline weight and weight change (kg)
Cussler 2008[148]	16 mo	12 mo	0 mo	2	Mean (SD) at baseline, mean change (SD) at 16 mo (12 mo since end of weight loss phase) BL 16 mo IG 84.4 (12.6) 0.7 (5.4) CG 82.0 (10.8) 1.0 (4.6)
Perri 1988[164]	24 mo	18 mo	6 mo	26	Mean at baseline, mean change (SD) at 6, 12, 18, and 24 mo BL 6 mo* 12 mo 18 mo 24 mo IG1 97.4 -13.2 (5.4) **-15.8 (11.8)** **-12.9 (12.4)** **-11.4 (12.1)** IG2 96.9 -11.3 (3.1) **-13.5 (6.2)** **-13.4 (7.4)** **-8.4 (7.5)** IG3 95.2 -13.1 (4.8) **-15.2 (6.2)** **-13.0 (7.6)** **-9.1 (6.4)** IG4 97.4 -13.7 (5.9) **-17.8 (11.7)** **-15.7 (14.3)** **-13.5 (15.2)** CG 89.0 -10.8 (7.6) **-8.9 (8.8)** **-5.7 (6.9)** **-3.6 (6.2)**
Svetkey 2008[170] (WLM)†	30 mo	24 mo	0 mo	IG1: 0** IG2: 30	Mean (SD) at baseline and 6 mo, mean change (SE) at 30 mo BL 6 mo* 30 mo IG1 97.2 (16.2) 88.6 (15.4) -3.3 (0.4) IG2 97.1 (17.5) 88.7 (16.9) **-4.2 (0.4)** CG 95.9 (16.2) 87.4 (15.3) **-2.9 (0.4)**

Bold=statistically significant difference between intervention and control groups.

* End of weight loss phase

** IG1 was a Web- and email-based intervention with no face-to-face or phone contact.

† Randomization occurred at the end of the weight loss phase, as apposed to the beginning (such as in Cussler et al and Perri et al).

Abbreviations: BL=baseline; CG=control group; IG=intervention group; mo=month; SD=standard deviation; SE=standard error; WLM= Weight Loss Maintenance.

Table 5. Trials Not Included in Meta-Analysis: Lipids Data in Behavioral Trials, 12- to 18-Month Outcomes

Study	Population risk status (risk group)	# of sessions in first 12 mo	N	Total cholesterol, HDL, LDL, and triglyceride outcomes (mg/dL)
Anderssen 1995[144]	Multiple risk factors	159	IG: 67 CG: 43	IG1(diet only): differs from control for **HDL** but not for total cholesterol or triglycerides IG2 (physical activity only): no group differences IG3 (diet+exercise): differs from control for **HDL and triglycerides** but not for total cholesterol
Woollard 2003[178]	Multiple risk factors	12	IG: 74 CG: 69	Total serum cholesterol, LDL, HDL, and triglycerides: group differences NS at both 12 and 18 mo (data shown in a figure only)
Kastarinen 2002[155] (LIHEF)	Hypertension	5	IG: 360 CG: 355	Mean at baseline (SD), mean change at 12 mo BL 12 mo *Total cholesterol* IG 218.5 (35.1) -1.9 CG 215.8 (35.9) -1.2 *LDL cholesterol* IG 140.5 (31.3) -2.3 CG 3.56 (0.79) -0.4 *HDL cholesterol* IG 51.0 (12.7) 0.8 CG 52.5 (14.7) 0.4 *Triglycerides* IG 138.1 (89.4) -2.7 CG 131.9 (88.5) -5.3
Burke 2005[145]	Hypertension	20	IG: 123 CG: 118	Group differences in LDL at 16 mo but no differences in total cholesterol or HDL at 16 mo (data shown in a figure only)
Narayan 1998[163]	Unselected/low risk	52	IG: 48 CG: 47	Median (range) at baseline, median change at 12 mo BL 12 mo *Total cholesterol* IG 173.7 (81.1-235.5) 7.7 CG 173.7 (123.6-239.4) 3.9 *Triglycerides* IG 123.9 (26.6-318.6) 0.5 CG 115.1 (53.1-123.9) 7.2

Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; HDL=high-density lipoprotein; IG=intervention group; LDL=low-density lipoprotein; Mo=month; NS=not statistically significant; SD=standard deviation.

Table 6. Trials Not Included in Meta-Analysis: Changes in Blood Pressure in Behavioral Trials, 12- to 18-Month Outcomes

Study	Population risk status (risk group)	# of sessions in first 12 mo	N	Blood pressure (mmHg)
Cohen 1991[147]	Hypertension	12	IG: 15 CG: 15	Mean change (SD) in arterial pressure at 12 mo IG 3.0 (14.2) CG -0.7 (11.3) No group difference in number of antihypertension medications
Davis 1992[149]	Hypertension	10	IG: 100 CG: 100	3 of the 4 medication groups showed differences in **DBP** between weight loss and usual care groups at 12 mo (p<0.05); SBP not reported (data shown in figure only)
Jones 1999[154] (HOT)	Hypertension	10	IG: 55 CG: 56	No group differences in % achieving target DBP at any time interval (3-30 mo); no group differences in average change in SBP or DBP
Kastarinen 2002[155] (LIHEF)	Hypertension	5	IG: 360 CG: 355	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Systolic blood pressure* IG 149 (16) -4.7 CG 148 (16) -3.4 *Diastolic blood pressure* IG 91(9) **-4.0** CG 91 (8) **-2.4**
Whelton 1998[175] (TONE)	Hypertension	26	IG: 147 CG: 147	Mean (SD) at baseline, mean change (95% SE) at last visit prior to attempted medication withdrawal (median, 3.2 mo) BL Last visit *Systolic blood pressure* IG 128.6 (10.8) -4.0 (1.3) CG 127.7 (12.1) -0.8 (0.8) *Diastolic blood pressure* IG 70.7 (9.6) -1.1 (0.8) CG 71.5 (8.5) -0.8 (0.5)
Hypertension Prevention Trial Research Group 1990[143]	Prehypertension	16	IG: 125 CG: 126	Mean at baseline, mean change (SE) at 36 mo BL 36 mo *Systolic blood pressure* IG 125.3 **-5.0 (0.9)** CG 124.7 **-2.6 (0.9)** *Diastolic blood pressure* IG 83.0 **-4.2 (0.8)** CG 83.3 **-2.4 (0.8)**
Langford 1985[157]	Prehypertension	18	IG: 52 CG: 31	% not taking antihypertension medication 56 weeks IG **59.5** CG **35.3**
Narayan 1998[163]	Unselected/low risk	52	IG: 48 CG: 47	Median (range) at baseline, median change at 12 mo BL 12 mo *Systolic blood pressure* IG 116 (90-146) 6.0 CG 116 (92-176) 4.1 *Diastolic blood pressure* IG 70 (48-90) 1.1 CG 72 (53-98) -1.0

Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; DBP=diastolic blood pressure; HOT=Hypertension Optimal Treatment; IG=intervention group; LIHEF=Lifestyle Intervention Against Hypertension in Eastern Finland; Mo=month; SBP=systolic blood pressure; SD=standard deviation; SE=standard error; TONE=Trial of Nonpharmacologic Interventions in the Elderly.

Table 7. Diabetes Incidence

Study	# Randomized	Time to followup (mo)	Population risk group	Weight loss (kg)	Diabetes incidence	NNT	Quality rating and issues noted with study
Behavioral							
DPP 2005	IG: 1079 CG: 1082	12, 36	Prediabetes	Mean (SD) at baseline, mean change (SE) at 12 mo BL 12 mo IG 94.1 (20.8) **-6.8 (0.2**) CG 94.3 (20.2) **-0.4 (0.2)**	Diabetes mellitus, crude cumulative incidence (cases/100 person-years) BL 36 mo IG -- 4.8 CG -- 11.0		Good
Tuomilehto 2001	IG: 265 CG: 257	12, 24, 72	Prediabetes	Mean (SD) BMI at baseline (kg/m^2), mean change (SD) at 12, 24 mo BL 12 mo 24 mo IG 31.3 (4.6) **-4.2 (5.1) -3.5 (5.5)** CG 31.0 (4.5) **-0.8 (3.7) 0.8 (4.4)**	n (%) BL 24 mo 72 mo IG -- **15 (5.7) 27(10.2)** CG -- **37 (14.4) 59(23.0)**	8	Good
Parikh 2010	IG: 50 CG: 49	12	Prediabetes	Mean (SD) at baseline, mean change (SD) at 12 mo BL 18 mo IG 79.1 (17.7) **-3.3 (3.3**) CG 73.6 (12.3) **-1.1 (3.7)**	Diabetes mellitus, crude cumulative incidence (cases/100 person-years) BL 12 mo IG -- 36 CG -- 33		Fair; high attrition; no report of blinding outcomes assessment or treatment allocation
Orlistat							
Richelsen 2007[198]	IG: 153 CG: 156	12, 18, 36	Prediabetes Predyslipidemia	Mean (SD) at baseline, mean change at 18 mo -2 mo BL 12 mo 18 mo IG 110.7 (17.9) -14.5 -- -11.7 CG 111.9 (16.0) -14.3 -- -9.6	n (%) BL 36 mo IG -- **8 (5.2)** CG -- **17 (10.9)**	18	Fair; high attrition
Torgerson 2004[202]	IG: 1650 CG: 1655	12, 48	Prediabetes	Mean (SD) at baseline, mean change at 12 mo BL 1 yr 4 yr* IG 110.4 (16.3) **-10.6** -- CG 110.6 (16.5) **-6.2** --	Diabetes mellitus, cumulative incidence (%) BL 4 yr IG 0 **102 (6.2)** CG 0 **149 (9.0)**	35	Fair; high attrition, especially by 48 mo
Metformin							
DPP 2005[212]	IG: 1073 CG: 1082	12, 36	Prediabetes	Mean (SD) at baseline, mean change (SE) at 12 mo BL 12 mo IG 94.3 (19.9) **-2.7 (0.2**) CG 94.3 (20.2) **-0.4 (0.2)**	Diabetes mellitus, crude cumulative incidence (cases/100 person-years) BL 36 mo IG -- 7.8 CG -- 11.0		Good
Fontbonne 1996[185]	IG: 227 CG: 230	12	Unselected/ low risk	Mean change (95% CI) at 12 mo BL 12 mo IG -- -2.0 (-3.0 to -1.1) CG -- -0.8 (-1.6 to 0.1)	# diagnosed with diabetes during course of trial IG: 0 CG: 5		Fair; participants were diagnosed with diabetes by local investigators; lack of central adjustments; high attrition

*Not abstracted due to high attrition.
Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; BMI=body mass index; CG=control group; CI=confidence interval; DPP=Diabetes Prevention Program; IG=intervention group; mo=months; NNT=number needed to treat; SD=standard deviation; SE=standard error.

Table 8. Trials Not Included in Meta-Analysis: Glucose Tolerance in Behavioral Trials, 12- to 18-Month Outcomes

Study	Population risk status (risk group)	# of sessions in first 12 mo	N	Glucose tolerance
Burke 2005[145]	Hypertension	20	IG: 123 CG: 118	No group differences at 16 mo (figure only)
Christian 2008[142]	Diabetes	4	IG: 155 CG: 155	Mean (SD) hemoglobin A_{1C} at baseline and 12 mo (%) BL 12 mo IG 8.08 (2.02) -0.141 (1.76) CG 8.29 (1.93) -0.46 (1.63)
Irwin 2003[152]	Unselected/low risk	128	IG: 87 CG: 86	Mean (95% CI) fasting glucose at baseline and 12 mo (mg/dL) BL 12 mo IG 97.8 (81.4-117.4) 98.9 (81.8-119.5) CG 97.4 (82.5-115.1) 98.4 (83.5-115.9)
Narayan 1998[163]	Unselected/low risk	52	IG: 48 CG: 47	Median (range) fasting glucose at baseline, median change at 12 mo (mg/dL) BL 12 mo IG **97.3 (81.1-117.1)** 1.8 CG **91.9 (75.7-109.9)** 1.8

Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; CI=confidence interval; IG=intervention group; Mo=month; SD=standard deviation.

Table 9. Behavioral Intervention Components

			Study	Estimated # sessions in 12 months	Physical activity sessions	Group sessions	Individual sessions	Technology-based	Primary care provider training	Involved spouse/family	Weight loss goal set	Addressed barriers	Addressed pros/cons or motivation	Active use of self-monitoring	Incentives	Support for weight maintenance
Diabetes, hypertension, or dyslipidemia	US	PC	Christian 2008[146]	4			X	X				X	X			
			Cohen 1991[147]	12			X		X							
			Mayer-Davis 2004[159] (POWER)*	30		X	X				X			X	X	X
		NPC	Jones 1999[154] (HOT)	10		X	X									X
			Davis 1992[149] (TAIM)*	16		X					X					X
			Langford 1985[157] (DISH)*	18		X	X			X	X			X		X
			Whelton 1998[175] (TONE)*	26		X	X				X	X		X		X
	Non-US	PC	Kastarinen 2002[155] (LIHEF)*	5		X	X									
			ter Bogt 2009[171]	5			X	X					X			X
			Woollard 2003[178]	12			X						X			
		NPC	Burke 2005[145] (ADAPT)*	20		X	X			X		X	X			X
			Anderssen 1995[144] (ODES)*	159	X	X	X				X					
Subclinical	US	NPC	Parikh 2010[204] (HEED)	8		X									X	
			HPT 1990[143]*	16		X					X	X	X	X		X
			DPP 2005[212]*	23		X	X				X			X	X	X
			Stevens 1993[168] (TOHP I)*	23		X	X					X		X		X
			Stevens 2001[169] (TOHP II)*	32		X	X			X	X	X	X	X		X
			Villareal 2008[173]*	208	X	X					X	X		X		
	Non-US	NPC	Mensink 2003[160]*	4	X	X	X									
			Tuomilento 2001[172] (FDPS)*	7**	X	X	X			X	X					
			Kulzer 2009[156] (PREDIAS)*	12		X				X		X	X			X
			Mitsui 2008[161]	24	X	X								X		X
Low risk or unselected	US	PC	Martin 2008[158]	6			X		X			X				
		NPC	Wood 1988[176]*	23		X	X									
			Simkin-Silverman 2003 (WHLP)[167]*	20		X	X				X	X		X	X	X
			Wood 1991[177]*	25	X	X								X		X
			Jeffery 1993[153]*	27		X					X			X	X	X
			Narayan 1998[163]	52	X	X										
			Fitzgibbon 2010[200] (ORBIT)	116		X	X				X	X	X	X		X
			Irwin 2003[152] (PATH)*‡	128	X	X	X							X	X	X
	Non-US	PC	Moore 2003[162]	.					X							X
			Pritchard 1999[165]*	8			X							X		
		NPC	Haapala 2009[151]*	0				X			X			X		
			Werkman 2010[174]	0				X								
			Silva 2009[166]*	30		X						X	X	X		X

***** Statistically significant between intervention and control groups for weight loss.
** Indicates an undetermined number of additional physical activity-focused sessions were offered.
‡ Intervention focus was physical activity.

Table 9. Behavioral Intervention Components

Abbreviations: ADAPT= Activity, Diet, and Blood Pressure Trial; DISH=Dietary Intervention to Study Hypertension; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HEED=Help Educate to Eliminate Diabetes; HOT=Hypertension Optimal Treatment; HPT=Hypertension Prevention Trial; LIHEF=Lifestyle Intervention Against Hypertension in Eastern Finland; NPC=non-primary care; ODES=Oslo Diet and Exercise Study; ORBIT=Obesity Reduction Black Intervention Trial; PATH=Physical Activity for Total Health; PC=primary care; POWER=Pounds Off With Empowerment; PREDIAS=Prevention of Diabetes Self-Management Program; TAIM=Trial of Antihypertensive Interventions and Management; TOHP=Trials of Hypertension Prevention; TONE=Trial of Nonpharmacologic Interventions in the Elderly; WHLP=Women's Healthy Lifestyle Project; US=United States.

Table 10. Trials Not Included in Meta-Analysis: Weight Loss in Medication Trials, 12- to 18-Month Outcomes

Study	Population risk status (risk group)	Behavioral intervention intensity	N	Weight loss (kg)
Orlistat trials				
Berne 2004[180]	Diabetes	Intense	IG: 111 CG: 109	Mean (SD) at baseline, % change at 12 mo BL 12 mo IG 95.3 (12.6) **-5.0** CG 95.7 (12.5) **-1.8**
Torgerson 2004[202]	Diabetes	Intense	IG: 1650 CG: 1655	Mean (SD) at baseline, % change at 12 mo BL 12 mo IG 110.4 (16.3) **-10.6** CG 110.6 (16.5) **-6.2**
Richelsen 2007[198]	Prediabetes/ hypertension	Intense	IG: 153 CG: 156	Mean (SD) at baseline, mean change at 18 mo -2 mo* BL 18 mo IG 110.7 (17.9) -14.5 -11.7 CG 111.9 (16.0) -14.3 -9.6
Finer 2000[184]	Unselected/low risk	NR	IG: 114 CG: 114	Mean (SD) at baseline, % change at 12 mo BL 12 mo IG 97.9 (12.9) -3.29 CG 98.4 (15.0) -1.31
Sjostrom 1998[200]	Unselected/low risk	NR	IG: 345 CG: 343	Mean (range) at baseline, mean change at 12 mo BL 12 mo IG 99.1 (61.0-148.6) **-10.3†** CG 99.8 (64.2-137.2) **-6.1**
Maintenance trial				
Hill 1999[190]	Unselected/low risk	Intense	IG: 181 CG: 188	Mean (SE) at -6 mo, mean change (SE) from -6 mo to baseline and 12 mo -6 mo* BL 12 mo IG 89.7 (0.9) -9.86 (0.27) **-7.24 (0.52)** CG 90.8 (0.9) -10.33 (0.31) **-5.93 (0.69)**

*Before a very low calorie diet.
† Change in weight at 12 months is measured from the start of the 4-week run-in period.
Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; IG=intervention group; mo=month; NR=not reported; SD=standard deviation; SE=standard error.

Table 11. Longer-Term Outcomes, Medication Trials

Study	Time to followup (mo)	Weight loss (kg)	Cholesterol (mg/dL)	Blood Pressure (mmHg)	Glucose tolerance
Orlistat					
Richelsen 2007[198]	36	Mean (SD) at baseline, mean change at 36 mo -2 mo 36 mo IG 110.7 (17.9) **-9.4** CG 111.9 (16.0) **-7.2**	Mean (SD) at baseline, mean change at 36 mo -2 mo 36 mo *LDL cholesterol* IG 143.2 (40.2) -13.1 CG 145.6 (36.3) -14.7 *HDL cholesterol* IG 43.6 (10.0) 1.5 CG 44.4 (10.0) 2.3	Mean (SD) at baseline, mean change at 36 mo -2 mo 36 mo *Systolic blood pressure* IG 144 (19.3) -7.8 CG 144 (17.3) -8.2 *Diastolic blood pressure* IG 90.8 (11.6) -3.7 CG 90.7 (10.4) -4.7	Mean (SD) at baseline, mean change at 36 mo -2 mo 36 mo *Hemoglobin A_{1C} (%)* IG 6.32 (0.93) -0.69 CG 6.28 (0.64) -0.51 *Fasting glucose (mg/dL)* IG 116.0 (33.0) -8.8 CG 113.0 (27.8) -5.8
Rossner 2000[199]	24	Mean (SD) at baseline, mean change (SD) from -4 weeks BL 24 mo IG 96.7 (13.8) **-7.4 (7.1)** CG 97.7 (14.6) **-4.3 (7.4)**	Mean (SD) at baseline and 24 mo BL 24 mo *Total cholesterol* IG 203.1 (37.5) **204.2 (37.1)** CG 209.7 (44.0) **221.6 (40.2)** *LDL cholesterol* IG 132.8 (33.2) **134.4 (33.6)** CG 137.1 (37.8) **147.9 (35.1)** *HDL cholesterol* IG 45.2 (11.6) 49.8 (12.4) CG 45.2 (13.9) 51.4 (13.1)	Mean (SD) at baseline and 24 mo BL 24 mo *Systolic blood pressure* IG 125.5 (14.9) 124.9 (16.5) CG 127.3 (16.1) 128.5 (17.5) *Diastolic blood pressure* IG 79.5 (9.4) 79.9 (9.5) CG 81.2 (9.8) 81.2 (9.9)	Mean (SD) at baseline and 24 mo BL 24 mo *Fasting glucose (mg/dL)* IG 98.6 (12.3) 99.3 (23.2) CG 100.2 (17.1) 99.8 (12.3)
Metformin					
DPP 2005[212]	34	Mean (SD) at baseline, mean change at 34 mo BL 34 mo IG 94.3 (19.9) -2.1 CG 94.3 (20.2) -0.1	Mean (SD) at baseline, % change at 36 mo BL 36 mo *LDL cholesterol* IG 123.6 -0.3 CG 123.6 -1.3 *HDL cholesterol* IG -- **-0.008** CG -- **-0.002**	Mean (SD) at baseline, mean change (SE) at 24, 36 mo BL 24 mo 36 mo *Systolic blood pressure* IG 124.0 (14.9) **-0.94 (0.4)** **-0.29 (0.5)** CG 123.5 (14.4) **-0.52 (0.4)** **-0.57 (0.5)** *Diastolic blood pressure* IG 78.2 (9.5) **-1.06 (0.2)** **-1.59 (0.3)** CG 78.0 (9.2) **-1.07 (0.2)** **-1.88 (0.3)**	NR

Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; DPP=Diabetes Prevention Program; HDL=high-density lipoprotein; IG=intervention group; LDL=low-density lipoprotein; mo=month; NR=not reported; SD=standard deviation; SE=standard error.

Table 12. Trials Not Included in Meta-Analysis: Central Adiposity in Orlistat Trials, 12- to 18-Month Outcomes

Study	Population risk status (risk group)	Behavioral intervention intensity	N	Waist circumference (cm)
Broom 2002[181]	Multiple risk factors	NR	IG: 265 CG: 266	Mean (SD) at baseline, mean change (SD) at 12 mo BL 12 mo IG 107.8 (15.6) **-5.99 (--)** CG 108.6 (16.4) **-2.60 (--)**
Lindgarde 2000[194]	Multiple risk factors	Intense	IG: 190 CG: 186	Mean (SD) at -2 weeks, mean change (SD) from -2 weeks at baseline and 12 mo -2 wk* BL 12 mo IG 106 (10.8) -- -4.8 (--) CG 106 (11.0) -- -4.1 (--)
Torgerson 2004[202]	Diabetes	Intense	IG: 1650 CG: 1655	Mean (SD) at baseline, mean change at 12 mo BL 12 mo IG 115.0 (10.4) **-9.6** CG 115.4 (10.4) **-7.0**
Richelsen 2007[198]	Prediabetes/ hypertension	Intense	IG: 153 CG: 156	Mean (SD) at -2 mo, mean change at baseline and 18, 36 mo -2 mo BL 12 mo 18 mo 36 mo IG 119 (12.1) -12 -- -12 **-7.7** CG 119 (10.9) -12 -- -9 **-5.4**
Rossner 2000[199]	Unselected/low risk	Intense	IG: 244 CG: 243	Mean (SD) at baseline, mean change (SD) at 12 mo BL 12 mo IG -- -6.2 CG -- -4.7
Maintenance trial				
Hill 1999[190]	Unselected/low risk	Intense	IG: 181 CG: 188	Reduced in 4 treatment groups during run-in weight loss phase. During 1-year treatment period, waist circumference increased slightly in all groups, and the resulting mean reductions (6 to 8 cm) after 1 year of treatment were not significantly different.

*Before a very low calorie diet.
Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; IG=intervention group; mo=month; NR=not reported; SD=standard deviation.

Table 13. Trials Not Included in Meta-Analysis: Lipids Data in Orlistat Trials, 12- to 18-Month Outcomes

Study	Population risk Status (risk group)	Behavioral intervention intensity	N	Total cholesterol, HDL, LDL, and triglyceride outcomes (mg/dL)
Broom 2002[181]	Multiple risk factors	NR	IG: 265 CG: 266	Mean (SD) at baseline, mean change (SD) at 12 mo BL 12 mo *Total cholesterol* IG 223.9 (42.5) **-4.6 (--)** CG 220.1 (38.6) **6.2 (--)** *HDL cholesterol* IG 54.1 (15.4) -- CG 54.1 (11.6) -- *LDL cholesterol* IG 146.7 (34.7) **-11.6 (--)** CG 146.7 (34.7) **-0.7 (--)** *Triglycerides* IG 159.3 (70.8) 38.9 CG 168.2 (88.5) 15.0
Torgerson 2004[202]	Diabetes	Intense	IG: 1650 CG: 1655	Mean (SD) at baseline, % mean change at 12 mo BL 12 mo *Total cholesterol* IG 223.9 (38.6) **-8.8** CG 223.9 (38.6) **-1.3** *HDL cholesterol* IG 46.3 (11.6) **3.4** CG 46.3 (11.6) **8.5** *LDL cholesterol* IG 142.9 (34.7) **-11.4** CG 146.7 (34.7) **-1.6** *Triglycerides* IG 168.2 (88.5) **-6.2** CG 168.2 (106.2) **-6.3**
Richelsen 2007[198]	Prediabetes/hypertension	Intense	IG: 153 CG: 156	Mean (SD) at -2 mo, mean change at baseline and 18 mo -2 mo* BL 18 mo *Total cholesterol* IG 228.2 (48.6) -46.3 -13.9 CG 232.4 (41.7) -46.3 -5.0 *HDL cholesterol* IG 43.6 (10.1) -1.9 2.3 CG 44.4 (10.0) -2.7 4.2 *LDL cholesterol* IG 143.2 (40.2) -29.0 -11.2 CG 145.6 (36.3) -30.9 -4.6 *Triglycerides* IG 208.9 (109.7) -78.8 -28.3 CG 221.3 (124.8) -83.2 -30.1
Davidson 1999[182]	Unselected/low risk	Intense	IG: 668 CG: 224	IG had greater reductions than CG; p<0.05 for **LDL** and **total cholesterol** (data shown in figure only)

Table 13. Trials Not Included in Meta-Analysis: Lipids Data in Orlistat Trials, 12- to 18-Month Outcomes

Study	Population risk Status (risk group)	Behavioral intervention intensity	N	Total cholesterol, HDL, LDL, and triglyceride outcomes (mg/dL)
Krempf 2003[193]	Unselected/low risk	Intense	IG: 346 CG: 350	Proportion of patients (%) at baseline and 18 mo BL 18 mo *Total cholesterol reduced by ≥20%* IG -- 10.1 CG -- 2.6 *LDL cholesterol reduced by ≥20%* IG -- 19.9 CG -- 6.6

*Before a very low calorie diet.
Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; HDL=high-density lipoprotein; IG=intervention group; LDL=low-density lipoprotein; mo=month; NR=not reported; SD=standard deviation.

Table 14. Trials Not Included in Meta-Analysis: Changes in Blood Pressure in Orlistat Trials, 12- to 18-Month Outcomes

Study	Population risk status (risk group)	Behavioral intervention intensity	N	Blood pressure (mmHg)
Broom, 2002[181]	Multiple risk factors	NR	IG: 265 CG: 266	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Systolic blood pressure* IG 141.1 (15.0) **-6.0** CG 139.2 (15.7) **-2.3** *Diastolic blood pressure* IG 89.0 (9.7) **-5.5** CG 88.1 (10.1) **-3.1**
Berne 2004[180]	Diabetes	Intense	IG: 111 CG: 109	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Systolic blood pressure* IG 145.0 (18.2) -3.2 CG 145.0 (16.1) -3.1 *Diastolic blood pressure* IG 84.5 (9.7) -2.4 CG 84.3 (10.0) -1.9
Hanefeld 2002[187]	Diabetes	Intense	IG: 195 CG: 188	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Systolic blood pressure* IG 148.0 (20.4) -4.96 CG 147.9 (17.8) -4.98 *Diastolic blood pressure* IG 87.0 (10.8) -4.78 CG 87.2 (10.7) -4.80
Richelsen 2007[198]	Prediabetes/ hypertension	Intense	IG: 153 CG: 156	Mean (SD) at baseline, mean change at 18 mo -2 mo* BL 18 mo *Systolic blood pressure* IG 144 (19.3) -13 -8.2 CG 144 (17.3) -12 -7.2 *Diastolic blood pressure* IG 90.8 (11.6) -7.2 -5.1 CG 90.7 (10.4) -7.6 -4.8
Torgerson 2004[202]	Prediabetes	Intense	IG: 1650 CG: 1655	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Systolic blood pressure* IG 130.8 (15.8) -7.3 CG 130.4 (15.4) -5.2 *Diastolic blood pressure* IG 82.0 (10.0) -3.6 CG 82.3 (10.0) -2.6

*Before a very low calorie diet.
Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; IG=intervention group; mo=month; NR=not reported; SD=standard deviation.

Table 15. Trials Not Included in Meta-Analysis: Changes in Glucose Tolerance in Medication Trials, 12- to 18-Month Outcomes

Study	Population risk Status (risk group)	Behavioral intervention intensity	N	Glucose tolerance
Orlistat trials				
Broom 2002[181]	Multiple risk factors	NR	IG: 265 CG: 266	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Fasting glucose (mg/dL)* IG -- **-3.4** CG -- **1.1**
Berne 2004[180]	Diabetes	Intense	IG: 111 CG: 109	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Fasting glucose (mg/dL)* IG 201.8 (46.9) **-34.2** CG 196.4 (45.1) **-4.7**
Richelsen 2007[198]	Prediabetes/ hypertension	Intense	IG: 153 CG: 156	Mean (SD) at baseline, mean change at 18 mo -2 mo* BL 18 mo *Fasting glucose (mg/dL)* **IG** 116.0 (33.0) -19.8 -12.1 **CG** 113.0 (27.8) -17.1 -8.1
Torgerson 2004[202]	Prediabetes	Intense	IG: 1650 CG: 1655	Mean (SD) at baseline, mean change at 12 mo BL 12 mo *Fasting glucose (mg/dL)* IG 82.9 (10.8) **1.8** CG 82.9 (10.8) **3.6**
Maintenance trial				
Hill 1999[190]	Unselected/low risk	Intense	IG: 181 CG: 188	Fasting glucose levels decreased slightly (0.4-1.8 mg/dL) in all groups during the 6-mo run-in period. After 12 mo of treatment, mean increases of 1%-2% above initial values were noted in the CG compared with slight (~1%) reductions in IG, but were not statistically significant.

*Before a very low calorie diet.

Bold=statistically significant difference between intervention and control groups.

Abbreviations: BL=baseline; CG=control group; IG=intervention group; mo=month; NR=not reported; SD=standard deviation.

Table 16. Harms Data Summary for Medication Interventions

Risk group	Reference; Medication type; Type of study	# Randomized	Average age (yrs)	% Female	% Nonwhite	Baseline BMI (kg/m^2) Mean, minimum	Dosage (mg)	Duration (wks)
With cardiovascular risk factors								
Diabetes	Berne 2005[180]; Orlistat; RCT	220	59.1	45.5	0	32.7 ≥28	120 tid	52
	Derosa 2010[215]; Orlistat; RCT	254	52.5	49.6	0	32.8 ≥30	120 tid	52
	Hanefeld 2002[187]; Orlistat; RCT	383	56.2	50.9	NR	34.1 ≥28	120 tid	48
	Hollander 1998[191]; Orlistat; RCT	322	55.1	48.9	12.5	34.3 ≥28	120 tid	52
	Kelley 2002[127]†; Orlistat; RCT	550	57.9	56	28	35.7 ≥28	120 tid	52
	Miles 2002[197]; Orlistat; RCT	516	53.1	48.0	18	NR ≥28	120 tid	52
Hypertension	Bakris 2002[126]†; Orlistat; RCT	554	52.8	61.1	14.5	35.6 ≥28	120 tid	52
Dyslipidemia	Broom 2002[132]†; Orlistat; RCT	142	51.6	60.5	NR	36.8 ≥30	120 tid	24
	Derosa 2003[183]; Orlistat; RCT	50	52.0	52.0	NR	31.9 >30	120 tid	52
	Muls 2001[130]†; Orlistat; RCT	294	48.6	80.7	NR	32.9 ≥27	120 tid	48
Multiple risk factors	Broom 2002[132] (UK Multimorbidity Study); Orlistat; RCT	531	46.0	78.4	NR	37.0 ≥28	120 tid	52
	Lindgarde 2000[194] (Swedish Multimorbidity Study); Orlistat; RCT	376	53.5	63.6	NR	33.2 ≥28	120 tid	52
	Swinburn 2005[201]; Orlistat; RCT	339	52.2	56.9	NR	37.8 ≥30	120 tid	52
Total trials (n) in subgroup: 12 (4,277)								
With subclinical increase in cardiovascular risk or risk factors								
Prediabetes	DPP 2005[142]; Metformin; RCT	2155	50.6	67.7	45.3	34.1 ≥24	850 bid	208
	Torgerson 2004[202] (XENDOS); Orlistat; RCT	3305	43.3	55.2	NR	37.4 ≥30	120 tid	208
Multiple risk factors	Richelsen 2007[198]; Orlistat; RCT	309	47.0	50.8	NR	37.5 ≥30	120 tid	156
Total trials (n) in subgroup: 3 (5,769)								
Without cardiovascular risk factors								
	Acharya 2006[133]†; Orlistat; Observational cohort	NR	45	80.1	NR	NR NR	120 tid	21
	Davidson 1999[182]; Orlistat; RCT	892	43.5	84.2	19.2	36.3 ≥30	120 tid	52
	Finer 2000[184]; Orlistat; RCT	228	41.5	88.5	5.1	36.8 ≥30	120 tid	52
	Fontbonne 1996[185] (BIGPRO); Metformin; RCT	457	49.5	66.7	NR	33.1 None (high WHR)	850 bid	52
	Gambineri 2006[186]; Metformin; RCT	40	27.0	100	NR	36.0 ≥28	850 bid	52

Table 16. Harms Data Summary for Medication Interventions

Risk group	Reference; Medication type; Type of study	# Randomized	Average age (yrs)	% Female	% Nonwhite	Baseline BMI (kg/m^2) Mean, minimum	Dosage (mg)	Duration (wks)
	Gokcel 2002[136]†; Metformin and orlistat; RCT	150	42.7	100	NR	37.2 >30	Sibutramine: 10 bid Orlistat:120 tid Metformin: 850 bid	26
	Hauptman 2000[189]; Orlistat; RCT	422	42.5	78.3	9.1	36.1 ≥30	120 tid	104
	Hill 1999[190]; Orlistat; RCT	369	46.3	84.0	11.7	32.8 ≥28	120 tid	52
	Krempf 2003[193]; Orlistat; RCT	696	41.0	86.4	NR	36.1 ≥28	120 tid	78
	Rossner 2000[199]; Orlistat; RCT	487	44.2	82.3	NR	35.0 ≥28	120 tid	104
	Sjostrom 1998[200]; Orlistat; RCT	688	44.8	83.0	NR	36.0 ≥28	120 tid	52
	Trolle 2007[131]†; Metformin; RCT	60	32	100	NR	33.8 NR	850 bid	26
	Van Gaal 1998[129]†; Orlistat; RCT	247	41.8	76.6	NR	34.6 ≥28	120 tid	24
Total trials (n) in subgroup: 13 (4,736)								
Total trials (n): 28 (14,782)								

† Trials included for key question 4 only.

Abbreviations: bid=twice a day; BIGPRO=Biguanides and Prevention of Risks in Obesity; BMI=body mass index; DPP=Diabetes Prevention Program; NR=not reported; RCT=randomized, controlled trial; tid=three times a day; UK=United Kingdom; WHR=waist-to-hip ratio; XENDOS=Xenical in the Prevention of Diabetes in Obese Subjects.

Table 17. Summary of Medication Harms

Adverse events	N Trials (meta-analysis, other)	Meta-analysis results RR (95% CI)	Weighted means	Results from studies not in meta-analysis	Dosage effects	Subgroup analysis	Comments
Orlistat							
Withdrawals due to adverse events	23, 0	1.67 (1.32- 2.13)	IG: 8% CG: 4%	--	3 of 4 studies present no difference; 1 study had slightly higher withdrawal rate with 120 mg (but no statistical testing)	Trials of unselected populations: RR, 2.2 (95% CI,1.6-3.0) Trials of those with CV risk: RR, 1.43 (95% CI, 0.99-2.06)	Gastrointestinal symptoms were main reason for withdrawal
Any	8, 0	1.10 (1.03-1.17)	IG: 78% CG: 70%	--	NR	--	Gastrointestinal symptoms were main reason for withdrawal
Serious	11, 2	1.21 (0.88-1.68)	IG: 10% CG: 9%	No serious adverse events in either treatment group in 2 trials	NR	Trials of unselected populations: RR, 2.0 (95% CI, 0.9-4.5) Trials of those with CV risk: RR, 1.1 (95% CI, 0.6-2.0)	Fecal incontinence, diverticulitis, abdominal pain
Gastrointestinal	18, 0	1.42 (1.33-1.52)	IG: 83% CG: 59%	--	3 of 3 studies did not report statistically high gastrointestinal adverse events with higher dose; 1 had slightly higher rate but was not labeled as statistically significant	--	Mild to moderate intensity and often resolved spontaneously
Hypoglycemia	0, 3	--	--	2 of 3 studies found increased incidence of hypoglycemia with orlistat	NR	NR	--
Bone mineral density	0, 1	--	--	In small subsample (N=30) of larger study, bone density did not differ between groups	--	--	--
Vitamin deficiency	0, 5	--	--	5 of 5 studies found lower vitamin E with orlistat; 4 of 4 studies found lower beta-carotene; 1 of 2 trials found lower vitamin A; 1 of 1 study found lower vitamin K; 5 of 5 studies found orlistat participants required more vitamin supplementation during the study	2 of 2 studies showed no clear relation to dose, although not clear if tested statistically	NR	--
Liver injury	0, 1 (event monitoring cohort)	--	--	UK monitoring study reported elevated liver tests in 2 cases; no cases of serious hepatic adverse reactions	NR	NR	FDA recently added warning to label about risk of severe liver disease with orlistat
Metformin							
Withdrawals	2, 0	3.92 (1.23-12.57)	IG: 5% CG: 1%	--	--	--	--
Any	2, 0	4.83 (0.84-27.63)	IG: 46% CG: 16%	--	--	--	--
Serious	0	--	--	--	--	--	--

Table 17. Summary of Medication Harms

Adverse events	N Trials (meta-analysis, other)	Meta-analysis results RR (95% CI)	Weighted means	Results from studies not in meta-analysis	Dosage effects	Subgroup analysis	Comments
Gastrointestinal	1, 3	--	--	Increased risk of gastrointestinal adverse events in metformin group	All same dosage	Not different by age	Main gastrointestinal symptoms included diarrhea, flatulence, nausea, vomiting
Hypoglycemia	0	--	--	--	--	--	--
Bone density	0	--	--	--	--	--	--

Abbreviations: CG=control group; CI=confidence interval; CV=cardiovascular; FDA=U.S. Food and Drug Administration; IG=intervention group; NR=not reported; RR=relative risk; UK=United Kingdom.

Table 18. Summary of Evidence

# of Studies	Design	Major limitations	Consistency	Applicability	Overall quality	Summary of findings
KQ1. Is there direct evidence that primary care screening programs for adult obesity improve health outcomes or result in short-term (12-18 months) or sustained (>18 months) weight loss or improved physiological measures?						
0 screening trials	RCT	No data	N/A	N/A	N/A	N/A
KQ1a. How well is weight loss maintained after an intervention is completed?						
0 screening trials	RCT	No data	N/A	N/A	N/A	N/A
KQ2. Do primary care–relevant interventions (behavioral-based interventions and/or pharmacotherapy) in obese or overweight adults lead to improved health outcomes?						
Behavioral-based interventions						
Death (M): 2 Cardiovascular disease (CVD): 4 Hospitalization (H): 1 Type 2 diabetes (DM): 3 HRQL/depression (Q): 3	RCT	M: Very low event rate; sparsely reported CVD, H: Low event rates, sparsely reported DM: Sparsely reported Q: Sparsely reported	M: High CVD: High H: N/A DM: High Q: High	M: Low–Moderate; US, self-identified non-primary care samples CVD: Moderate; 2 conducted in US (not primary care) in self-identified samples. 2 conducted in study-identified samples in primary care outside US H: Low–Moderate; US, self-identified non-primary care samples DM: Moderate; conducted in US (not primary care) in self-identified samples. 2 conducted in study-identified samples outside US Q: Low–Moderate; 2 in US, self-identified samples; 1 nonUS recruitment sample NR	M: Good CVD: Fair–Good DM: Fair–Good Q: Fair	M: No differences in death rate, but small number of deaths limits conclusions. CVD: No differences in CVD events, deaths, or CVD-related deaths at 2.5, 3, and 10 years in 3 large, good-quality trials. Additional fair-quality trial showed no difference in % taking cardiovascular medication at 1 year. H: No differences in hospitalization, but low hospitalization rate limits conclusions. DM: In DPP, twice as many in control group than lifestyle intervention group developed diabetes at 3 years (28.9% vs. 14.4%; NNT=7); similar results in similar Finnish trial, but no DM reduction in small trial with very high base rates of elevated fasting glucose. Q: None of 3 trials found group differences in depression outcomes (% screening depressed, depressive symptomatology); small change in HRQL correlated with weight change in DPP.
Pharmacotherapy						
Orlistat Death (M): 4 Type 2 diabetes (DM): 2 HRQL/depression (Q): 2	RCT	M: Very low event rate; sparsely reported DM: Sparsely reported, high attrition Q: Sparsely reported; nonstandard quality of life measure in 1 study	M: High DM: High Q: N/A	M: Moderate; all conducted in primary care setting; 1 in US DM: Low; nonUS, not primary care; 1 trial required 5% weight loss during run-in phase Q: Low; nonUS setting with no connections to primary care	Fair	M: Each study only had 1 death; in all studies deaths were in orlistat group, but no clear relationship with treatment. DM: Both trials reported low incidence of diabetes, by 9-10 percentage points. Q: No difference in depression scores. Orlistat group had greater satisfaction with treatment and less overweight distress. 1 of 8 (vitality) subscales of SF-36 improved with orlistat.

Table 18. Summary of Evidence

# of Studies	Design	Major limitations	Consistency	Applicability	Overall quality	Summary of findings
Metformin Death (M): 2 Hospitalization (H): 1 Cardiovascular disease (CVD): 2 Type 2 diabetes (DM): 2 HRQL/depression (Q): 1	RCT	M: Very low event rate; sparsely reported H: Sparsely reported CVD: Sparsely reported DM: Sparsely reported Q: Sparsely reported	M: High H: N/A CVD: High DM: High Q: N/A	M, CVD, DM: Low–Moderate; 1 conducted in self-identified samples, no connection to primary care; 1 study in Europe with no connection to primary care H, Q: Low–Moderate; US, self-identified sample, no connection to primary care	Fair–Good	M: No difference between groups, but small number of deaths limits conclusions. H: No difference in hospitalization. CVD: No difference in CVD events. DM: Incidence of diabetes was reduced in good-quality trial in prediabetics after 3 years (21.7% vs. 28.9%; NNT=14). Smaller trial with unclear adjudication also found decreased risk of diabetes in those randomized to metformin. Q: No difference in depression.
KQ2a. What are common elements of efficacious interventions?						
Behavioral-based interventions						
N/A	N/A	N/A	N/A	N/A	N/A	Insufficient data to examine.
KQ2b. Are there differences in efficacy between patient subgroups?						
Behavioral-based interventions						
Death, hospitalization (M, H): 1 Type 2 diabetes (DM): 1 HRQL/depression (Q): 2	RCT	M, H: Sparsely reported; not powered to look for subgroup effects DM: Sparsely reported; not powered to look for subgroup effects Q: Sparsely reported	M, H, DM: N/A Q: High	All: Moderate; both conducted in US, not in primary care, in self-identified samples	M, H, DM: Good Q: Fair–Good	M, H: DPP found no treatment-by-age interactions in hospitalizations or deaths. DM: DPP found that diabetes incidence decreased in the older age groups in the behavioral intervention group; there was no difference in incidence in age groups in the placebo group. Intervention had greater effects among persons with lower baseline glucose concentrations after a 2-hour glucose load. Q: Neither trial found that treatment affected depression, nor did either report that men and women differed in their response to treatment.
Pharmacotherapy						
Orlistat: 0	N/A	N/A	N/A	N/A	N/A	No studies examined health outcomes by subgroups and subgroup analyses could not be conducted.
Metformin Death, hospitalization (M, H): 1 Type 2 diabetes (DM): 1 HRQL/depression (Q): 1	RCT	M, H: Sparsely reported; not powered to look for subgroup effects DM: Sparsely reported; not powered to look for subgroup effects Q: Sparsely reported	All: N/A	All: Moderate; one in US, neither in primary care, both in self-identified samples	M, H, Q: Good DM: Good–Fair	M, H: DPP found no treatment-by-age interactions in hospitalizations or deaths. DM: DPP found that diabetes incidence was lower in younger age groups in metformin intervention group; there was no difference in incidence in age groups in placebo group. The effect of metformin was less in those with a lower BMI or lower fasting glucose. Treatment effects did not differ according to sex or ethnicity. Q: DPP did not find that treatment affected depression, nor did it report that men and women differed in their response to treatment.

Table 18. Summary of Evidence

# of Studies	Design	Major limitations	Consistency	Applicability	Overall quality	Summary of findings
KQ3. Do primary care–relevant interventions (behavioral-based interventions and/or pharmacotherapy) in obese or overweight adults lead to short-term or sustained weight loss, with or without improved physiological measures?						
Behavioral-based interventions						
Weight loss (W): 38 Adiposity (A): 14 Lipids (L): 16 Blood pressure (BP): 22 Glucose tolerance (GT): 12 (7 in populations selected for impaired glucose tolerance or diabetes)	RCT	All: High variability in design, setting population, and statistical heterogeneity in outcomes Lipids and glucose tolerance somewhat sparsely reported and subject to reporting bias.	All: Moderate	All: Moderate; two thirds conducted in US, but only 4 in US primary care, most in self-identified samples.	All: Fair–Good	W: Average of 3.0 kg more weight lost in intervention than control groups, ranging from no effect to 8.3 kg greater weight loss in intervention group. Group differences remain in long term, especially for higher-intensity interventions. A: Waist circumference reduced by average of 2.7 cm more in intervention than control groups. L: Little evidence that behavioral treatment improves lipids. Meta-analysis results likely overestimate lipid changes. BP: Average of 2.5/1.9 mmHg greater reduction in blood pressure in intervention than control groups. Reductions frequently maintained beyond 18 months with continued support. Risk of hypertension reduced with behavioral treatment in those with prehypertension; NNT for hypertension was 14 in large, good-quality trial. GT: Average of 5.3 mg/dL greater decline in fasting glucose in intervention than control groups in trials targeting patients with diabetes or impaired glucose tolerance. Little evidence that behavioral treatment improves glucose in other populations, where meta-analysis results likely overestimate glucose changes.
Pharmacotherapy						
Orlistat Weight loss (W): 18 Adiposity (A): 12 Lipids (L): 18 Blood pressure (BP): 14 Glucose tolerance (GT): 14	RCT	All: Most had high attrition; slightly over 60% of trials required successful run-in phase BP: Half could not be included in meta-analysis of SBP, and more than half (8 of 14) could not be included in meta-analysis of DBP	W: Moderate A: Moderate L: Moderate–High BP: Moderate GT: Low–Moderate	All: Low; only 5 conducted in US, only 1 in US primary care, almost all self-identified samples, most trials with run-in phase lost 10-20% of participants before randomization	All: Fair (17) –Good (1)	W: Average of 3.0 kg more weight lost in orlistat than placebo groups. Both groups also received behavioral interventions that were more intensive than would be typically found in primary care. Relative risk of losing 5% or more of initial weight was 1.57 (NNT=5). A: Waist circumference reduced by average of 2.3 cm more among those taking orlistat than those taking placebo. L: Orlistat was associated with greater average declines in total cholesterol (12.6 mg/dL) and LDL (11.4 mg/dL), but also with greater declines in HDL (0.9 mg/dL). BP: Small (2.0/1.3 mm Hg) or no greater reduction in blood pressure in those taking orlistat than those taking placebo. GT: Average of 5.7 mg/dL greater decrease in fasting glucose in those taking orlistat than those taking placebo, larger effects in studies of those with type 2 diabetes.

Table 18. Summary of Evidence

# of Studies	Design	Major limitations	Consistency	Applicability	Overall quality	Summary of findings
Metformin Weight loss (W): 3 Adiposity (A): 2 Lipids (L): 3 Blood pressure (BP): 2 Glucose tolerance (GT): 3	RCT	Few trials total, with very different populations	All: Low–Moderate	All: Low (for general US primary care) Moderate (for patients at risk of diabetes); only 1 conducted in US, all involved selected samples, none conducted in primary care	All: Fair–Good	W: The good-quality trial of patients with prediabetes showed the largest effects (2.3 kg statistically greater weight loss with metformin), and included only a brief behavioral intervention. A trial of those with high WHR found that those on metformin lost a nonsignificant 1.2 kg more than those on placebo. A small trial of those with PCOS found no difference in weight loss between metformin and placebo. A: In DPP, waist circumference declined by an average of 1.5 cm more in those taking metformin than those taking placebo. A very small trial in women with PCOS did not find a significant difference. L: Metformin did not have favorable effects on total cholesterol, HDL, LDL, or triglycerides. Long-term metformin in DPP had favorable but small (<1mg/dL) effects on HDL. BP: Metformin did not improve blood pressure. GT: In DPP, metformin led to greater reductions in fasting glucose (4.2 mg/dL) compared with placebo (0.6 mg/dL). 2 smaller studies did not find effects of metformin on glucose measures.
KQ3a. How well is weight loss maintained after an intervention is completed?						
Behavioral-based interventions						
Maintenance trials (M): 3 Followup 4+ months after treatment ended (F): 6	RCT	M: Few trials F: Few trials, very heterogeneous in terms of study design, outcomes reported, quality, and intensity of interventions.	M: Fair F: Low	M: Moderate; all 3 set in US, using self-identified samples, not connected to primary care F: Low; half conducted in US with self-identified participants and no connection to primary care; only 1 of nonUS trials in primary care	M: Fair–Good F: Fair–Good	M: Interventions involving 26 or more sessions over 18-24 months improved weight maintenance after weight loss, but no group differences were seen in less intensive programs. Only one of the more intensive trials had a period of at least 6 months of no contact at the end of the maintenance intervention; the others measured outcomes at the end of the maintenance intervention. F: 4 of 6 trials showed continued benefit 4-18 months after treatment ended; intensity of these programs ranged from 5 to 30 contacts.
Pharmacotherapy						
Orlistat Maintenance trials (M): 1 Followup 4+ months after treatment ended (F): 0	RCT	M: Few trials	M: N/A	M: Low; maintenance after a very low calorie diet	M: Fair	M: Those randomized to 120 mg tid of orlistat regained less weight than those randomized to placebo. 60 mg tid of orlistat was not as effective. F: No trials examined maintenance of weight loss after treatment with orlistat had ended.
Metformin: 0	RCT	N/A	N/A	N/A	N/A	No trials examined maintenance of weight loss after treatment with metformin had ended.

Table 18. Summary of Evidence

# of Studies	Design	Major limitations	Consistency	Applicability	Overall quality	Summary of findings
KQ3b. What are common elements of efficacious interventions?						
Behavioral-based interventions						
38	RCT	Variability in intervention details reported; most trials were efficacious; many sources of variability besides treatment components that may influence effect size	N/A	All: Moderate; two thirds conducted in US, but only 4 in US primary care; most in self-identified samples.	All: Fair–Good	Number of sessions in first year was the only element consistently related to effect size. No association was found for physical activity sessions, group sessions, individual sessions, technology-based intervention, specific weight loss goals, spouse or family involvement, addressing barriers to weight loss, motivational assessment (i.e., pros and cons of weight loss), self-monitoring, incentives for weight loss or participation, or support after active intervention phase.
KQ3c. Are there differences in efficacy between patient subgroups?						
Behavioral-based interventions						
Age (A): 5 Sex (S): 8 Race (R): 6 Baseline BMI (B): 4 CV risk status (CVRS): 38	RCT	All: Sparsely reported, trials often not powered for subgroup effects CVRS: Individual trials did not perform subgroup analysis; results summarized here are comparisons of results from studies of participants with CVRS with studies of unselected or low-risk participants	A: Moderate S: Low–Moderate R: Low–Moderate B: Moderate CVRS: Moderate	All: Moderate	All except CVRS: Good (most trials reporting subgroup analyses rated good-quality) CVRS: Fair–Good	A: Good-quality trials found larger improvements in weight, waist circumference, and incident diabetes in older participants; 3 found no age effects on weight. S: Men lost more weight than women in 4 of 5 trials testing effect of sex, but other variables eliminated this effect in 2 trials. No to minimal differences in other intermediate outcomes of blood pressure and lipids. R: Black participants lost less weight than nonblacks in 3 of 4 trials testing effect of race; mixed results for incident hypertension in 2 trials. B: Baseline BMI predicted weight loss in only 1 of 4 trials at 12 months or beyond. CVRS: Weight loss did not vary by CV risk status; effect on glucose appears larger in trials of participants with diabetes or prediabetes; no apparent effect of CV risk status on other intermediate health outcomes.
Pharmacotherapy						
Orlistat Age (A), Sex (S), Race (R), Baseline BMI (B): 0 CV risk status (CVRS): 18	RCT	CVRS: Individual trials did not perform subgroup analysis; results summarized here are comparisons of results from studies of participants with CVRS with studies of unselected or low-risk participants	CVRS: Moderate–High	All: Low; only 5 conducted in US, only 1 in US primary care; almost all self-identified samples; most trials with run-in phase lost 10-20% of participants before randomization	CVRS: Fair (17)–Good (1)	A, S, R, B: No trials examined effects of age, sex, race, or baseline BMI. CVRS: Weight loss did not vary by CV risk status. Greater improvements in glucose seen in trials of patients with diabetes.
Metformin Age (A), Race (R), Sex (S): 1	RCT	A, R, S: Not powered for subgroup effects.	A, R, S: N/A	All: Low–Moderate; US, self-identified sample, no connection to primary care	All: Good	A: Weight loss and waist circumference reductions greatest in oldest age group (ages 60-85 years). R, S: Treatment effects did not differ by sex or race.

Table 18. Summary of Evidence

# of Studies	Design	Major limitations	Consistency	Applicability	Overall quality	Summary of findings
KQ4. What are the adverse effects of primary care–relevant interventions in obese or overweight adults?						
Behavioral-based interventions						
Bone mineral density (BMD): 4 Serious adverse event (SAE): 2 Serious injury (SI): 2 Mild musculoskeletal injury (MI): 1 Eating disorder (ED): 1	RCT	Fair studies: High attrition and/or small numbers of participants or followup of less than 1 year	BMD: Low–Moderate SAE: High SI: High MI: N/A Eating disorder: N/A	All: Moderate; most conducted in US	All: Good–Fair	BMD: 3 of 4 studies noted a decrease in total or hip bone density with weight loss. SAE: No serious adverse events reported in any treatment group. SI: No serious injuries reported in any treatment group. MI: Increase in mild musculoskeletal injuries with supervised exercise program, but did not affect daily activities or work attendance. ED: 1 study showed improvement, not worsening, of eating disorder symptoms with behavioral weight loss treatment.
Pharmacotherapy						
Orlistat Withdrawals (W): 23 Any adverse event (AE): 8 Serious adverse event (SAE): 13 Bone mineral density (BMD): 1 Vitamin deficiency (V): 5 Liver injury (L): 1	RCT (23) Event monitoring (1)	RCT: Most had high attrition; many had run-in phase with required compliance and/or weight loss requirement Event monitoring: Retrospective reporting and low response rate	W: Moderate AE: Moderate SAE: Moderate BMD: N/A V: Moderate L: N/A	All: Low; few conducted in US, even fewer in US primary care; almost all self-identified samples; most trials with run-in phase lost 10-20% of participants before randomization	All: Fair	W: More withdrawals in orlistat group than placebo; primarily due to gastrointestinal side effects of orlistat. AE: More adverse events in orlistat group than placebo; primarily due to gastrointestinal side effects of orlistat. SAE: No increase in serious adverse events in orlistat group. BMD: Data insufficient. V: Orlistat most closely associated with lower vitamin E and beta-carotene. Some evidence for lower vitamin A and K. Orlistat participants required more vitamin supplementation during the study. L: UK monitoring study reported elevated liver tests in 2 cases; no cases of serious hepatic adverse reactions.
Metformin Withdrawals (W): 2 Total adverse events (AE): 2 Serious adverse events (SAE): 0 Bone mineral density (BMD): 0	RCT	High attrition or small number of participants	W: High AE: Moderate SAE: N/A BMD: N/A	All: Low (for general US primary care) Moderate (for patients at risk of diabetes); only 1 conducted in US, all involved selected samples, none conducted in primary care	All: Fair	W: More withdrawals in metformin group than placebo; primarily due to gastrointestinal side effects of metformin. AE: More adverse events in metformin group than placebo; primarily due to gastrointestinal side effects of metformin. SAE: No data. BMD: No data.

Table 18. Summary of Evidence

# of Studies	Design	Major limitations	Consistency	Applicability	Overall quality	Summary of findings
KQ4c. Are there differences in efficacy between patient subgroups?						
Behavioral-based interventions						
0 trials examined subgroups	RCT	No data	N/A	N/A	N/A	
Pharmacotherapy						
Orlistat CV risk status (CVRS): 23	RCT	Individual trials did not perform subgroup analysis; results summarized here are comparisons of results from studies of participants with CVRS with studies of unselected or low-risk participants	Fair	Low; few conducted in US, even fewer in US primary care; almost all self-identified samples; most trials with run-in phase lost 10-20% of participants before randomization	Fair–Good	Those with CV risk factors were less likely to withdraw due to adverse events or to experience serious adverse events compared with those who were unselected for CV risk factor/at low risk.
Metformin Gastrointestinal adverse events (GI): 1	RCT	Not powered to examine subgroup effects	N/A	Low–Moderate; US, self-identified nonprimary care samples	Good	GI: Did not differ by age.

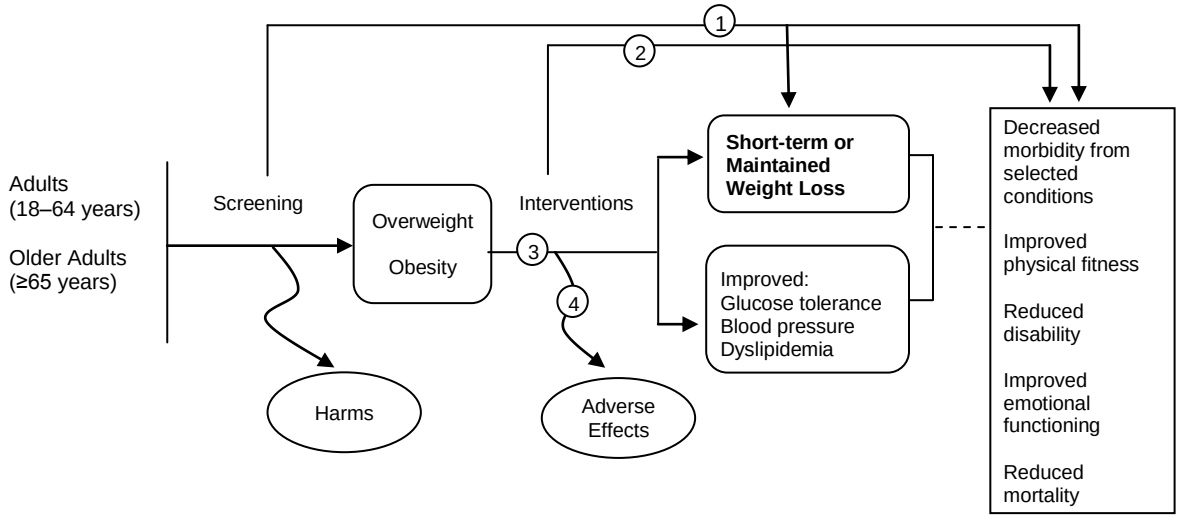
Abbreviations: BMI=body mass index; CV=cardiovascular; DBP=diastolic blood pressure; DPP=Diabetes Prevention Program; HDL=high-density lipoprotein; HRQL=health-related quality of life; KQ=key question; LDL=low-density lipoprotein; N/A=not applicable; NNT=number needed to treat; NR=not reported; PCOS=polycystic ovary syndrome; RCT=randomized, controlled trial; SF-36=36-item Short-form Health Survey; SBP=systolic blood pressure; tid=three times a day; UK=United Kingdom; US=United States; WHR=waist-to-hip ratio.

Table 19. Interquartile Range* of Weight Change in Intervention and Control/Placebo Groups

Type of trial	No or minimal treatment (+ placebo for medication trials)	Behavioral treatment** (+ placebo for medication trials)	No or minimal treatment + medication	Behavioral treatment** + medication
Behavioral	+0.5 to -0.9 kg (27 trials)	*0-11 sessions:* -1.5 to -4.2 kg (10 trials) *12-26 sessions:* -3.8 to -6.8 kg (11 trials)	(--)	(--)
Orlistat	(--)	-3.3 to -6.4 kg (12 trials)	(--)	-5.6 to -9.5 kg (12 trials)
Metformin	-0.4 to -0.8 (2 trials)	-5 kg (1 trial)	-2.0 to -2.7 kg (2 trials)	-4 kg (1 trial)

* Full range provided if fewer than four trials.
** Behavioral treatment in medication trials rated as “intense” (i.e., more than could be expected in usual care).

Figure 1. Analytic Framework: Primary Care Screening and Interventions for Obesity and Overweight in Adults



Key Questions

Key Question 1. Is there direct evidence that primary care screening programs for adult obesity or overweight improve health outcomes or result in short-term (12 months) or sustained (>12 months) weight loss or improved physiological measures (i.e., glucose tolerance, blood pressure, or dyslipidemia)?

1a. How well is weight loss maintained after an intervention is completed?

Key Question 2. Do primary care–relevant interventions (behavioral-based interventions and/or pharmacotherapy) in obese or overweight adults lead to improved health outcomes?

2a. What are common elements of efficacious interventions?

2b. Are there differences in efficacy between patient subgroups (i.e., ages 65 years or older, sex, race/ethnicity, degree of obesity, or baseline cardiovascular risk status)?

Key Question 3. Do primary care–relevant interventions in obese or overweight adults lead to short-term or sustained weight loss, with or without improved physiological measures?

3a. How well is weight loss maintained after an intervention is completed?

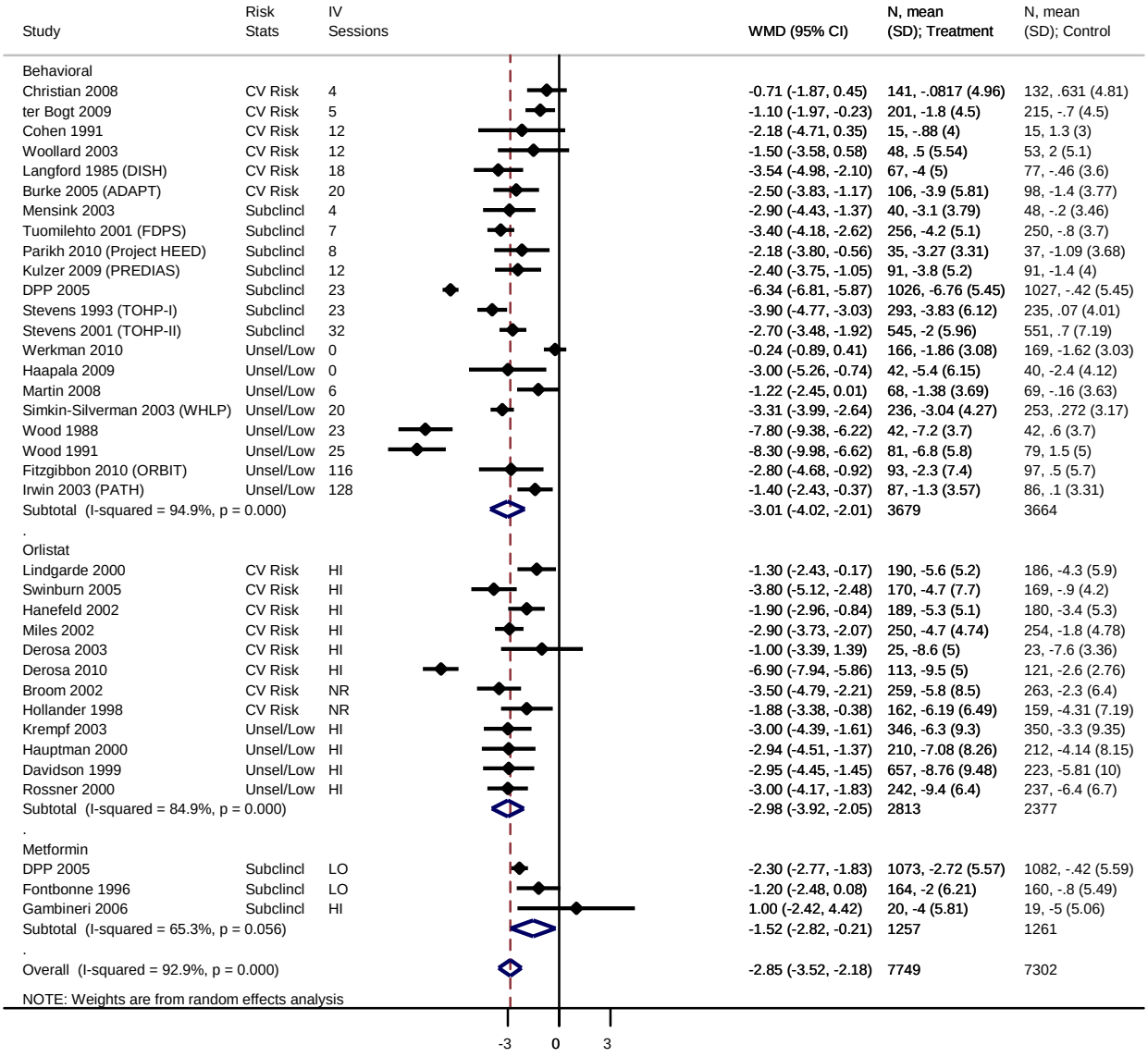
3b. What are common elements of efficacious interventions?

3c. Are there differences in efficacy between patient subgroups (i.e., ages 65 years or older, sex, race/ethnicity, degree of obesity, or baseline cardiovascular risk status)?

Key Question 4. What are the adverse effects of primary care–relevant interventions in obese or overweight adults (e.g., nutritional deficits, cardiovascular disease, bone mass loss, injuries, or death)?

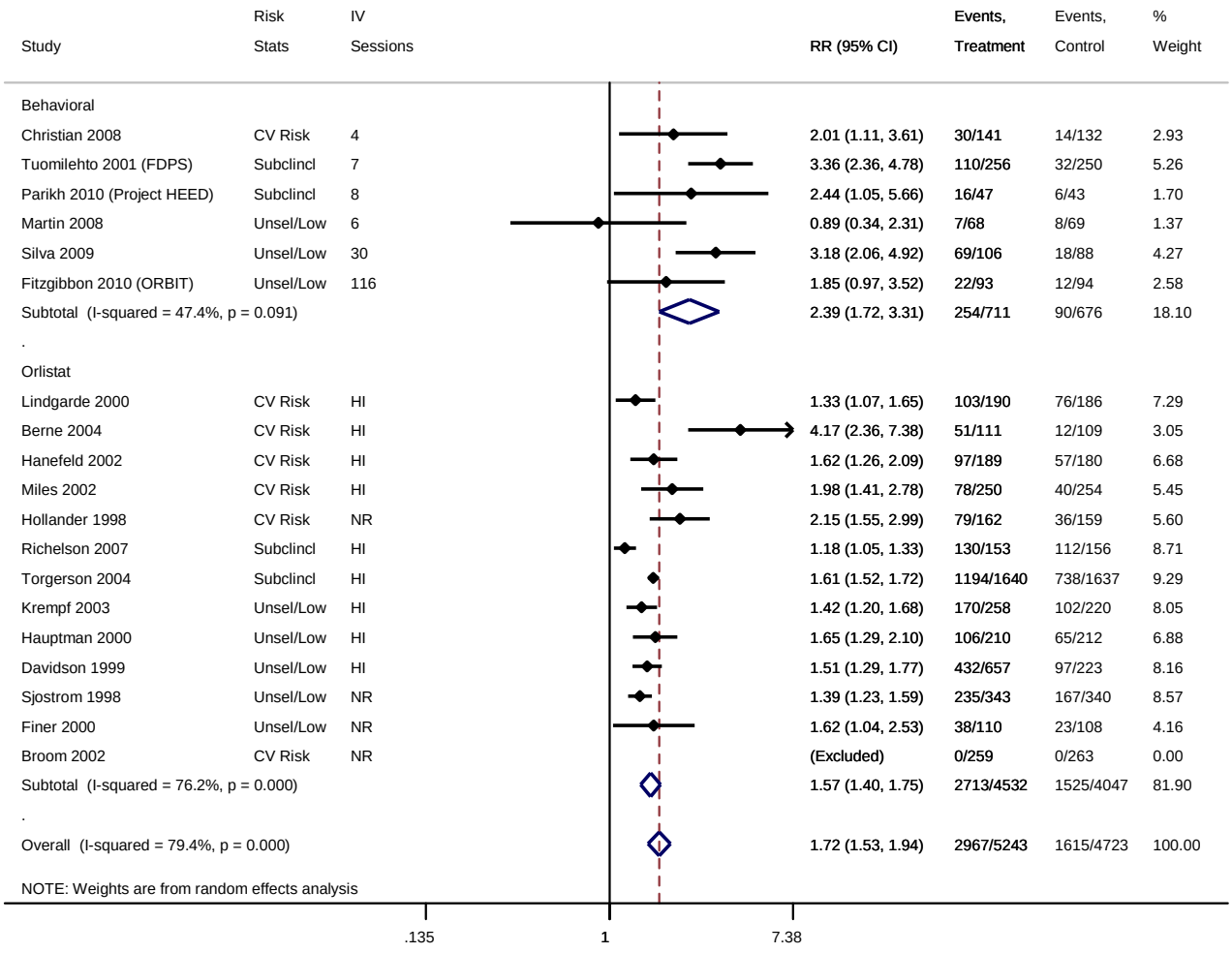
4a. Are there differences in adverse effects between patient subgroups (i.e., ages 65 years or older, sex, race/-ethnicity, degree of obesity, or baseline cardiovascular risk status)?

Figure 2. Difference Between Intervention and Control Groups in Weight Change (kg) at 12 to 18 Months



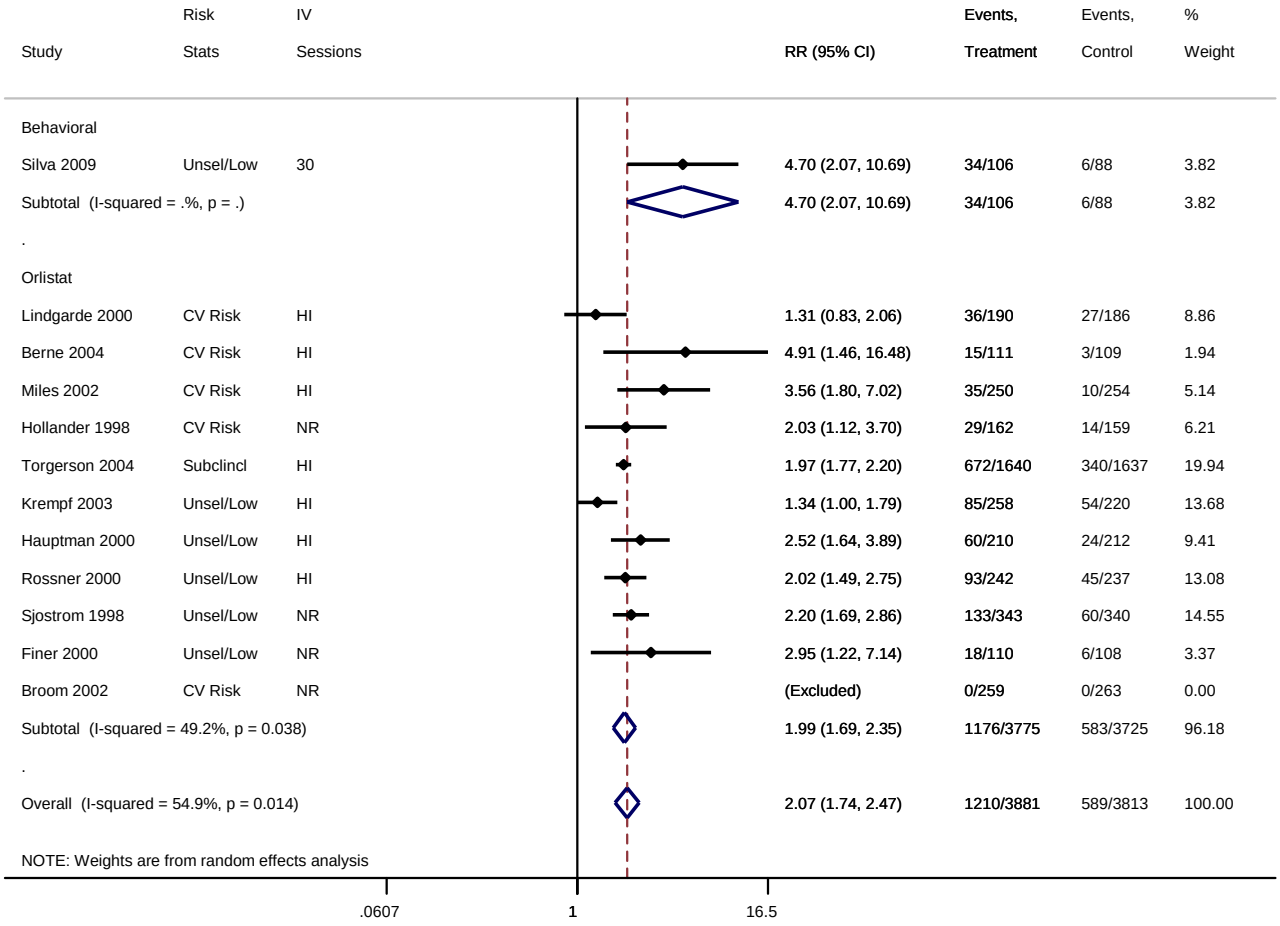
Abbreviations: ADAPT=Activity, Diet, and Blood Pressure Trial; CI=confidence interval CV=cardiovascular; DISH=Dietary Intervention to Study Hypertension; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HEED=Help Educate to Eliminate Diabetes; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; ORBIT=Obesity Reduction Black Intervention Trial; PATH=Physical Activity for Total Health; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; TOHP=Trials of Hypertension Prevention; WHLP=Women's Healthy Lifestyle Project; Unsel=unselected; WMD=weighted mean difference.

Figure 3. Relative Risk of Participants Losing at Least 5% of Baseline Weight in Intervention Group Compared With Control Group



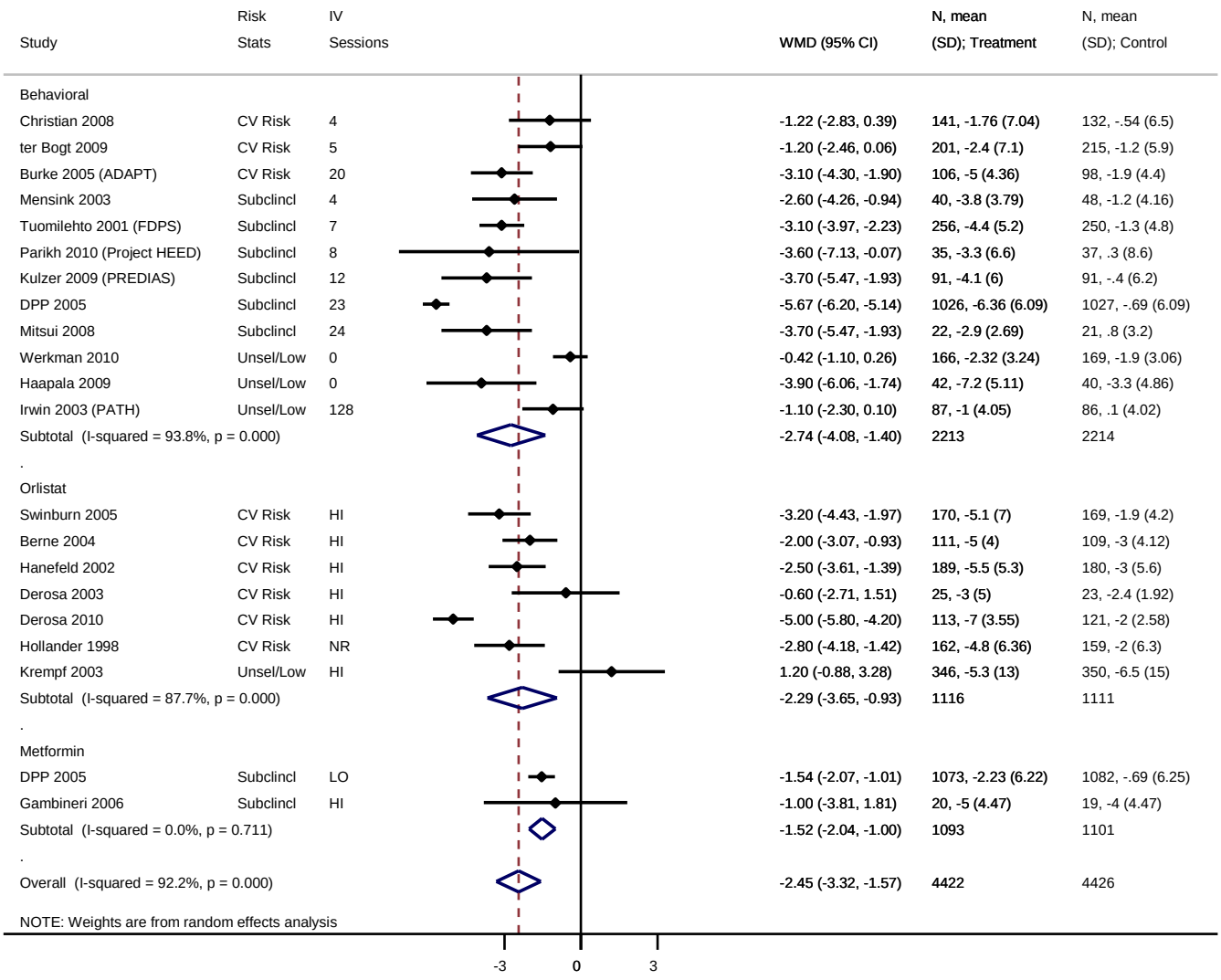
Abbreviations: CI=confidence interval; CV=cardiovascular; FDPS=Finnish Diabetes Prevention Study; HEED=Help Educate to Eliminate Diabetes; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; ORBIT= ORBIT=Obesity Reduction Black Intervention Trial; RR=relative risk; SD=standard deviation; Subclincl=subclinical; Unsel=unselected.

Figure 4. Relative Risk of Participants Losing at Least 10% of Baseline Weight in Intervention Group Compared With Control Group



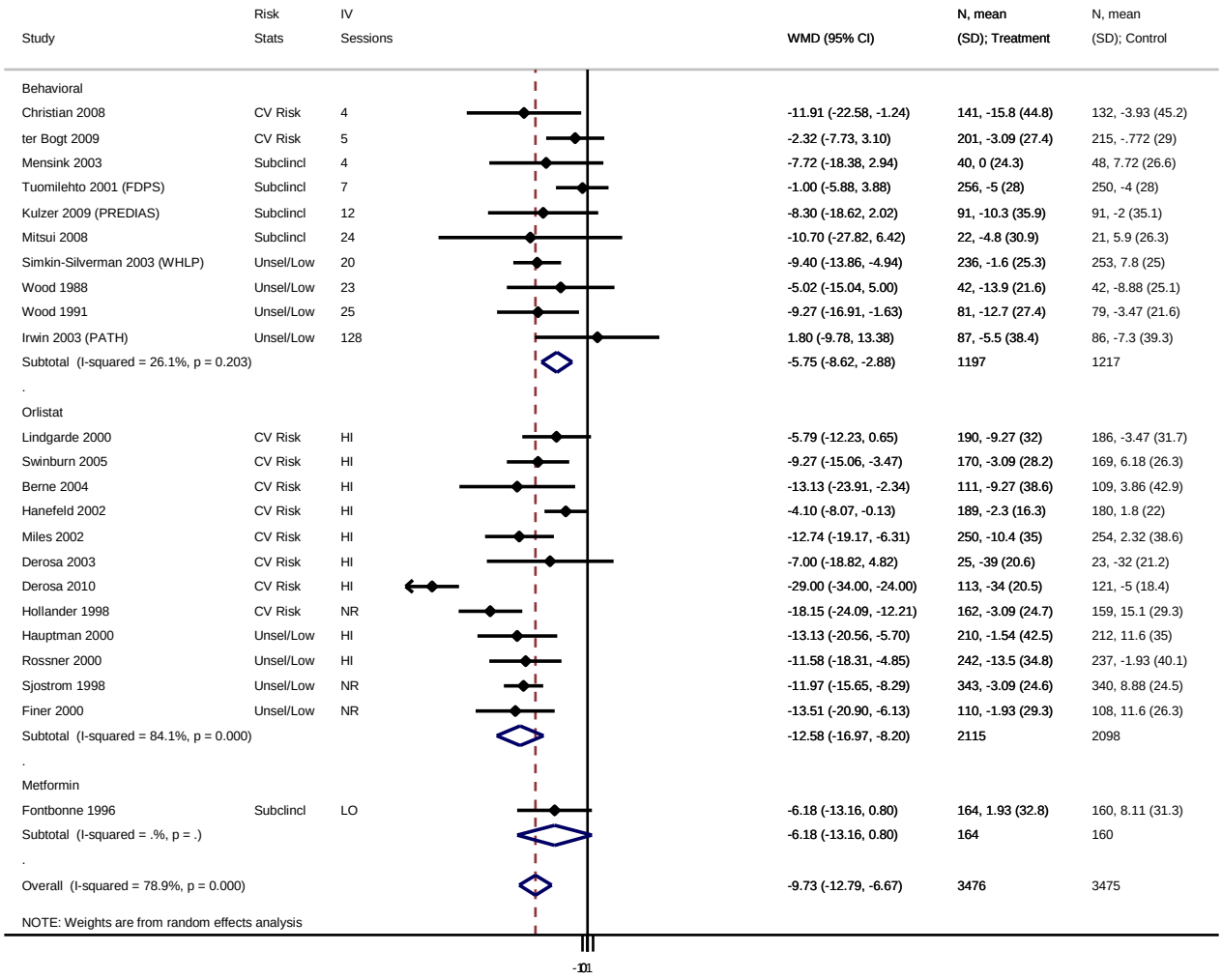
Abbreviations: CI=confidence interval; CV=cardiovascular; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; RR=relative risk; SD=standard deviation; Subclincl=subclinical; Unsel=unselected.

Figure 5. Difference Between Intervention and Control Groups in Change in Waist Circumference (cm) at 12 to 18 Months



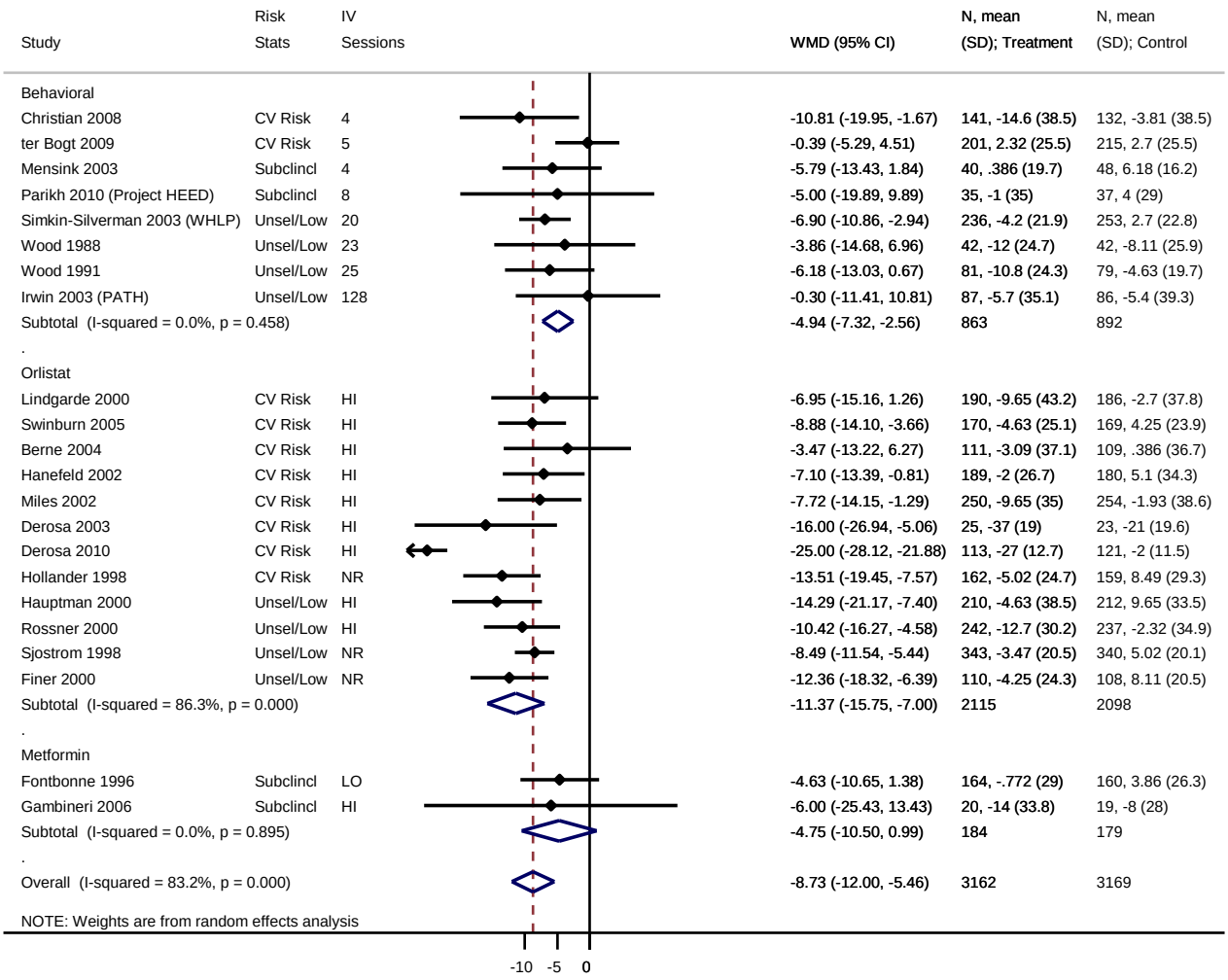
Abbreviations: ADAPT=Activity, Diet, and Blood Pressure Trial; CI=confidence interval; CV=cardiovascular; DISH=Dietary Intervention to Study Hypertension; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HEED=Help Educate to Eliminate Diabetes; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; PATH=Physical Activity for Total Health; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; TOHP=Trials of Hypertension Prevention; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 6. Difference Between Intervention and Control Groups in Total Cholesterol (mg/dL)



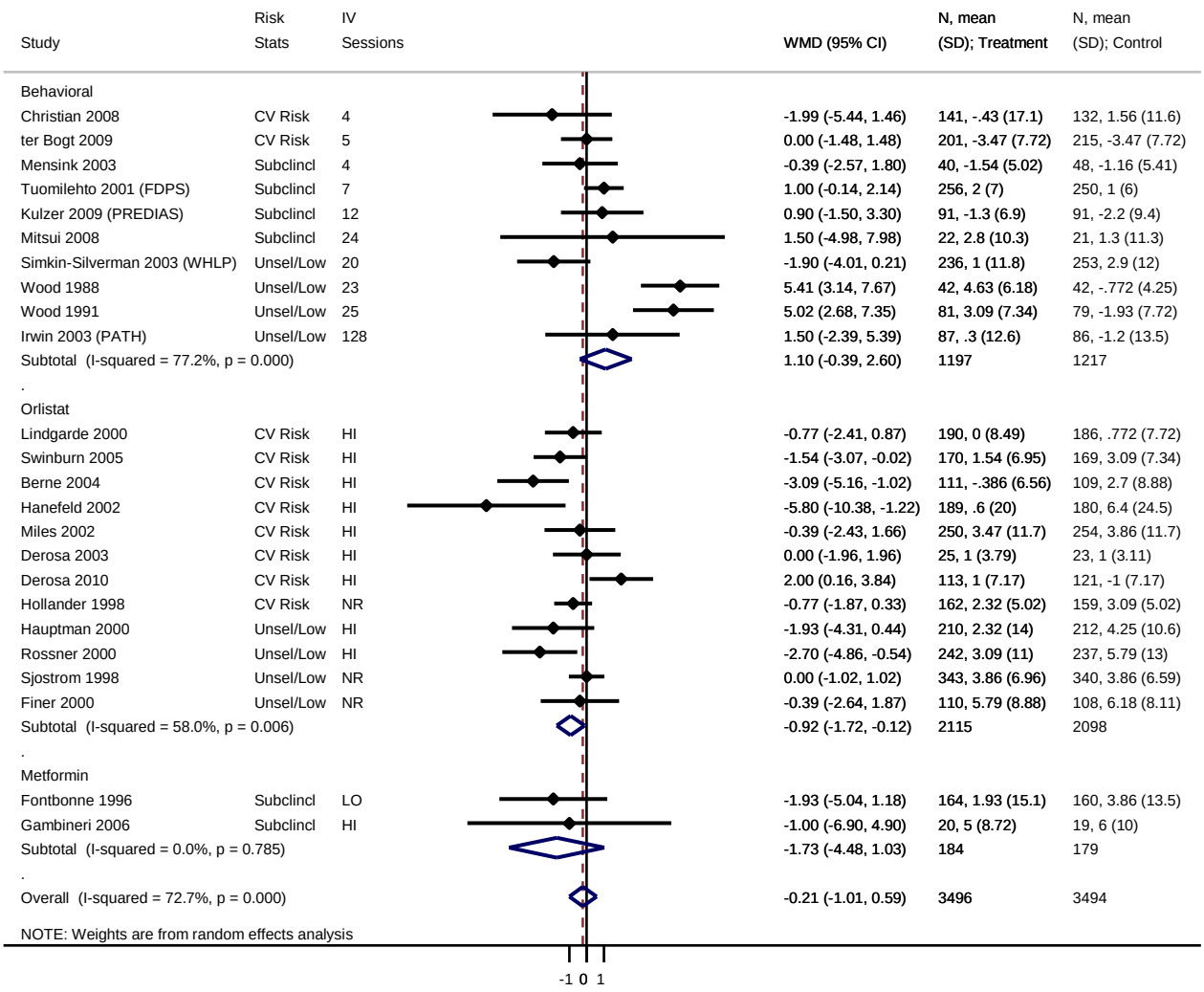
Abbreviations: CI=confidence interval; CV=cardiovascular; FDPS=Finnish Diabetes Prevention Study; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; PATH=Physical Activity for Total Health; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 7. Difference Between Intervention and Control Groups in Change in Low-Density Lipoprotein (mg/dL)



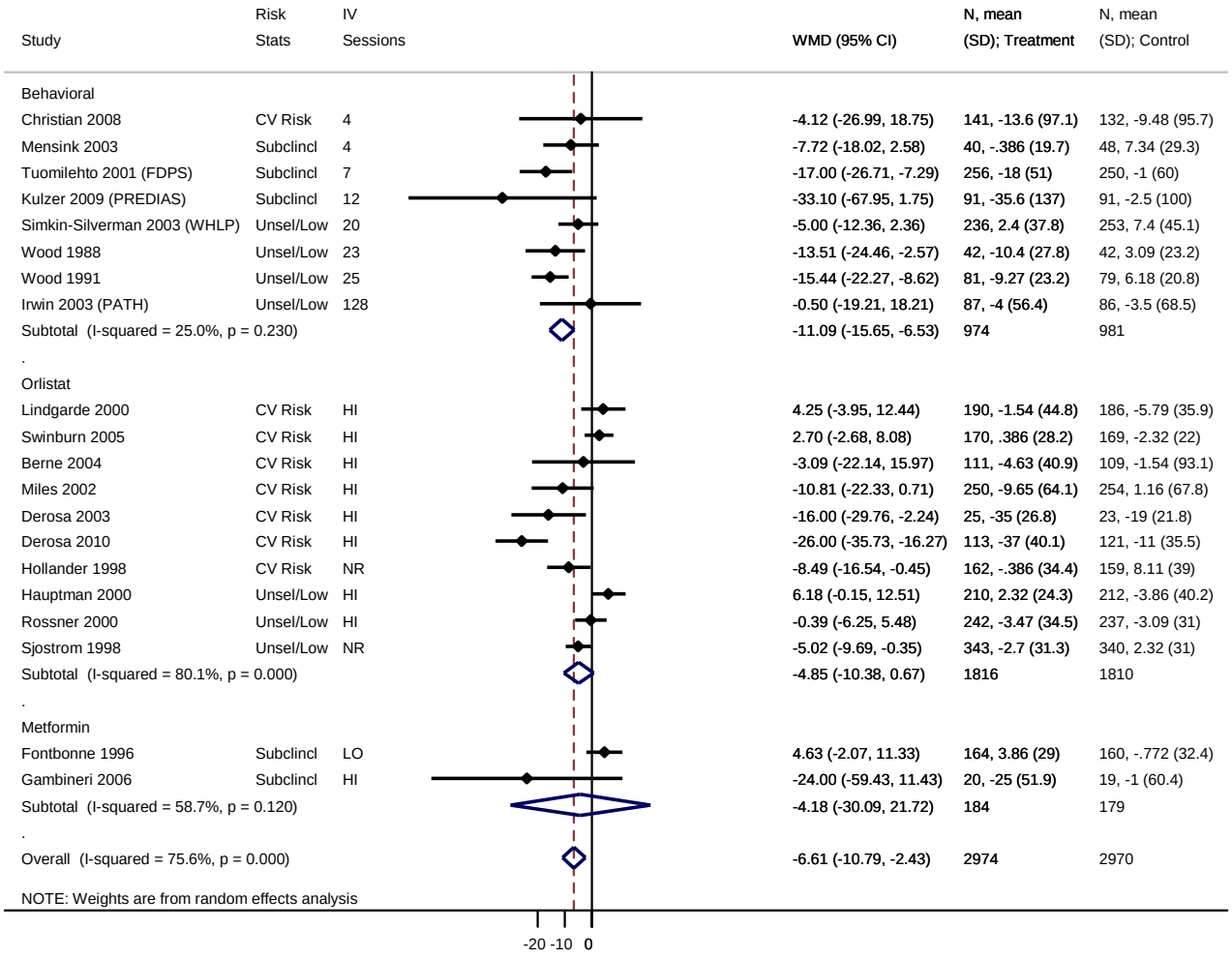
Abbreviations: CI=confidence interval; CV=cardiovascular; HEED=Help Educate to Eliminate Diabetes; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; PATH=Physical Activity for Total Health; SD=standard deviation; Subclincl=subclinical; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 8. Difference Between Intervention and Control Groups in Change in High-Density Lipoprotein (mg/dL)



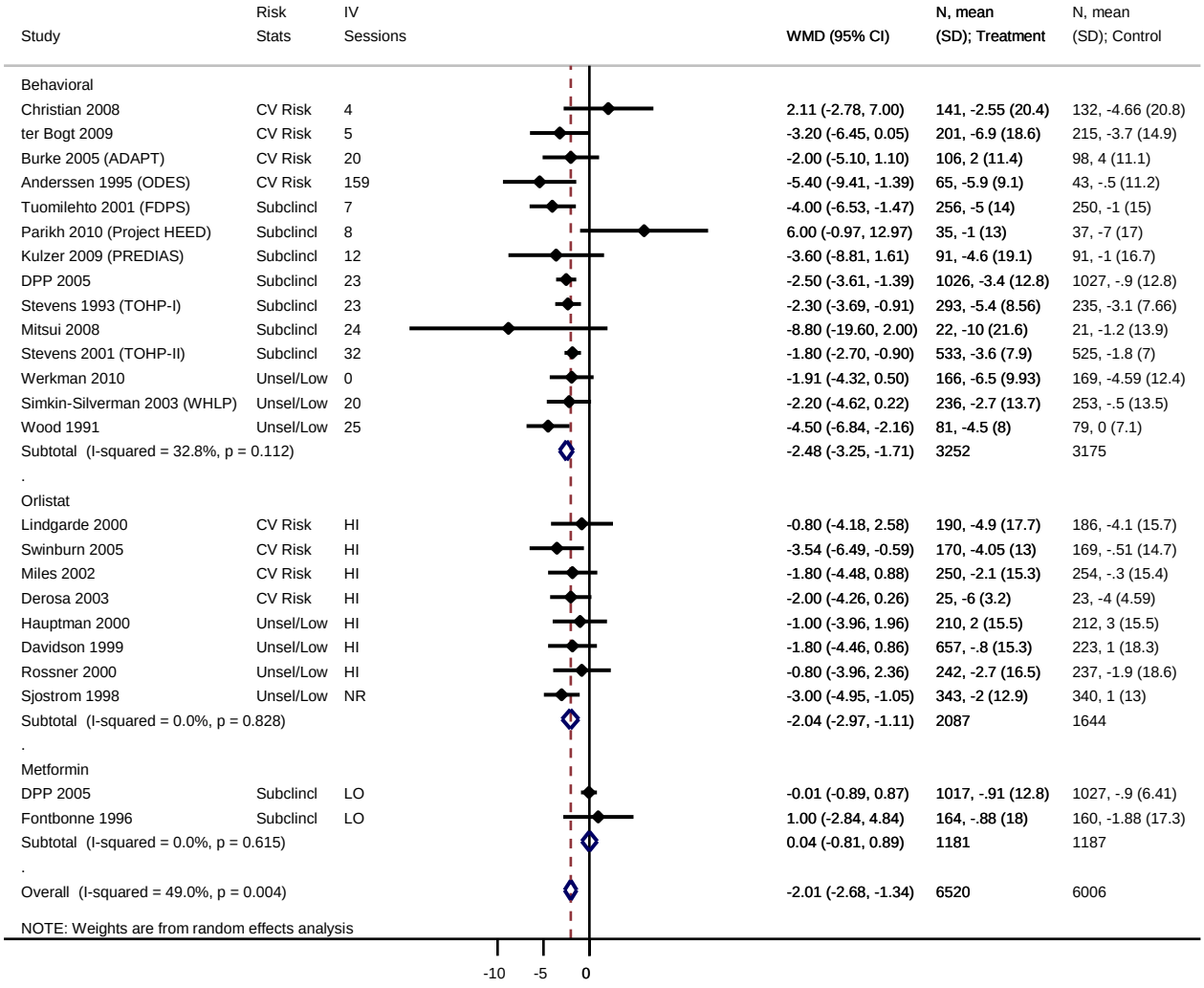
Abbreviations: CI=confidence interval; CV=cardiovascular; FDPS=Finnish Diabetes Prevention Study; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; PATH=Physical Activity for Total Health; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 9. Difference Between Intervention and Control Groups in Change in Triglycerides (mg/dL)



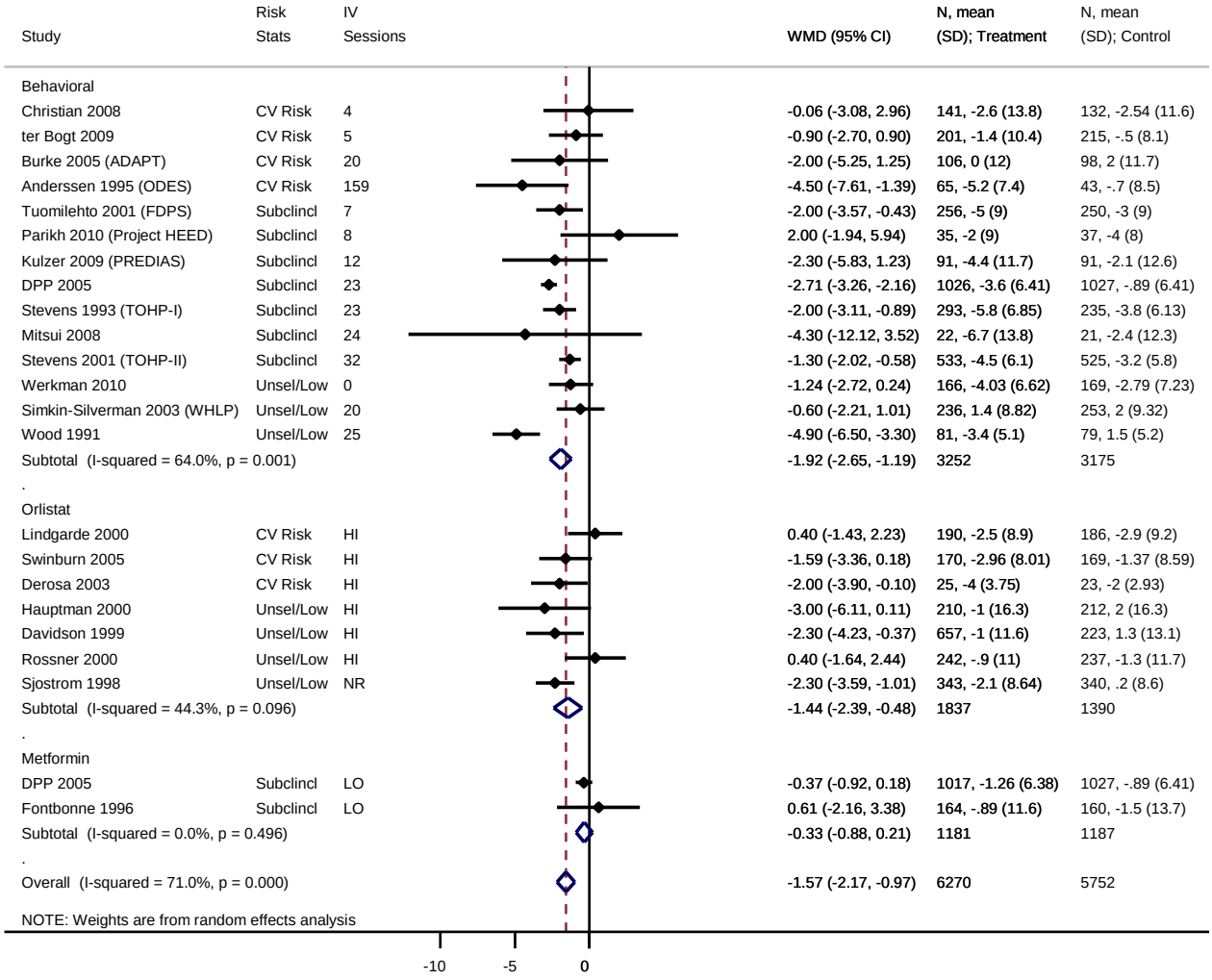
Abbreviations: CI=confidence interval; CV=cardiovascular; FDPS=Finnish Diabetes Prevention Study; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; PATH=Physical Activity for Total Health; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 10. Difference Between Intervention and Control Groups in Change in Systolic Blood Pressure (mm Hg)



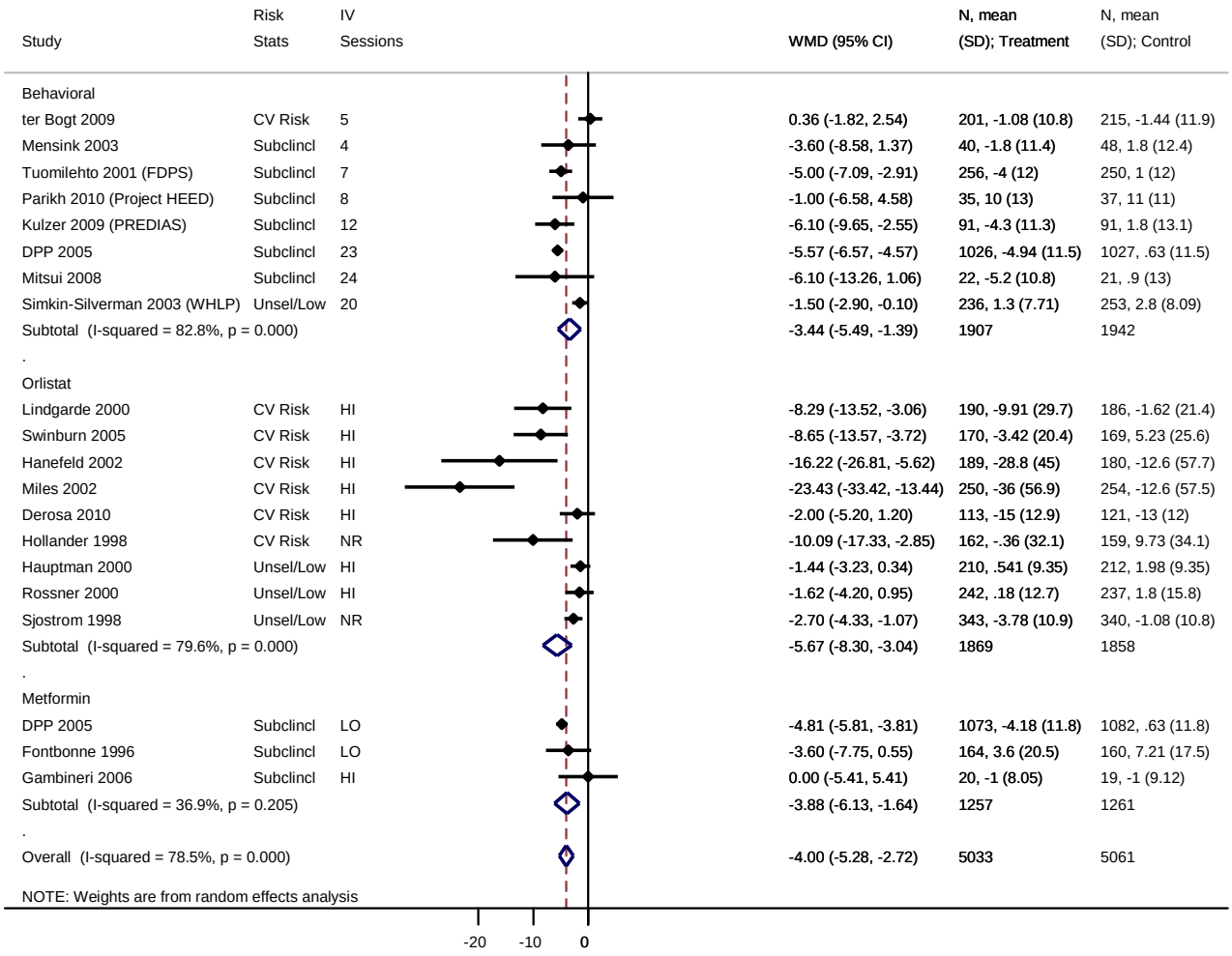
Abbreviations: ADAPT=Activity, Diet, and Blood Pressure Trial; CI=confidence interval; CV=cardiovascular; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HEED=Help Educate to Eliminate Diabetes; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; ODES=Oslo Diet and Exercise Study; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; TOHP=Trials of Hypertension Prevention; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 11. Difference Between Intervention and Control Groups in Change in Diastolic Blood Pressure (mm Hg)



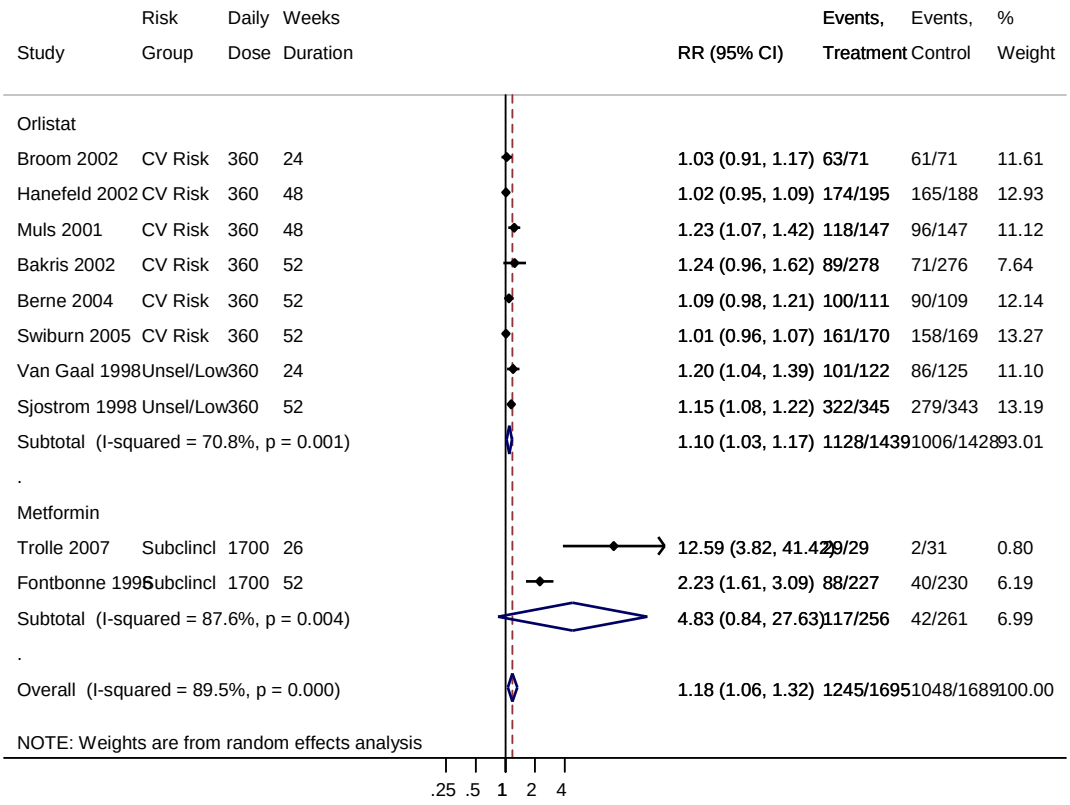
Abbreviations: ADAPT=Activity, Diet, and Blood Pressure Trial; CI=confidence interval; CV=cardiovascular; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HEED=Help Educate to Eliminate Diabetes; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; ODES=Oslo Diet and Exercise Study; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; TOHP=Trials of Hypertension Prevention; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 12. Difference Between Intervention and Control Groups in Change in Plasma Glucose (mg/dL)



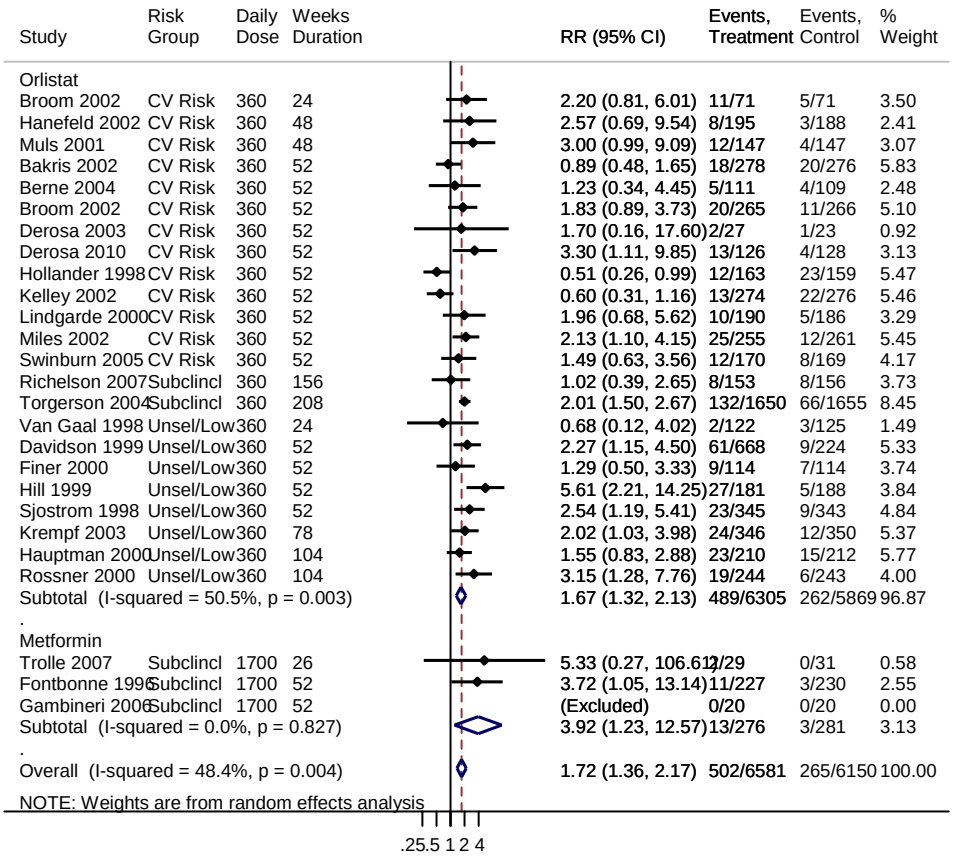
Abbreviations: CI=confidence interval; CV=cardiovascular; DPP=Diabetes Prevention Program; FDPS=Finnish Diabetes Prevention Study; HEED=Help Educate to Eliminate Diabetes; HI=intensive intervention; IV=intervention; LO=brief intervention; N=number; NR=not reported; PREDIAS=Prevention of Diabetes Self-Management Program; SD=standard deviation; Subclincl=subclinical; Unsel=unselected; WHLP=Women's Healthy Lifestyle Project; WMD=weighted mean difference.

Figure 13. Relative Risk of Experiencing Any Adverse Effects



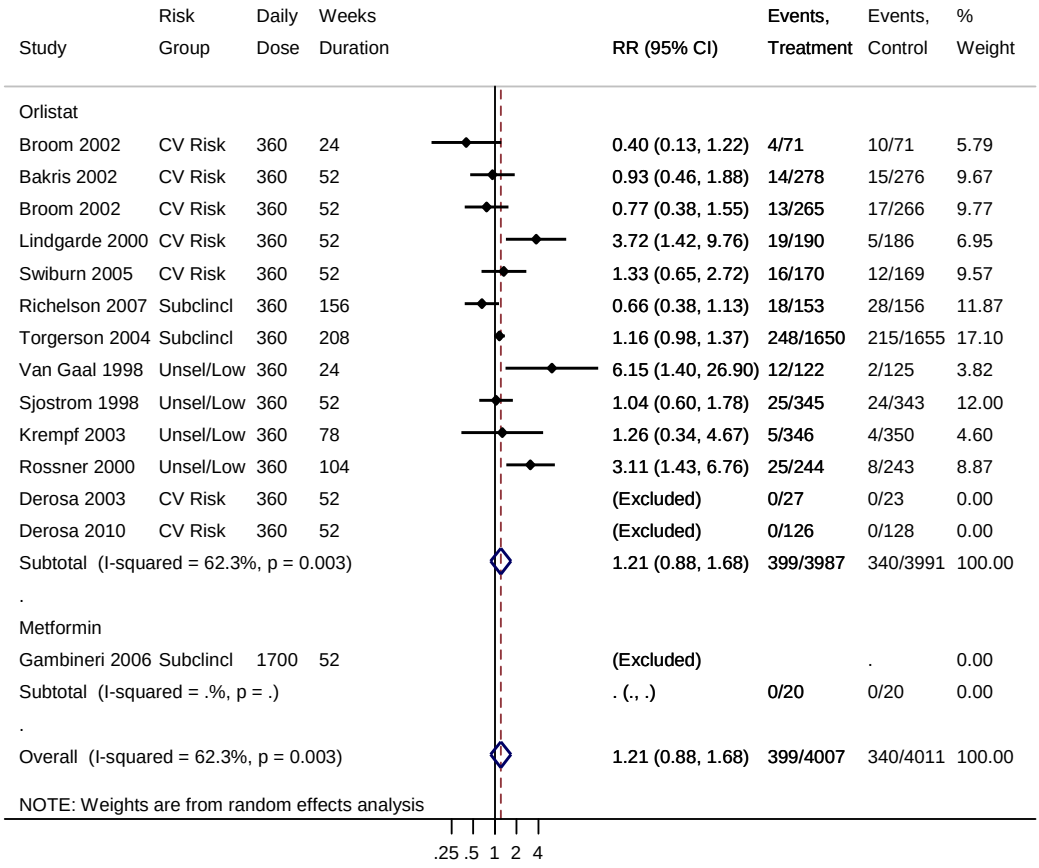
Abbreviations: CI=confidence interval; CV=cardiovascular; IV=intervention; N=number; RR=relative risk; SD=standard deviation; Subclincl=subclinical; Unsel=unselected.

Figure 14. Relative Risk of Study Withdrawal Due to Adverse Effects



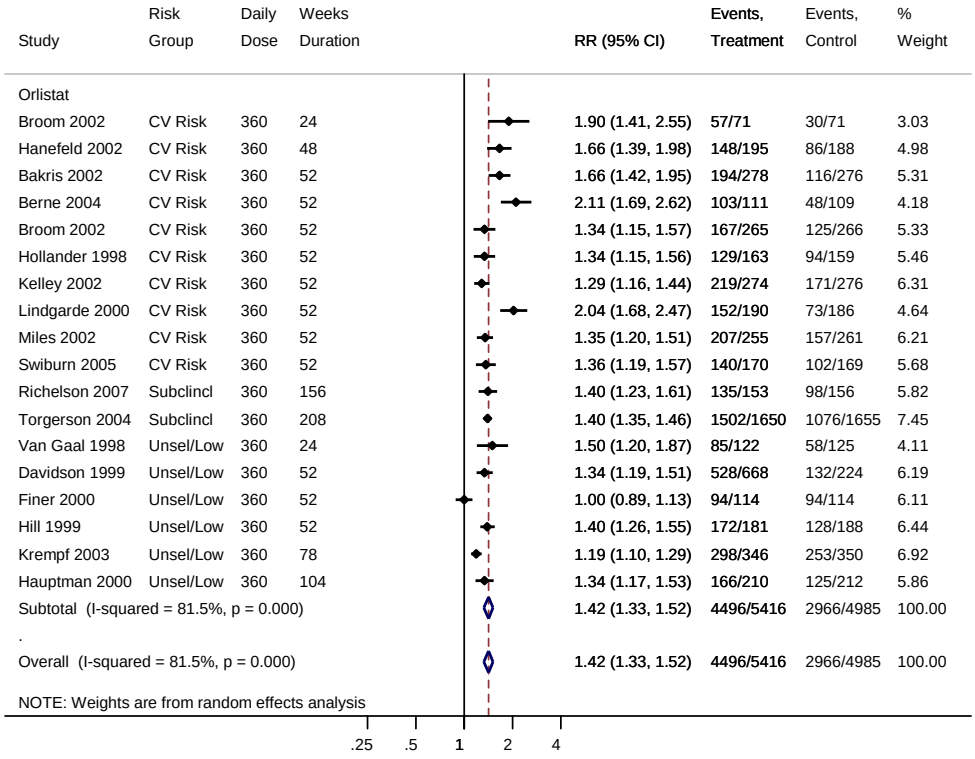
Abbreviations: CI=confidence interval; CV=cardiovascular; IV=intervention; N=number; RR=relative risk; SD=standard deviation; Subclincl=subclinical; Unsel=unselected.

Figure 15. Relative Risk of Experiencing Serious Adverse Effects



Abbreviations: CI=confidence interval; CV=cardiovascular; IV=intervention; N=number; RR=relative risk; SD=standard deviation; Subclincl=subclinical; Unsel=unselected.

Figure 16. Relative Risk of Experiencing Gastrointestinal Adverse Effects in Orlistat Trials



Abbreviations: CI=confidence interval; CV=cardiovascular; IV=intervention; N=number; RR=relative risk; SD=standard deviation; Subclincl=subclinical; Unsel=unselected.

Study Selection

Two investigators independently reviewed all abstracts and articles against inclusion and exclusion criteria. Discrepancies were resolved by consensus. Articles excluded for not meeting inclusion criteria or for poor quality are listed in Appendix D Tables 1–4. Inclusion and exclusion criteria are detailed in Appendix B Table 1, and are summarized here.

Study design. We included only English-language, randomized or controlled clinical trials evaluating the effectiveness and safety of weight loss interventions in adults. Large cohort studies or case-control studies reporting serious adverse effects related to weight loss interventions were included to assess harms only (key question [KQ] 4 only). All trials had to include a true control group that received no intervention. More specifically, an acceptable control group could not receive a personalized intervention, at-home workbook materials, advice more frequently than annually, or participate in frequent weigh-ins (less than every 3 months). A healthy lifestyle message was considered too similar to weight loss messages for attention control groups.

Population and setting. We included trials conducted among adults (ages ≥18 years) who were obese or overweight. Populations must either have been unselected, selected for low cardiovascular disease risk, or selected for increased risk for specified conditions (cardiovascular disease, hypertension, dyslipidemia, or type 2 diabetes). Trials limited to participants with cardiovascular disease were not included, though trials could include some participants with cardiovascular disease. We included trials conducted in settings generalizable to U.S. primary care, feasible for conducting in primary care, feasible for referral from primary care, or conducted in commercial settings (e.g., Weight Watchers). We excluded trials conducted in hospitals, institutionalized settings, school-based programs, occupational settings, churches, and other settings deemed not generalizable to primary care, such as those with existing social networks among participants or the ability to offer intervention elements that could not be replicated in a health care setting.

Intervention. We included only interventions focusing on weight loss, including behavioral-based, pharmacological (orlistat and metformin), or a combination of both. We excluded behavioral interventions that did not focus primarily on weight or that did not report weight-related outcomes, surgical interventions, primary prevention programs that did not involve a weight loss goal for all participants, and trials focusing on pharmacological agents other than orlistat or metformin.

Outcomes. We included multiple health outcomes: decreased morbidity from diabetes mellitus, cardiovascular disease, cancer, arthritis, asthma, and sleep apnea; improved depression; improved emotional function (scores on emotional subscales of quality of life instruments); physical fitness capacity or performance (not behavioral); physical functioning (scores on physical subscales of quality of life measures); disability (global measures of disability, such as activities of daily living); and mortality. Intermediate outcomes included a reduction of weight or adiposity (a required outcome). Acceptable measures included weight, relative weight, total adiposity measures, or change in any of these measures. Other intermediate outcomes included weight maintenance after an intervention has ended and metabolic consequences (e.g., glucose

tolerance, blood pressure, dyslipidemia). Adverse outcomes included serious treatment-related harms at any time point after an intervention began (e.g., death, medical issue requiring hospitalization or urgent medical treatment) or other treatment-related harms reported in trials. Outcomes reported more than 12 months after the start of the intervention were included. Trials of treatment-related harms had no minimum followup requirement.

Data Extraction and Quality Assessment

Two independent investigators dual-reviewed 5,869 abstracts and 623 articles (Appendix B Figure 1) for inclusion and critically appraised all included articles using design-specific criteria (Appendix B Table 2) and USPSTF methods.[125] The USPSTF has defined a three-category quality rating of "good," "fair," and "poor" based on specific criteria. Discrepancies in quality ratings were resolved by consultation with a third investigator. All studies rated as poor quality were excluded from the review.

Briefly, for KQs 1–3, we assessed the validity of the randomization and measurement procedures, attrition, similarities between the groups in baseline characteristics and attrition, intervention fidelity, and statistical methods. Among other things, good-quality trials blinded staff members to the participants' treatment assignments (or future treatment assignment) if they performed tasks related to assessment or randomization, had followup data on 90 percent or more of participants, reported group-specific followup with less than 10 percentage points difference between groups, and described important details related to the measurement of anthropomorphic measures, such as how participants were dressed, what type of scale was used, how they determined where to measure waist circumference, or how many times blood pressure measures were taken and how they were combined. Trials were rated as "poor" if attrition in the treatment and control groups differed by more than 20 percentage points or if overall attrition was higher than 40 percent, or had other important flaws. If a study was conducted for more than 12 months, only data from time points with adequate followup were included. For example, if the study's attrition met our standards at 12 months but not at 24 months, only 12-month data was abstracted. However, we made an exception to this rule for outcomes that were reported as cumulative incidence. For example, we did not abstract 24-month weight or blood pressure data from a study that had low attrition at 24 months; however, we did abstract the incidence of diabetes during the entire study period if it was reported as cumulative incidence and the attrition at 12 months was not higher than our quality criteria.[202] All trials meeting quality criteria for KQs 1–3 were also examined for KQ 4 outcomes.

In addition, we developed separate quality assessment procedures for trials that were not included for KQs 1–3 (either due to quality issues or other inclusion criteria) but reported harms outcomes, so some trials that were excluded from KQs 1–3 for poor quality were included for KQ 4. The quality rating of KQ 4-only studies focused specifically on the assessment and analysis of harms (and not other outcomes). In addition, we did not have minimum attrition standards, both because harms of treatment could appear at any time after treatment began and because we were concerned that if medications had high rates of adverse events, attrition could be very high, and only a very selected sample would be evaluated for harms if we maintained the same attrition standards. We only examined harms outcomes that were cumulative (i.e., percent withdrawing from the trial due to adverse effects, percent experiencing any serious adverse

effect, percent experiencing any adverse effect, and percent experiencing any gastrointestinal adverse effects) in these trials that did not meet the attrition standards of KQs 1–3. Because we had different standards for KQ 4 that focused only on factors specifically related to the assessment of harms, we did not distinguish between "good" and "fair" trials, but simply rated them as "acceptable" or "poor." A poor-quality study was one that had a fatal flaw that made the harms data of questionable validity.

One investigator abstracted data from included studies into evidence tables and a second investigator reviewed abstracted data for accuracy. We abstracted prespecified study details into evidence tables that included the following items: study design; setting (location, target population, recruitment strategy); population characteristics (study inclusion and exclusion criteria, participant age, sex, race/ethnicity, and socioeconomic status, as defined by income or education); baseline health status (body mass index; percent with diabetes, hypertension, and dyslipidemia); intervention characteristics (aim/theory, intervention/control description, duration, incentives, and who administered the intervention); outcomes; and adverse events. Relevant outcomes for abstraction included anthropomorphic measures (weight/relative weight, central adiposity, overall adiposity), intermediate outcomes (lipids, glucose tolerance, blood pressure), and health outcomes (depression, decreased morbidity, physical fitness capacity, mortality). Complete evidence tables are included in Appendix C Tables 1–3.

For KQs 1–3, this review included 140 articles representing 61 unique trials, 27 of which were conducted in the United States.

In addition to evaluating the studies from KQs 1–3 for harms, we abstracted harms data from 25 additional weight loss studies (table of harms data studies not in main analysis). These studies were not included in KQs 1–3 for various reasons, including poor quality, short duration (<12 months), or not a qualified methodology (not a controlled trial). For KQ 4, this review included 167 articles representing 85 unique trials.

Data Synthesis and Analysis

We separately synthesized evidence for trials of weight loss medications and trials of behavioral-based interventions. Behavioral and medication trials were combined in a single forest plot for each outcome, but results were pooled separately for the behavioral trials, and each medication was synthesized separately given their different mechanisms of action. Within each intervention type, trials were grouped according to the risk status of the study samples, and then ordered by the intensity of the behavioral interventions within each risk status. We grouped the trials according to risk status as follows: 1) trials limited to people with known risk factors related to cardiovascular disease (operationalized as hypertension, diabetes, or dyslipidemia and termed "CV risk" trials); 2) trials limited to those with elevated risk but without known disease (prehypertension, impaired glucose tolerance or elevated fasting glucose, borderline high total cholesterol, low-density lipoprotein, or triglyceride levels, low high-density lipoprotein levels, or abdominal obesity; termed "subclinical" trials); and 3) trials that either did not limit samples on the basis of cardiovascular risk or that excluded people with the risk factors described above (termed "unselected/low risk" trials).

We captured the intensity of the behavioral interventions differently in behavioral-based and medication trials. For behavioral-based interventions, we usually had enough detail to estimate the number of sessions offered in the first year of the intervention, and used this continuous variable as our indicator of intensity in the forest plots. Medication trials typically provided limited detail about the behavioral interventions they offered as adjuncts to medication management, but we were able to identify two levels of intensity: brief intervention only, comparable with what might be offered in primary care (labeled "LO" in the forest plots and referred to as "brief" in the text), and more intensive than would likely be offered in primary care (labeled "HI" in the forest plots and referred to as "intensive" in the text). Trials that had insufficient detail to determine intensity were labeled "NR" (not reported) in the forest plots. The "brief" interventions did not require participants to attend a specific session on diet. These three studies offered handouts and regular visits with a physician while subjects received the medication. The "intensive" counseling interventions generally involved regular (generally four to 12 sessions over 12 months) contact with a dietitian or counselor, most often with monthly medication monitoring and weigh-ins. Only one of the trials with 12 or more sessions explicitly reported discussing behavioral management principles with participants, but most of the trials with only four sessions did report providing some instruction in behavior management principles. Thus, although 12 sessions is considerably more than four, we did not feel that the 12-session interventions could necessarily be described as more intensive than the four-session interventions that included behavioral management, so we decided to group them together under the label "intensive" (or "HI" in the forest plots).

We conducted random effects meta-analyses to estimate the effect size of weight loss interventions on intermediate health outcomes (adiposity, systolic and diastolic blood pressure, total cholesterol, high- and low-density lipoprotein cholesterol, triglycerides, and glucose). For continuous outcomes, we analyzed change in outcome from baseline. Risk ratios were analyzed for dichotomous outcomes. Absolute risk difference was also estimated through meta-analysis in many cases so the number needed to treat could be calculated. We selected a single intervention arm for trials that included multiple active treatment arms and calculated change from baseline and standard deviations based on the information provided in the individual articles if they were not provided. We converted measurements into common units using standard conversion factors, which are provided below.

We assessed the presence of statistical heterogeneity among studies using standard chi-square tests and the magnitude of heterogeneity was estimated using the I^2 statistic.[139] We considered an I^2 of <50 percent to represent low heterogeneity, 50 to 75 percent to represent moderate heterogeneity, and >75 percent to indicate high heterogeneity among studies. Tests of publication bias on whether the distribution of the effect sizes was symmetric with respect to the precision measure were performed using funnel plots and Egger's linear regression method,[140] when the number of studies was about 10 or more.[141]

Meta-regression was used to explore heterogeneity in effect sizes among the KQs 1–3 trials. Due to concerns about type I errors, we limited most exploration of heterogeneity to a single outcome of weight loss. Some factors were explored for the entire body of trials, combining behavioral and all three medication types. Some factors were run separately for the medication trials only

and the behavioral trials only. Continuous variables were left as continuous variables, and categorical variables were converted to one or more dummy variables.

A prominent source of clinical heterogeneity was population risk status. Thus, we created two dummy variables, using the unselected/low-risk category as the reference group, and included these variables in all meta-regression models. All regression models involving the full set of KQs 1–3 trials also included a variable to indicate whether the trial was a medication or behavioral-based intervention trial.

Another factor we explored was the participant identification approach. Trials that identified specific potentially eligible patients prior to recruitment and used individual outreach and screening for recruitment (referred to as "study-identified") were contrasted with trials that used broad-based media approaches that required potential participants to contact study staff in order to be screened for study eligibility (referred to as "self-identified"). Trials that did not report enough detail to determine recruitment approach were assumed to be self-identified. Additional factors explored for the entire combined body of literature were: percent of participants retained at 12 to 18 months, whether the trials focused on weight maintenance as opposed to weight loss, whether primary care was the setting for either recruitment or the intervention, whether the trial was set in the United States, study quality rating (on a subjective scale of 1–4, where 1=barely acceptable and 4=good), and selected patient-level characteristics (average age, percent female, percent nonwhite, and baseline body mass index).

For behavioral trials, we also examined the number of sessions in the first year and, in separate models, the presence of each of the following intervention components: supervised physical activity sessions, group sessions, individual sessions, technology-based assessment or intervention, specific weight loss goal, spouse or family involvement, barriers to weight loss addressed, pros and cons of weight loss or similar motivational assessment, self-monitoring expected, use of incentives for weight loss or intervention participation, and support for weight loss or lifestyle maintenance after active intervention phase. The variables examined in the combined medication and behavioral trials were also examined separately in the behavioral subgroup. Number of sessions in the first year and patient risk status were included in all models.

Additional variables were explored for the medication and behavioral trials separately. For medication trials, we also examined the percent of participants that were retained after a run-in phase (scored as 100 if there was no run-in phase, and dropped from the analysis if a run-in phase was present but we could not determine the percent who dropped out), the specific type of medication, and whether the behavioral intervention was more intensive than would be delivered in primary care (see intensity definitions described above). The variables explored for the entire group of trials listed above were also examined separately in the medication trials. All meta-regression of the medication trials controlled for medication type and population risk status. All analyses were performed using Stata 10.0 (StataCorp, College Station, TX).

Meta-analysis decisions. Meta-analysis involves a number of decisions and calculations, and this document details the main decision rules we developed for data abstraction and analysis, and formulas used to calculate missing statistics.

Selecting intervention arm. For trials with multiple intervention arms, we selected the intervention that was most similar to other interventions included in the meta-analysis, if applicable (e.g., most orlistat trials used 120 mg daily dosage, so if a trial included treatment arms using 120 mg and another amount, we selected the arm that used 120 mg), or the most intensive arm. In one case, one treatment arm was diet-only and one arm was exercise-only, and we used the diet-only arm.

Selecting number of participants. If the study did not report some kind of data substitution for missing followup data (e.g., last observation carried forward) or an analysis that used all observations (e.g., random effects models, general estimating equations), then we used the number of participants with followup in each group, if available. If not available, we used the number of participants randomized. If the trial did report data substitution or analysis techniques such those described above, then we used the number randomized in each group, if they were not given specifically for each analysis. For adverse events (KQ 4), when only a proportion and not a number was provided, we assumed the denominator to be the total number randomized.

Baseline values. If a trial reported values at run-in (prior to randomization) and at randomization (post-run-in), we used the baseline values at randomization. If a trial only reported change from before run-in, we calculated changes from that point but did not enter standard deviations.

Followup time. If a study had a 12-month followup, we used that in the meta-analysis. If a trial did not have a 12-month followup, we accepted outcomes with up to 18 months of followup, preferentially selecting the closest to12 months if multiple followup times were reported.

For weight maintenance trials (and those with a weight loss requirement during run-in), we considered baseline to be the beginning of the weight maintenance phase (randomization, for those trials with weight loss run-in). For calculating the number of sessions, we counted the number of sessions in the weight maintenance phase only. For estimating followup time, we counted time to followup from the end of the weight-loss phase for the outcome of weight loss. When entering 5% or 10% weight loss in maintenance trials, we accepted whatever was reported by the trial, which in all cases was counted from the beginning of the initial weight-loss phase.

Calculations. If a trial reported results separately for subgroups, we combined the subgroup scores to calculate a single overall score for each intervention and control group participants. We used the following formulas to calculate combined means and standard deviations:[292]

$$\text{Mean}_{\text{combined}} = N_1M_1 + N_2M_2 / N_1 + N_2$$

$$\text{SD}_{\text{combined}} = \sqrt{\frac{(N_1 - 1)\,SD_1^2 + (N_2 - 1)\,SD_2^2 + \frac{N_1N_2}{N_1 + N_2}\left(M_1^2 + M_2^2 - 2M_1M_2\right)}{N_1 + N_2 - 1}}$$

We used standard calculations to convert standard errors and 95% confidence intervals to standard deviations:

$$\text{SD}_{\text{mean}} = \text{SE}_{\text{mean}} * \text{sqrt}(n) \text{ or}$$
$$\text{SD}_{\text{mean}} = (\text{CI}_{\text{upper}} - \text{CI}_{\text{Lower}}) * \text{sqrt}(n) / 3.29$$

If only baseline and followup values were reported, we calculated the crude mean change by subtracting the baseline mean from the followup mean for each group, and estimated the standard deviation using the following formula:

$$SD_{change} = Sqrt(SD^2_{base} + SD^2_{post} - 2 * SD_{base} * SD_{post} * r_{base,post})$$

In order to use this formula, we estimated the correlation between baseline and followup for each outcome. To do this, we examined studies that reported mean change as well as baseline and followup means, and used the formula above to determine the correlations in their samples. These studies were quite variable in the resulting correlations, the time of followup, the quality of the study, and the number of estimates we were able to find. Because of this variability, both in quality of the estimate and the absolute value of the correlations, we grouped like outcomes and used what we believed to be reasonable, somewhat conservative (lower) values for that set of outcomes. The final correlations used are listed in Table 1.

Other analyses. When summary means were calculated for groups of trials (such as average age among all behavioral trials), mean values were weighted by the number of participants randomized in the relevant treatment arms of the trial.

Table 1. Estimated Correlation Between Baseline and Followup for Analyzed Outcomes, Used in Calculation of Change Score Standard Deviations

Outcome	Control Group Correlation	Intervention Group Correlation
Weight	0.95	0.9
Waist circumference	0.9	0.9
Total cholesterol	0.55	0.55
High-density lipoprotein	0.55	0.55
Low-density lipoprotein	0.55	0.55
Triglycerides	0.55	0.55
Systolic blood pressure	0.43	0.43
Diastolic blood pressure	0.37	0.37
Glucose	0.6	0.6

Table 2. Conversion Factors

Measure	Original Metric	Final Metric	Conversion Factor	Reverse Conversion (1/x)
Total cholesterol*	mg/dL	mmol/L	0.0259	38.61
High-density lipoprotein*	mg/dL	mmol/L	0.0259	38.61
Low-density lipoprotein*	mg/dL	mmol/L	0.0259	38.61
Triglycerides*	mg/dL	mmol/L	0.0113	88.50
Glucose*	mg/dL	mmol/L	0.0555	18.02
Energy**	kcal	kJ	4.184	0.239
Weight***	lb	kg	0.4541	2.202

* From: Instructions for authors. *JAMA.* 2006;295(1):103-11. http://jama.ama-assn.org/content/295/1/103.full
** From: Thompson A, Taylor BN. Guide for the Use of the International System of Units (SI). NIST Special Publication No. 811. Gaithersburg, MD: National Institute of Standards and Technology; 2008. http://www.nist.gov/pml/pubs/sp811/
*** From: Federal Highway Administration. SI (Modern Metric) Conversion Factors.Washington, DC: U.S. Department of Transportation; 2003. http://www.fhwa.dot.gov/publications/convtabl.cfm

Systematic Evidence Review Search

Databases: PubMed, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effectiveness, National Institute for Health and Clinical Excellence, Institute of Medicine, National Institutes of Health
Dates: 2001 to January 2009

1. "Obesity"[Majr:NoExp] OR "Obesity, Morbid"[Majr] OR "Overweight"[Majr:NoExp]
2. "Anti-Obesity Agents"[Majr:NoExp] OR "Appetite Depressants"[Majr] OR "Anti-Obesity Agents "[Pharmacological Action] OR "Appetite Depressants "[Pharmacological Action] OR "sibutramine "[Substance Name] OR "orlistat "[Substance Name]
3. "Bariatric Surgery"[Majr:NoExp] OR "Gastric Bypass"[Majr] OR "Gastroplasty"[Majr]
4. "Body Mass Index"[Majr] OR "Weight Loss"[Majr:NoExp]
5. #1 OR #2 OR #3 OR #4
6. #5 AND systematic[sb]
7. #5 AND systematic[sb] Limits: All Child: 0-18 years
8. #5 AND systematic[sb] Limits: All Adult: 19+ years
9. #7 NOT #8
10. #6 NOT #9
11. #6 NOT #9 Limits: Humans
12. #6 NOT #9 Limits: Animals
13. #12 NOT #11
14. #10 NOT #13
15. obesity[ti] OR obese[ti] OR overweight[ti]
16. bariatric[ti] OR gastroplasty[ti] OR "gastric bypass"[ti] OR "gastric banding"[ti]
17. bmi[ti] OR "body mass index"[ti]
18. #15 OR #16 OR #17
19. #18 AND systematic[sb]
20. #19 AND (publisher[sb] OR in process[sb] OR pubmednotmedline[sb])
21. #14 OR #20
22. #14 OR #20 Limits: Publication Date from 2001 to 2009, English

Key Question Search

Databases: MEDLINE, Cochrane Central Register of Controlled Trials
Dates: 2005 to March 10, 2010

1. Obesity
2. Obesity, Morbid
3. Overweight
4. 1 or 2 or 3
5. Mass Screening
6. screen$.ti,ab.
7. 5 or 6
8. 4 and 7
9. limit 8 to "all child (0 to 18 years)"

10. limit 8 to "all adult (19 plus years)"
11. 9 not 10
12. 8 not 11
13. limit 12 to animals
14. limit 12 to humans
15. 13 not 14
16. 12 not 15
17. limit 16 to english language
18. limit 17 to yr="2005 - 2009"
19. from 18 keep 1-500

Metformin Search

Database: MEDLINE
Dates: 2001–2005

1. Metformin
2. metformin.ti,ab.
3. glucophage.ti,ab.
4. 1 or 2 or 3
5. Obesity
6. Obesity, Morbid
7. Overweight
8. Weight Loss
9. obes$.ti,ab.
10. overweight.ti,ab.
11. weight loss.ti,ab
12. 5 or 6 or 7 or 8 or 9 or 10 or 11
13. diabetes.ti,ab,hw
14. 4 and 12 and 13
15. limit 14 to (clinical trial or controlled clinical trial or meta analysis or randomized controlled trial) (159)
16. clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/
17. Meta-Analysis as Topic
18. (control$ adj3 trial$).ti,ab.
19. random$.ti,ab.
20. clinical trial$.ti,ab.
21. 16 or 17 or 18 or 19 or 20
22. 14 and 21
23. 15 or 22
24. limit 23 to "all child (0 to 18 years)"
25. limit 23 to "all adult (19 plus years)"
26. 24 not 25
27. 23 not 26
28. limit 27 to animals

29. limit 27 to humans
30. 28 not 29
31. 27 not 30
32. limit 31 to english language
33. limit 32 to yr="2001 - 2005"
34. remove duplicates from 33

Appendix B Table 1. Review Inclusion and Exclusion Criteria

Populations	Include	• Adults ages 18 years and older who are obese or overweight. • Study participants are either: 1) unselected or low-risk; 2) selected for increased risk of cardiovascular disease, including hypertension, dyslipidemia, or type 2 diabetes mellitus; or 3) selected populations, restricted to patients who are postpartum or have polycystic ovary syndrome.
	Exclude	• Children and adolescents younger than age 18 years. • Adults with secondary causes of obesity, such as steroid use. • Restricted patient subgroups (i.e., that are not listed above as included, such as pregnant women or people with arthritis, eating disorders, or cardiovascular disease). • Populations that do not demonstrate obesity or overweight using body mass index (BMI) or other weight-related measurements • Cancer survivors or people who have arthritis, osteoporosis, or liver disease (because of different motivation).
Settings	Include	• Studies conducted in primary care, feasible for conducting in primary care, or feasible for referral from primary care. In order for an intervention to be feasible for primary care referral, it needs to be conducted as part of a health care setting or be widely available in the community at a national level. • Studies conducted in commercial settings (e.g., Weight Watchers). • Geographic settings generalizable to United States (all countries listed as "high" human development on the Human Development Index [>0.90]: Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Hong Kong, Iceland, Ireland, Israel, Italy, Japan, Korea, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, Singapore, Slovenia, Spain, Sweden, Switzerland, and United Kingdom).
	Exclude	• Settings not generalizable to primary care (e.g., inpatient hospital units, emergency departments, nursing home and other institutionalized settings, school-based programs, occupational settings, churches and faith-based and other community-based settings), unless intervention is primary care feasible. • Studies performed in countries with populations not similar to the United States.

Interventions	Include	• Interventions focusing on weight loss, including the following broad types:
		  ○ Behavioral-based interventions
		  ○ Pharmacological (orlistat, sibutramine, and metformin) interventions
		  ○ Combination of behavioral-based and pharmacological treatment
		• Must be conducted in a primary care setting, judged to be feasible in "usual" primary care, or feasible for referral. Criteria for primary care feasible are:
		  ○ Could target patients seeking care in primary care settings
		  ○ The skills to deliver the intervention are or could be present in clinicians and/or related staff in the primary care setting
		  ○ Could generally be ordered/initiated by a primary care clinician

	Exclude	• Nonbehavioral or nonpharmacological interventions.
		• Surgical interventions (addressed as a contextual question).
		• Pharmacological agents that are not FDA approved for long-term weight loss:
		  ○ New agents being evaluated for FDA approval (e.g., rimonabant)
		  ○ Older amphetamine-like agents that have been taken off the market (e.g., fenfluramine and dexfenfluramine), are listed on the FDA site as discontinued (e.g., phenmetrazine or mazindol), or are only approved for short-term weight loss (e.g., phentermine)
		• Complementary and alternative treatments (e.g., chitosan, acupuncture)
		• Primary prevention programs
		• Community-level, population-based strategies

Appendix B Table 1. Review Inclusion and Exclusion Criteria

		• Sibutramine trials

Outcomes	Include	• **Health outcomes** (reported at ≥12 months after start of intervention or baseline assessment [if intervention start cannot be determined]):
		  ○ Decreased morbidity from diabetes mellitus, cardiovascular disease, cancer, arthritis, asthma, or sleep apnea
		  ○ Improved depression
		  ○ Improved emotional functioning (scores on emotional subscales of quality of life instruments)
		  ○ Physical fitness capacity or performance (not behavioral), physical functioning (scores on physical subscales of quality of life measures), or disability (global measures of disability, such as activities of daily living)
		  ○ Mortality
		• **Intermediate outcomes** (reported at ≥48 weeks after start of intervention or baseline assessment [if intervention start cannot be determined]):
		  ○ Reduction of weight or adiposity (required outcome); acceptable measures include weight (e.g., kilograms or pounds), relative weight (e.g., BMI, % overweight), total adiposity measures (e.g., DEXA, underwater weight, or comparable), or change in any of these measures.
		  ○ Weight maintenance after intervention has ended
		  ○ Metabolic consequences: glucose tolerance, blood pressure, dyslipidemia
		• **Adverse outcomes:**
		  ○ Serious treatment-related harms at any time point after an intervention began (e.g., death, medical issue requiring hospitalization or urgent medical treatment)
		  ○ Other treatment-related harms reported in trials meeting inclusion criteria for intermediate or health outcomes (e.g., inducement of eating disorders)

	Exclude	• Improved functioning (except as enumerated under health outcomes). • Cost effectiveness • Intermediate physiological outcomes other than glucose tolerance, blood pressure, or dyslipidemia • Behavioral changes (e.g., physical activity or diet) • Outcomes reported <12 months after start of intervention or baseline assessment (if time from intervention start cannot be determined), except for harms resulting in death, hospitalization, or the need for urgent medical treatment.
Study Designs	Include	• Randomized, controlled trials (RCTs) • Controlled clinical trials (CCTs) • Harms only: large cohort studies or case-control studies; must have an appropriate comparison group; large event monitoring, systematic evidence reviews of RCTs or CCTs (if useful information)
	Exclude	• Ecological studies • Case reports • Case series or other noncomparative designs • Nonsystematic reviews • Letters to the editor • Systematic evidence reviews of RCT or CCTs (look at reference list for references and considering including for harms if serious harms or otherwise adds to information)

Appendix B Table 2. Quality Rating Criteria

Design	USPSTF Quality Rating Criteria[293]	NICE Methodology Checklists[294]
Systematic reviews and meta-analyses	• Comprehensiveness of sources considered/ search strategy used • Standard appraisal of included studies • Validity of conclusions • Recency and relevance, especially for systematic reviews	• Study addresses an appropriate and clearly focused question • Description of the methodology used is included • Literature search is sufficiently rigorous to identify all relevant studies • Study quality is assessed and taken into account • Enough similarities between selected studies to make combining them reasonable
Case-control studies	• Accurate ascertainment of cases • Nonbiased selection of cases/controls with exclusion criteria applied equally to both • Response rate • Diagnostic testing procedures applied equally to each group • Measurement of exposure accurate and applied equally to each group • Appropriate attention to potential confounding variables	• Study addresses an appropriate and clearly focused question • Cases and controls are taken from comparable populations • Same exclusion criteria are used for both cases and controls • Percentage of each group (cases and controls) that participated in the study is specified • Participants and nonparticipants are compared to establish their similarities or differences • Cases are clearly defined and differentiated from controls • Controls are clearly established as noncases • Measures are taken to prevent knowledge of primary exposure influencing case ascertainment • Exposure status is measured in a standard, valid, and reliable way • Main potential confounders are identified and taken into account in the design and analysis • Confidence intervals are provided
Randomized, controlled trials	• Initial assembly of comparable groups employs adequate randomization, including first concealment and whether potential confounders were distributed equally among groups • Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination) • Important differential loss to followup or overall high loss to followup • Measurements are equal, reliable, and valid (includes masking of outcome assessment) • Clear definition of interventions • All important outcomes considered	• Study addresses an appropriate and clearly focused question • Assignment of subjects to treatment groups is randomized • Adequate concealment method is used • Subjects and investigators are kept blind about treatment allocation • Treatment and control groups are similar at the start of the trial • Only difference between groups is the treatment under investigation • All relevant outcomes are measured in a standard, valid, and reliable way • Percentage of individuals or clusters recruited into each treatment arm of the study who dropped out before completion is provided • All subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis) • When the study is carried out at more than one site, results are comparable for all sites

Appendix B Table 2. Quality Rating Criteria

Design	USPSTF Quality Rating Criteria[293]	NICE Methodology Checklists[294]
Cohort studies	• Initial assembly of comparable groups employs consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts • Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination) • Important differential loss to followup or overall high loss to followup • Measurements are equal, reliable, and valid (includes masking of outcome assessment) • Clear definition of interventions • All important outcomes considered	• Study addresses an appropriate and clearly focused question • Two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation • Study indicates how many of participants asked to take part did so, in each group being studied • Likelihood that some eligible subjects might have the outcome at the time of enrollment is assessed and taken into account in the analysis • Percentage of individuals or clusters recruited into each arm of the study who dropped out before completion is provided • Full participants and those lost to followup are compared, by exposure status • Outcomes are clearly defined • Assessment of outcome is made blind to exposure status • Where blinding is not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome • Measure of assessment of exposure is reliable • Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable • Exposure level or prognostic factor is assessed more than once • Main potential confounders are identified and taken into account in the design and analysis • Confidence intervals are provided
Diagnostic accuracy studies	• Screening test is relevant, available for primary care, and adequately described • Study uses a credible reference standard, performed regardless of test results • Reference standard interpreted independently of screening test • Handles indeterminate results in a reasonable manner • Spectrum of patients included in study • Sample size • Administration of reliable screening test	• Nature of the test being studied is clearly specified • Test is compared with an appropriate gold standard • Where no gold standard exists, a validated reference standard is used as a comparator • Patients for testing are selected either as a consecutive series or randomly, from a clearly defined study population • Test and gold standard are measured independently (blind) of each other • Test and gold standard are applied as close together in time as possible • Results are reported for all patients that are entered into the study • Prediagnosis is made and reported

Hierarchy of research design:

I	Properly conducted randomized, controlled trial
II-1	Well-designed controlled trial without randomization
II-2	Well-designed cohort or case-control analytic study
II-3	Multiple time series with or without the intervention; dramatic results from uncontrolled experiments
III:	Opinions of respected authorities, based on clinical experience; descriptive studies or case reports; reports of expert committee

Appendix B Table 3. Inclusion or Exclusion of Articles From the 2003 U.S. Preventive Services Task Force Review, Behavioral Trials

Author, Year	Included in Review	Reason for Exclusion
Wadden, 2001		Comparative effectiveness
Kuller, 2001	X	NA*
Tuomilehto, 2001	X	NA
Rothacker, 2001		Comparative effectiveness
Jones, 1999	X	NA
Stevens, 2001	X	NA
Swinburn, 1999		Worksite related
Jakicic, 1999		Comparative effectiveness
Leermakers, 1999		Comparative effectiveness
Sbrocco, 1999		Comparative effectiveness
Fogelholm, 2000		Comparative effectiveness
Jeffery, 1997		Weight gain prevention
Wing, 1996		Comparative effectiveness
Lindholm, 1995		Comparative effectiveness
OXCHECK, 1995		Not focused on weight loss
Knowler, 2002	X	NA
Ashley, 2001		Comparative effectiveness

* Secondary article to an included article.

Abbreviation: NA=not applicable.

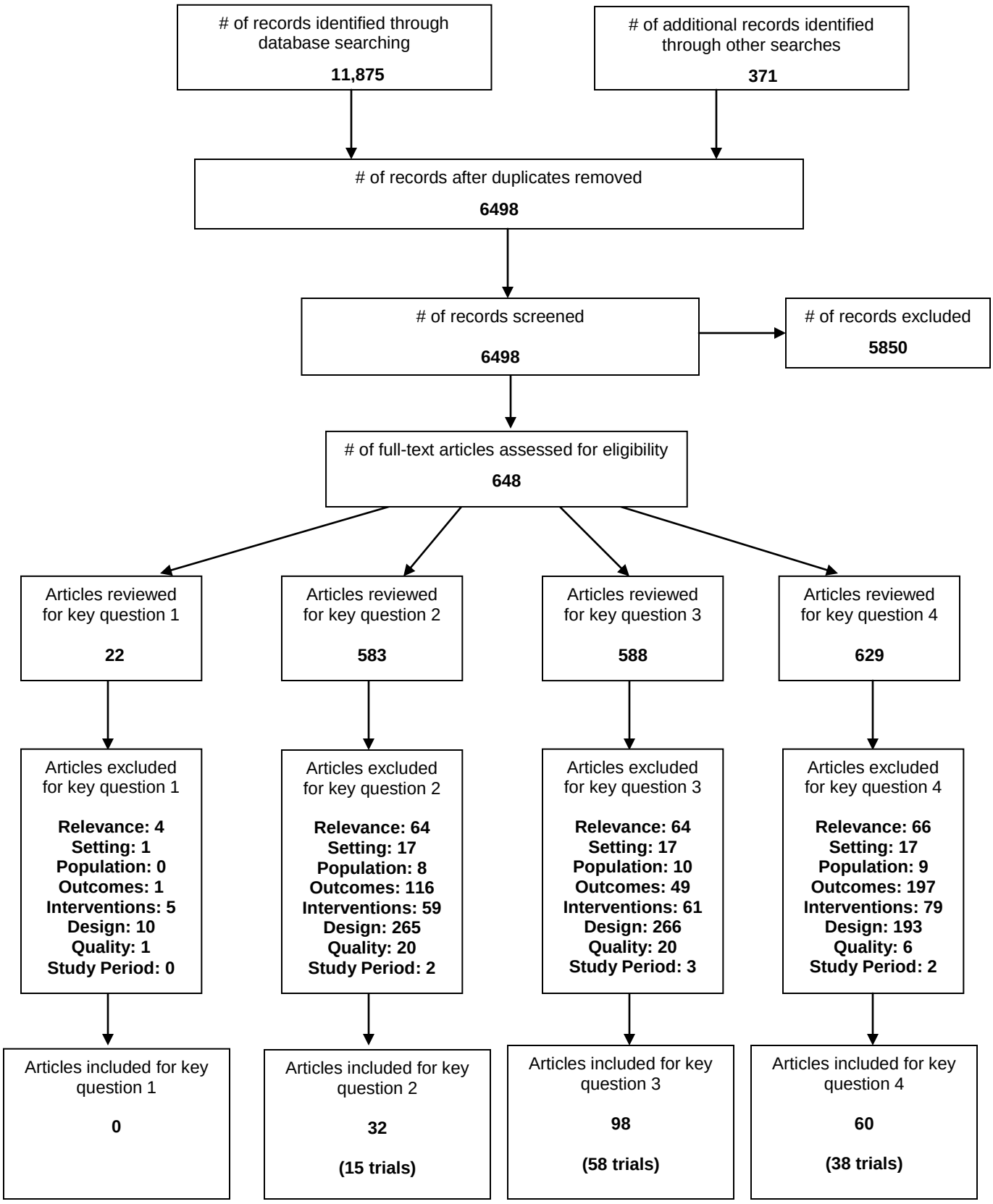
Appendix B Table 4. Inclusion or Exclusion of Articles From the 2003 U.S. Preventive Services Task Force Review, Medication Trials

Author, Year	Included for KQs 1–3	Reason for Exclusion	Included for KQ 4	Reason for Exclusion
James, 2000		Sibutramine study		Sibutramine study
Fujioka, 2000		Sibutramine study		Sibutramine study
Gokcel, 2001		Sibutramine study		Sibutramine study
Smith, 2001		Sibutramine study		Sibutramine study
Wirth, 2001		Sibutramine study		Sibutramine study
Dujovne, 2001		Sibutramine study		Sibutramine study
Van Gaal, 1998		<12 months of followup	X	NA
Hill, 1999	X	NA	X	NA
Karhunen, 2000	X	NA*	X	NA*
Micic, 1999		<12 months of followup		No harms outcomes
Muls, 2001		<12 months of followup	X	NA
Giugliano, 1993		<12 months of followup		No harms outcomes
Rissanen, 1998	X	NA*	X	NA*

* Secondary article to an included article.

Abbreviations: KQ=key question; NA=not applicable.

Appendix B Figure 1. Search Results and Article Flow



Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Anderssen, 1995[144] ODES (Oslo Diet and Exercise Study) Fair	**Design:** RCT **Location:** Norway **Recruitment Setting:** Ongoing screening examination of 40 year-olds in Oslo **Self-selected:** No	**Inclusion:** Aged 41-50 years; physically inactive (exercising at most once per week); BMI>24 kg/height^2; DBP 86-99 mmHg; total serum cholesterol 5.20-7.74 mmol/L; HDL cholesterol <1.20 mmol/L, and fasting serum triglycerides >1.4 mmol/L; based on the screening examination performed 1-10 years prior to baseline measurements **Exclusion:** Overt cardiovascular disease; diabetes; treated with antihypertensive drugs, acetylsalicylic acid, or other drugs that might interfere with the test results; diseases or personal traits that make them unsuited for participation; already on a lipid-lowering diet; regular endurance training 2 times per week or more	**N recruited or assessed for eligibility:** 25,000 **N eligible:** 660 **N excluded:** NR **N refused or other reason:** NR **N Randomized:** Total: 219 IG1 (diet): 55 IG2 (exercise): 54 IG3 (diet+exercise): 67 CG: 43 **Followup (12 mo), n (%):** Total: 209 (95*) IG1: 52 (95*) IG2: 49 (91*) IG3: 65 (97*) CG: 43 (100*) * *calc* **Cluster information:** NA	**Age (mean):** 44.9* **Sex (% female):** 9.6* **Race/Ethnicity:** NR **SES (income, education):** NR **BMI:** 28.8* **% Hypertension:** 0% taking hypertension meds **% Diabetes: 0%** **% Dyslipidemia:** NR * Age and BMI based on n with followup (n=209), sex based on n randomized (n=219)
Burke, 2005[145] ADAPT Fair	**Design:** RCT **Location:** Australia **Recruitment Setting:** Advertising **Self-selected:** Yes	**Inclusion:** Aged 40-70; BMI >25 kg/m^2; treated with 1-2 antihypertensive drugs for at least 3 months **Exclusion:** Clinic blood pressure >160/90 mmHg; consumption of >2 fish meals or >4 fish-oil capsules per week; alcohol intake >4 standard drinks/day for women and >6 standard drinks/day for men; drug- or insulin-treated diabetes; chronic renal failure (serum creatinine >120 nmol/L); chronic liver disease; symptomatic CVD of <3 months duration; other chronic debilitating disease; use of antihypertensive drugs for indications other than hypertension	**N recruited or assessed for eligibility:** 2252 **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N Randomized:** Total: 241 (calc) IG: 123 CG: 118 **Followup (16 mo), n (%):** *16 months* Total: 192 (79.7) (calc) IG: 102 (82.9) CG: 90 (76.3) **Cluster information:** NA	**Age (mean):** 56.2 (calc) **Sex (% female):** 55.6 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** 100 **% Diabetes:** 0% treated for DM **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Christian, 2008[146] Fair	**Design:** RCT **Location:** Colorado, US **Recruitment Setting:** Community-based health centers **Self-selected:** No	**Inclusion:** Latino/Hispanic in ethnicity with a language preference of either English or Spanish; aged 18 to 75 years; diagnosis of type 2 diabetes; BMI ≥25 kg/m^2; uninsured, Medicaid eligible, or Medicare beneficiaries **Exclusion:** Substance use or abuse; severe arthritis or other medical conditions limiting physical activity; recent myocardial infarction or stroke; peripheral vascular disease; undergone or scheduled for gastric bypass surgery	**N recruited or assessed for eligibility:** 322 **N eligible:** 310 **N excluded:** 4 **N refused or other reason:** 8 **N Randomized:** Total: 310 IG: 155 CG: 155 **Followup (12 mo), n (%):** Total: 273 (88.1) IG: 141 (91.0) CG: 132 (85.2) **Cluster information:** NA	**Age (mean):** 53.2 (calc) **Sex (% female):** 66.1 (calc) **Race/Ethnicity:** % Hispanic/Latino: 100 **SES (income, education):** "More than 65% of patients at both sites had family incomes at or below 100% of the US poverty level ($20,650 annually for a family of 4)." **% Hypertension:** NR **% Diabetes:** 100% **% Dyslipidemia:** NR **Other health problems (list):** NR
Cohen, 1991[147] Fair	**Design:** Cluster RCT **Location:** Pennsylvania, US **Recruitment Setting:** Family health center **Self-selected:** No (assumed)	**Inclusion:** Patient of physician participating in the study; diagnosis of hypertension; BMI ≥27.8 in men and ≥27.3 kg/m^2 in women; aged 20-75 years **Exclusion:** NR, although one patient excluded post-randomization "because of another health problem"	**N recruited or assessed for eligibility:** NR **N eligible:** 67 **N excluded:** 1 **N refused or other reason:** 36 **N Randomized (by physician):** Total: 30 IG: 15 (of 10 physicians) CG: 15 (of 8 physicians) **Followup (12 mo), n (%):** Total: 30 (100) IG: 15 (100) CG: 15 (100) **Cluster information:** Analysis Adjusted for Clustering: N Number of clusters: 18 Average cluster size: 2 (calc) Inter-cluster correlation: NR	**Age (mean):** 59.5 (calc) **Sex (% female):** NR **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** 100 **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Cussler, 2008[148] Fair	**Design:** RCT **Location:** Arizona, US **Recruitment Setting:** Newspaper and television advertisements **Self-selected:** Yes	**Inclusion:** 40-55 years of age; BMI between 25.0 and 38.0 kg/m^2; nonsmoker; free from major illnesses **Exclusion:** NR	**N recruited or assessed for eligibility:** ~300 **N eligible:** 161 **N excluded:** ~140 **N refused or other reason:** NR **N completed 4 mo intervention:** 136 **N randomized:** Total: 135 IG (Internet): 66 CG (Self-directed): 69 **Followup (16 mo), n (%):** Total: 111 (82.2) IG: 52 (78.8) CG: 59 (85.5) **Cluster information:** Randomized by wt loss group Analysis Adjusted for Clustering: Y Number of clusters: 6 Average cluster size: 22 Inter-cluster correlation: 0.02	**Age (mean):** 48.2 **Sex (% female):** 100 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR
Davis, 1992[149] Langford, 1991[260] Davis, 1989[261] TAIM Fair	**Design:** RCT **Location:** New York, Alabama, and Mississippi, US **Recruitment Setting:** Newspaper, radio, television advertising, referrals from private physicians or other sources of medical care, brochures distributed by mail, through community centers, or the workplace, etc. **Self-selected:** Yes	**Inclusion:** 21-65 years; at a preliminary screen: DBP of 100 mmHG or less for participants taking antihypertensive medicine or DBP between 90-104 mmHg for those on no treatment, between 110-160% of ideal weight by recall; at a secondary screen: No antihypertensive medication (participants on prior antihypertensive medication had their medication reduced then discontinued over a time period of up to 8 weeks), DBP between 90-100 mmHg, between 100-160% of ideal weight by clinic measurement **Exclusion:** History or other evidence of myocardial infarction, stroke, or bronchial asthma; creatine level ≥180 µmol/L; diabetes requiring insulin therapy; allergy to thiazides or β-blockers; actual or contemplated pregnancy; likelihood of difficulty in complying with the interventions	**N recruited or assessed for eligibility:** 10,148 **N eligible for first clinic visit:** 4985 **N at first clinic visit:** 1949 **N at second clinic visit:** 881 **N randomized:** Total: 200 (878 to all groups)* IG: 100* CG: 100* ** Note: 678 others were randomized to groups that couldn't be used (sodium restriction/potassium reduction diet; prescribed a diuretic or β-blocker)* **Followup (6, 24 mo), n (%):** *6 mo* Total: 179 (89.5) IG: 89 (89.0) CG: 90 (90.0) *24 mo* Total: 118 (59.0) IG: 57 (57.0) CG: 61 (61.0) **Cluster information:** NA	**Age (mean):** 47.7 (calc) **Sex (% female):** 50 (calc) **Race/Ethnicity:** % White: 66 (calc) % Black: 34 (calc) **SES (income, education):** % Education ≥ college: 64 (calc) **% Hypertension:** 100% **% Diabetes:** 0% DM requiring insulin% **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Diabetes Prevention Program Research Group, 1999[142] Diabetes Prevention Program Research Group, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2005[205] Diabetes Prevention Program Research Group, 2005[207] Ackermann, 2009[211] Diabetes Prevention Program Good	**Design:** RCT **Location:** 27 clinical centers, US **Recruitment Setting:** Mass media, mail, telephone contacts, and recruitment through employment or social groups or health care systems **Self-selected:** Yes (assume mostly volunteer)	**Inclusion:** Fasting plasma glucose 95-125 mg/dL (≤125 mg/dL in American Indian clinics); impaired glucose tolerance (2-hour postchallenge glucose 140-199 mg/dL after a 75 g glucose load); aged ≥25 years; BMI ≥24 kg/m^2 (≥22 kg/m^2 for Asian Americans) **Exclusion:** Recent MI, sx of CHD, diabetes at baseline; medical conditions likely to limit life span and/or increase risk of intervention; conditions or behaviors likely to affect conduct of the trial; medications and medical conditions likely to confound the assessment for diabetes	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N Randomized:** Total: 3234 IG-Metformin: 1073 IG-Lifestyle: 1079 CG: 1082 **Followup (12, 24, 36 mo), n (%):** *12 mo* Total: 3070 (94.9) (calc) IG-M: 1017 (94.8 (calc)) IG-L: 1026 (95.1 (calc)) CG: 1027 (94.9 (calc)) *36 mo* Total: 1921 (59.4) (calc) IG-M: 626 (58.3 (calc)) IG-L: 638 (59.1 (calc)) CG: 657 (60.7 (calc)) **Cluster information:** NA	**Age (mean):** 50.6 **Sex (% female):** 67.7 **Race/Ethnicity:** *% White:* 54.7 *% African American:* 19.9 *% Hispanic:* 15.7 *% American Indian:* 5.3 *% Asian/Pacific Islanders:* 4.4 **SES (income, education):** NR **% Hypertension:** 29.6% HTN, 45% HTN or meds for HTN **% Diabetes:** 0 **% Dyslipidemia:** 44.1% had elevated LDL or taking medication **Other health problems (list):** History of stroke, revascularization, MI, MI by ECG, elevated TG, Metabolic syndrome
Fitzgibbon, 2010[204] ORBIT Fair	**Design:** RCT **Location:** Illinois, US **Recruitment Setting:** University of Illinois (mass email and face-to-face recruitment near intervention site) **Self-selected:** Mixed	**Inclusion:** Women; BMI between 30-50 kg/m^2; self-identified as African American or Black; 30-65 years of age; able to participate in an activity program requiring 30 minutes of uninterrupted moderate activity; able to attend class sessions **Exclusion:** Unable to exercise because of emphysema, chronic bronchitis, or asthma; used a cane, walker, or wheelchair for mobility; planning to move out of the area; treated for cancer (excluding skin cancer other than melanoma) in the past 5 years; participating in a formal weight-loss program or taking weight-loss medications prescribed by a doctor; pregnant, nursing, or planning a pregnancy; using illegal drugs or consuming >2 alcoholic drinks per day on a daily basis	**N recruited or assessed for eligibility:** 690 **N eligible:** 482 **N excluded:** 229 **N refused or other reason:** 248 **N randomized:** Total: 213 IG: 107 CG: 106 **Followup (18 mo), n (%):** Total: 190 (89.2) IG: 93 (86.9) CG: 97 (91.5) **Cluster information:** NR	**Age (mean):** 46.0 **Sex (% female):** 100 **Race/Ethnicity:** *% Black:* 100 **SES (income, education):** *Mean years of education (SD):* 14.9 (2.0) *Median household income/year (25th, 75th percentiles):* $42,500 (30,000, 62,500) **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Haapala, 2009[151] Fair	**Design:** RCT **Location:** Finland **Recruitment Setting:** Newspaper advertisement and telephone screening **Self-selected:** Yes	**Inclusion:** Aged 24-44 years; BMI 25-36 kg/m^2; access to a mobile phone and an internet connection; no diagnosed chronic disease; no major psychiatric disease; no current, planned, or previous pregnancy within 6 months **Exclusion:** NR	**N recruited or assessed for eligibility:** NR **N eligible:** 156 **N excluded:** 23 **N refused or other reason:** 8 **N randomized:** Total: 125 IG: 62 CG: 63 (1 refused to participate after randomization) **Followup (12 mo), n (%):** Total: 85 (68.0) IG: 45 (72.6) CG: 40 (63.5) **Cluster information:** NA	**Age (mean):** 38.1 (calc) **Sex (% female):** 77.4 **Race/Ethnicity:** NR **SES (income, education):** % Vocational school: 16.9 % College degree: 60.5 % Graduate degree: 15.3 p<0.05 for chi-square test between IG and CG **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR
Hypertension Prevention Trial Research Group, 1990[143] HPT Good	**Design:** RCT **Location:** US (multiple states) **Recruitment Setting:** Direct mailings from various lists depending on the location (e.g., students, magazine subscribers, registered voters) **Self-selected:** Yes	**Inclusion:** Men and women aged 25-49 years at entry; diastolic blood pressure of 76-99 mmHg at the first baseline visit; 78-89 mmHg at the second visit 7-30 days later **Exclusion:** Using hypertensive medication; evidence of cardiovascular disease; BMI of 35 or more; dietary requirements incompatible with the dietary counseling regimen; drank 21 or more alcoholic beverages per week; perceived as unable to comply with the counseling regimens or data collection schedule	**N recruited:** 223,815 (mailings) **N assessed for eligibility:** 11,810 **N eligible:** NR **N excluded:** 8599 **N refused or other reason:** 2370 **N randomized:** Total: 251 (590 other participants randomized to other groups) IG (Cal): 125 CG (Na-Cal control): 126 **Followup (6, 12, 36 mo), n (%):** *6 months* Total: 233 (92.8) IG: 121 (96.0) CG: 112 (89.6) *12 months* Total: 229 (91.2 (calc)) IG: 113 (90.4) CG: 116 (92.1) *36 months* Total: 233 (92.8) IG: 116 (92.0) CG: 117 (93.6) **Cluster information:** NA	**Age (mean):** 38.8 (calc) **Sex (% female):** 32.7 (calc) **Race/Ethnicity:** % White: 80.1 (calc) **SES (income, education):** % College graduate: 49.8 (calc) **% Hypertension:** 0% using HTN meds or have DBP>89 **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Irwin, 2003[152] Frank, 2005[263] Mohanka, 2006[264] PATH Good	**Design:** RCT **Location:** Washington, US **Recruitment Setting:** Mass mailing and media placements **Self-selected:** Yes	**Inclusion:** Postmenopausal women aged 50-75 years; sedentary (<60 min/wk of moderate- and vigorous-intensity recreational activity and maximal oxygen consumption <25.0 mL/kg per minute); BMI >25.0 or BMI 24-25 and body fat >33.0%; fasting blood glucose <140 mg/dL **Exclusion:** Taking hormone replacement therapy; clinical diagnosis of diabetes; smokers	**N recruited or assessed for eligibility:** 102,459 letters sent in mass mailing 7,830 interested in trial **N eligible:** NR **N excluded:** 6451 **N refused or other reason:** 1,206 **N randomized:** Total: 173 IG: 87 CG: 86 **Followup (12 mo), n (%):** Total: 170 (98.3 (calc)) IG: 84 (96.6 (calc)) CG: 86 (100) **Cluster information:** NA	**Age (mean):** 60.8 **Sex (% female):** 100 **Race/Ethnicity (calc):** % Non-Hispanic white: 87 % African American: 3 % Asian American: 5 **SES (income, education):** % Education level (calc) High school graduate: 11.0 Some college: 41.0 College graduate: 8.7 Graduate degrees: 39.3 **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems (list):** NR
Jeffery, 1993[153] Jeffery, 1995[289] Trial of Food Provision and Monitary Incentives Fair	**Design:** RCT **Location:** Pennsylvania and Minnesota, US **Recruitment Setting:** Newspaper and radio advertisements, mailed invitations **Self-selected:** Yes	**Inclusion:** 14-32 kg overweight according to 1983 insurance industry standards; aged 25-45 years; non-smoker; drink <3 alcoholic beverages/day; not on a special diet or allergic to any foods; able to exercise; free of current serious diseases; not taking prescription medications including oral contraceptives **Exclusion:** NR	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 202 IG1 (standard behavioral therapy): 40 IG2 (SBT + food provision): 40 IG3 (SBT + incentive): 41 IG4 (SBT + FP + I): 41 CG: 40 **Followup (12 mo), n (%):** Total: 176 (calc) (87) IG: NR CG: NR **Followup (18 mo), n (%):** Total: 172 (calc) (85) IG: NR CG: NR **Followup (30 mo), n (%):** Total: 177 (88) IG: NR CG: NR **Cluster information:** NA	**Age (mean):** 37.5 (calc) **Sex (% female):** 50 (calc) **Race/Ethnicity:** *% White:* 92.1 (calc) **SES (income, education):** *% Non-college grad:* 42.6 (calc) **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Jones, 1999[154] Hansson, 1994[265] The HOT Study Group, 1993[266] Hypertension Optimal Treatment (HOT) Substudy Fair	**Design:** RCT **Location:** US **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Age 50-80 years; DBP 100-115; BMI ≥27 kg/m^2 **Exclusion:** Malignant hypertension; secondary hypertension; stroke or MI within 12 months prior to randomization; decompensated congestive heart failure; other serious concomitant disease which, in the opinion of the investigator, could affect survival during the next 2-3 years; patients who, in the opinion of the investigator, require a beta-blocker, ACE-inhibitor or diuretic for reasons other than hypertension; patients who, in the opinion of the investigator, require antiplatelet or anticoagulant treatment; insulin-treated DM; patients with known hypersensitivity to felodipine; patients with known contraindications to low-dose ASA	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: says 112, but IG+CG=111, not sure which numbers are accurate IG: 55 CG: 56 **Followup (30 mo), n (%):** Total: 102 (91.1 (calc)) IG: 51 CG: 51 **Cluster information:** NA	**Age (mean):** 58 (calc)* **Sex (% female):** 52.0 (calc)* **Race/Ethnicity:*** *% African-American:* 40.2 *% White:* 59.8 **SES (income, education):** NR **% Hypertension:** 100 **% Diabetes:** 0% insulin-treated DM **% Dyslipidemia:** NR **Other health problems (list):** NR *for those analyzed (n=102)
Kastarinen, 2002[155] LIHEF Study (Lifestyle Intervention against Hypertension in Eastern Finland) Fair	**Design:** RCT **Location:** Finland **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Aged 25-74 years; systolic blood pressure 140-179 mmHg and/or diastolic blood pressure 90-109 mmHg or on antihypertensive drug therapy **Exclusion:** Secondary hypertension, mental or physical illness serious enough to potentially influence the compliance with study procedures; alcoholism; type 1 diabetes; current or planned pregnancy; history of myocardial infarction or stroke within the preceding 3 months	**N recruited or assessed for eligibility:** NR **N eligible:** 813 **N excluded:** NR **N refused or other reason:** 98 **N Randomized:** Total: 715 IG: 360 CG: 355 **Followup (12 mo), n (%):** Total: 592 (83) (calc) IG: 317 (88) CG: 275 (77) **Followup (24 mo), n (%):** Total: 587 (82) (calc) IG: 304 (84) CG: 283 (80) **Cluster information:** NA	**Age (mean):** 54.3 **Sex (% female):** 53 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** 100 **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** History of CVD: 4%

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Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Kulzer, 2009[156] Fair	**Design:** RCT **Location:** Germany **Setting:** NR **Self-selected:** NR	**Inclusion:** Aged 20-70 years; BMI ≥26 kg/m2; impaired glucose tolerance or impaired fasting glucose; ability to read and understand German; elevated diabetes risk based on a Diabetes Risk Score of >10 or according to assessment of a primary care physician **Exclusion:** Manifest diabetes or diagnosis of a serious illness (e.g., cancer)	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N Randomized:** Total: 182 IG: 91 (assumed) CG: 91 (assumed) **Followup (12 mo), n (%):** Total: 165 (90.7) IG: NR CG: NR **Cluster information:** NA	**Age (mean):** 56.3 **Sex (% female):** 43 **Race/Ethnicity:** NR **SES (income, education):** 13.2 year education **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** NR
Langford, 1985[157] Wassertheil-Smoller, 1985[267] DISH Fair	**Design:** RCT **Location:** Multiple states, US **Recruitment Setting:** Hypertension Detection and Follow-up Program (HDFP) clinics **Self-selected:** No	**Inclusion:** Active, controlled former Stepped Care HDFP participants who were originally identified through population-based screening; DBP of 95 mmHg or higher on first screening and 90 mmHg or higher on confirmation; BP controlled in past year (no SBP>180 past yr, average DBP<95 past yr, average of last 2 DBP <91 and neither >95 **Exclusion:** History of congestive heart failure; history or ECG evidence of myocardial infarction; history of stroke or transient ischemic attacks; creatine level of 2.5 mg/dL or more on at least two determinations; history of personal problems or intercurrent illness making compliance with dietary regimen difficult or impossible; severe alcoholism; pregnancy; β-blocker therapy for angina; glucocorticoid therapy for an indefinite period	**N recruited or assessed for eligibility:** 865 **N eligible:** 584 **N excluded:** 281 **N refused or other reason:** 88 **N Randomized:** Total: 496 *Overweight* IG1 (Weight reduction): 87 IG2 (Sodium restriction): 101 CG1 (no medications): 89 CG2 (continue medications): 48 *Not overweight* IG (sodium restriction): 68 CG1 (no medications): 70 CG2 (continue medications): 33 *Note: IG1 and CG1 from the overweight group are the only 2 groups of interest, n=176.* **Followup (13 mo), n (%):** Total: 144 (81.8) IG: 67 (77.0) CG: 77 (86.5) **Cluster information:** NA	**Age (mean):** 56.7 (calc) **Sex (% female):** 65.9 (calc) **Race/Ethnicity:** *% Black:* 65.9 (calc) **SES (income, education):** NR **% Hypertension:** 100 % Mild hypertensives: 42.6 (calc) **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Martin, 2008[158] Martin, 2006[268] Fair	**Design:** RCT **Location:** Louisiana, US **Recruitment Setting:** Primary care physician office waiting rooms **Self-selected:** No	**Inclusion:** Women between 18 and 65 years old; overweight or obese (BMI≥25 kg/m^2); low income (<$16,000 annual income); attendees of the primary care clinic for at least 1 year; free of serious or uncontrolled medical conditions (e.g. renal or hepatic failure, cancer, immunological disease, uncontrolled hypertension) **Exclusion:** Use of weight-altering medications; pregnancy; severe psychiatric illness; alcohol intake >14 drinks per week; serious physical illness	**N recruited or assessed for eligibility:** 256 **N eligible:** 144 **N excluded:** 91 **N refused or other reason:** 21 **N Randomized:** 144 IG: 71 CG: 73 **N ITT:** Total: 137 IG: 68 CG: 69 **Followup (9, 12, 18 mo), n (%):** *9 months* Total: 102 (70.8) IG: NR CG: NR *12 months* Total: 93 (64.6) IG: NR CG: NR *18 months* Total: 91 (63.2) IG: NR (56) CG: NR (77) **Cluster information:** Analysis Adjusted for Clustering: Y Number of clusters: 8 Average cluster size: 17 Inter-cluster correlation: NR	**Age (mean):** 41.8 (calc) **Sex (% female):** 100 **Race/Ethnicity:** *% African American:* 100 **SES (income, education):** *% Completed high school/GED:* 74.3 (calc) **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR
Mayer-Davis, 2004[159] POWER Fair	**Design:** RCT **Location:** South Carolina, US **Recruitment Setting:** Rural primary health care centers **Self-selected:** No	**Inclusion:** Aged 45 years and older; clinical diagnosis of diabetes; BMI ≥25 kg/m^2 **Exclusion:** Any limitation that would prohibit full participation in the study (e.g., metastatic cancer, multiple or recent MI or stroke, dialysis for end-stage renal disease, severe psychiatric disease or dementia, or inability to walk)	**N recruited or assessed for eligibility:** 717 (calc) **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 187 IG (R-L): NR IG (I-L): NR CG: NR **Followup (12 mo), n (%):** Total: 152 (81.3) IG1: 47 (NR) IG2: 49 (NR) CG: 56 (NR) **Cluster information:** NA	**Age (mean):** 60.4 (calc) **Sex (% female):** 80.3 (calc) **Race/Ethnicity:** *% Black:* 81.6 (calc) *% Non-Hispanic White:* 17.8 (calc) *% Other:* 0.6 (calc) **SES (income, education):** *% Less than HS:* 48.7 (calc) **% Hypertension:** 77.6 (calc) **% Diabetes:** 100 **% Dyslipidemia:** NR **Other health problems (list):** NR Baseline characteristics for participants still present at 12 mo

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Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Mensink, 2003[160] Mensink, 2003[269] Fair	**Design:** RCT **Location:** The Netherlands **Recruitment Setting:** Selected from an existing cohort of participants from civil registries **Self-selected:** No	**Inclusion:** Aged 40-70 years and a family history of diabetes or a BMI ≥25 kg/m^2; mean 2-hour glucose concentration of two oral glucose-tolerance tests between 7.8-12.5 mmol/L; mean fasting blood glucose ≤7.8 mmol/L; Caucasian **Exclusion:** Known or overt diabetes; previously diagnoses diabetes, excluding gestational diabetes; mean 2-hour blood glucose >12.5 mmol/L; mean fasting blood glucose >7.8 mmol/L; medication use known to interfere with glucose tolerance; participation in regular vigorous exercise or an intensive weight reduction program during the last year before the start of the study; presence of any chronic disease that hampered participation in a lifestyle intervention program; improbability of a 5-year survival	**N recruited or assessed for eligibility:** 6108 **N eligible:** NR **N excluded:** 2504 **N refused or other reason:** 3490 **N Randomized:** Total: 114 IG: 55 CG: 59 **Followup (24 mo), n (%):** Total: 92 (80.7) IG: 41 (74.5) CG: 51 (86.4) **Cluster information:** NA	**Age (mean):** 56.7 (calc) **Sex (% female):** 43.9 (calc) **Race/Ethnicity:** % Caucasian: 100 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 0 100% impaired glucose tolerance **% Dyslipidemia:** NR **Other health problems (list):** NR
Mitsui, 2008[161] Fair	**Design:** RCT **Location:** Japan **Recruitment Setting:** Public announcement **Self-selected:** Yes	**Inclusion:** 50-69 years of age; waist circumference ≥85 cm (men) or ≥90 cm (women); no regular exercise for the past 6 months; present non-smoker; ambulant; no history of serious disease such as diabetes, cancer, stroke, heart disease, or kidney disease requiring dialysis **Exclusion:** NR	**N recruited or assessed for eligibility:** NR **N eligible:** 46 **N excluded:** NR **N refused or other reason:** NR **N Randomized:** Total: 46 IG: 24 CG: 22 **Followup (12 mo), n (%):** Total: 43 (93.5) IG: 22 (91.7) CG: 21 (95.5) **Cluster information:** NA	**Age (mean):** 63.3 (calc) **Sex (% female):** 54.3 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** % Taking medication for hypertension: 17.4 (calc) **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

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Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Moore, 2003[162] Fair	**Design:** Cluster randomized trial **Location:** England **Recruitment Setting:** General practices **Self-selected:** No	**Inclusion:** Obese adults (BMI ≥30 kg/m^2); aged 16 to 64 years **Exclusion:** NR	**N recruited or assessed for eligibility:** NR **N eligible:** 991 **N excluded:** NR **N refused or other reason:** NR **N Lost during run-in:** 148 **N Randomized:** Total: 843 IG: 415 CG: 428 **Followup (12, 18 mo), n (%):** *12 months* Total: 565 (67.0) IG: 279 (67.2) CG: 286 (66.8) *18 months* Total: 531 (63.0) IG: 256 (61.7) CG: 275 (64.3) **Cluster information:** Analysis Adjusted for Clustering: Y	**Age (mean):** 48.6 (calc) **Sex (% female):** 73.9 (calc) **Race/Ethnicity:** NR **SES (income, education):** *Median (IQR) SES in practice:* IG: 3.4 (-0.9, 5.8), CG: 2.4 (0.1, 7.1) **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR
Narayan, 1998[163] Fair	**Design:** RCT **Location:** Arizona, US **Recruitment Setting:** Residents of Gila River Indian Community through direct invitation and media ads **Self-selected:** Mixed (84/95 invited, 11 self-selected)	**Inclusion:** Obesity (BMI ≥27 kg/m^2 for men and ≥25 kg/m^2 for women); normoglycemia (2-hour post-load plasma glucose <7.8 mM); aged 25-54 years **Exclusion:** Previous diagnosis of diabetes; current self-reported physical activity ≥20 hours/week; prescribed low-fat diet; randomization of another member of the household to the study; evidence of ischemic heart disease; chronic illness; current treatment with steroids, thiazides, or beta blockers; pregnancy or intention to become pregnant soon; conditions likely to interfere with informed consent or participation	**N recruited or assessed for eligibility:** 404 **N screened:** 190 **N eligible:** 130 **N excluded:** 60 **N refused or other reason:** 35 **N randomized:** Total: 95 IG: 48 CG: 47 **Followup (6, 12 mo), n (%):** *6 mo* Total: 87 (91.6) IG: NR CG: NR *12 mo* Total: 88 (92.6) IG: NR CG: NR **Cluster information:** NA	**Age (mean):** 33.5 (calc) **Sex (% female):** 75.8 (calc) **Race/Ethnicity:** *% Pima Indian:* 100 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems (list):** NR

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Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Parikh, 2010[208] Project HEED Fair	**Design:** RCT **Location:** New York, US **Recruitment Setting:** Community **Self-selected**: NR	**Inclusion**: Aged ≥ 18 years; East Harlem resident; English or Spanish speaking; BMI ≥ 25 kg/m^2; not pregnant; no diabetes; did not use glucose-altering medications; and able to participate in group sessions; pre-diabetes glucose levels **Exclusion:** Normal or diabetes-level glucose readings	**N recruited or assessed for eligibility: 555** **N eligible:** 103 **N excluded:** 75 **N refused or other reason: 310** **N randomized:** Total: 99 IG: 50 CG: 49 **Followup, n (%):** *12 mo* Total: 72 (72.7) IG: 35 (70.0) CG: 37 (75.5) **Cluster information:** NA	**Age (mean):** 48 **Sex (% female):** 85 **Race/Ethnicity:** *% Hispanic:* 89 *% Black:* 9 **SES (income, education):** *% No high school diploma:* 58 *% Annual income:* < $15,000: 62 $15,000-30,000: 26 > $30,000: 12 **% Hypertension:** 31 **% Diabetes:** 0% (all pre-diabetic) **% Dyslipidemia:** 25 **Other health problems (list):** Depressive symptoms, food insufficiency, family history of diabetes
Perri, 1988[164] Fair	**Design:** RCT (all groups received treatment for 6 months, but then treatment differed for a maintenance period) **Location:** NR (authors from New York and Indiana, US) **Recruitment Setting:** Advertisements **Self-selected:** Yes	**Inclusion:** 20-100% over ideal body weight based on Metropolitan Life Insurance Company norms; not currently involved in other weight-loss programs; not suffering from any significant health disorders; not taking any medication that would affect weight loss; willing to commit themselves to involvement in the study over a 24-month period; not pregnant or planning to become pregnant during the course of the study **Exclusion:** NR	**N recruited or assessed for eligibility:** 182 **N eligible:** 123 **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 123 IG1 (BC): 25 IG2 (BCS): 25 IG3 (BCA): 26 IG4 (BCAS): 26 CG (B): 21 **Followup (6, 24 mo), n (%):** *6 months (initial tx phase)* Total: 94 (76.4) IG1 (BC): 19* (76.0) IG2 (BCS): 18* (73.1) IG3 (BCA): 20* (76.0) IG4 (BCAS): 20* (76.9) CG (B): 17* (81.0) *24 months* Total: 91 (74.0) IG1 (BC): 19 (76.0*) IG2 (BCS): 19 (76.0*) IG3 (BCA): 18 (69.2*) IG4 (BCAS): 19 (73.1*) CG (B): 16 (76.2*) * calc **Cluster information:** NA	**Age (mean):** NR (range 22-59) **Sex (% female):** 78.9 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

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Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Pritchard, 1999[165] Fair	**Design:** RCT **Location:** Australia **Recruitment Setting:** Screened opportunistically when attending university general practice **Self-selected:** No	**Inclusion:** Aged between 25 and 65 years; pre-existing diagnosis of overweight, hypertension, or type 2 diabetes or without pre-existing diagnosis but appeared to be overweight on presentation at reception **Exclusion:** Mentally ill; intellectually handicapped; terminally ill; acutely ill; pregnant; participating in other health education programs	**N recruited or assessed for eligibility:** 296 **N eligible:** NR **N excluded:** NR **N refused or other reason:** 44 **N randomized:** Total: 273 (270*) IG1 (dietitian): 88* IG2 (doctor + dietitian): 92* CG: 90 **Followup (12 mo), n (%):** Total: 177 (65.6)* IG1: 48 (54.5)* IG2: 65 (70.6)* CG: 64 (71.1)* **Cluster information:** NA * *Note: This includes only those who were overweight.Patients did not have to be overweight for inclusion.Followup rates for the whole sample are not available. Results are only abstracted for the overweight sample.*	**Age (mean):** NR (73% of patients were less than 50 years old) **Sex (% female):** 72.5 (calc) **Race/Ethnicity:** NR **SES (income, education):** 58% of patients in most disadvantaged quartile, 20% were more disadvantaged, 20% were less disadvantaged, and 2% were least disadvantaged **% Hypertension:** 32 (calc) **% Diabetes:** 2 (calc) **% Dyslipidemia:** NR **Other health problems (list):** Overweight *Note: Baseline characteristics include all participants, including those who were not overweight.*
Silva, 2009[166] Silva, 2008[270] Teixeira, 2009[271] Fair	**Design:** RCT **Location:** Portugal **Recruitment Setting:** Website, newspapers, TV and radio ads, and fliers distributed in health care centers, local services, schools, etc. **Self-selected:** Yes	**Inclusion:** Female; 25-50 years old; premenopausal; BMI between 25-40 kg/m^2; willing to attend weekly meetings for 1 year and be tested regularly for 3 years; be free from major illness; not taking or having taken in the previous year medication known to interfere with body weight regulation (namely anti-depressive medication); willing to not participate in any other formal or informal weight loss program during the first year of the study (intervention group only); not pregnant or lactating **Exclusion:** NR	**N recruited or assessed for eligibility:** 943 **N eligible:** 290 met initial crit **N excluded:** 653 (+19 excluded post-rand) **N refused or other reason:** NR **N randomized:** Total: 258 IG: NR CG: NR **N excluded after randomization:** 19 **N "valid initial sample":** Total: 239 IG: 123 CG: 116 **Followup (12 mo), n (%):** Total: 208 (87.0) (80.6 of all rand) IG: 115 (93.5) CG: 93 (80.2) **Cluster information:** NA	**Age (mean):** 37.6 **Sex (% female):** 100 **Race/Ethnicity:** NR **SES (income, education):** *% Higher education:* 67 **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Simkin-Silverman, 2003[167] Simkin-Silverman, 1998[272] Kuller, 2001[273] Park, 2007[274] Women's Healthy Lifestyle Project (WHLP) Good	**Design:** RCT **Location:** Pennsylvania, US **Recruitment Setting:** Mass mailing to registered voters **Self-selected:** Yes	**Inclusion:** Women aged 44-50; <3 months amenorrhea in the 6 months prior to the initial telephone interview; not taking HRT; no surgically induced menopause (hysterectomy or bilateral oophorectomy); DBP <95 mmHg; BMI 20-34 kg/m2; fasting glucose <140 mg/dl; LDL 80-160 mg/dl; total cholesterol 140-260 mg/dl; not taking any lipid-lowering agents, insulin, thyroid, antihypertensive, or psychotropic medications; not treated for cancer in the past 5 years; not having participated in a weight reduction program within the past 4 months **Exclusion:** NR	**N recruited or assessed for eligibility:** 2115 **N eligible for initial screening:** 1021 **N eligible among screened:** 637 **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 535 IG: 260 CG: 275 N complete 6- and 18-mo data: Total: 489 (91.4) IG: 236 (85.8) CG: 253 (97.3) **Followup (54 mo), n (%):** Total: 509 (95.1) (calc) IG: 246 (94.6 (calc)) CG: 263 (95.6 (calc)) **Cluster information:** NA	**Age (mean):** 47 **Sex (% female):** 100 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** 0% HTN meds or DBP≥95 **% Diabetes:** NR **% Dyslipidemia:** 0% lipid lowering meds or TC≥260 **Other health problems (list):** NR
Stevens, 1993[168] Whelton, 1992[275] The Trials of Hypertension Prevention Collaborative Research Group, 1992[276] Trials of Hypertension Prevention Phase I Good	**Design:** RCT **Location:** 10 clinical centers, US **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Aged 30-54 years; high-normal DBP (80-89 mmHg); BMI <36 kg/m^2 **Exclusion:** Hypertensive (DBP ≥90 mmHg or use of BP meds within 2 months of the first evaluation); CVD; contraindication to any of the TOHP Phase I interventions; might have difficulty complying with the treatment or follow-up requirements of the trial; DM; gastrointestinal tract disease; chronic renal failure; malignant neoplasm; current pregnancy or intent to become pregnant during the study; recent history of psychiatric disorders	**N recruited or assessed for eligibility:** 16,821 **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 2182 overall, 564 to weight loss IG and CG IG: 308 CG: 256 **Followup (18 mo), n (%):** Total: 528 (93.6 (calc)) IG: 293 (95.1 (calc)) CG: 235 (91.8 (calc)) **Cluster information:** NA	**Age (mean):** 43.0 **Sex (% female):** 29.9 (calc) **Race/Ethnicity:** *% White:* 82.2 *% Black:* 15.0 **SES (income, education):** College graduates: 52.5% **% Hypertension:** 0 **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Stevens, 2001[169] Hollis, 1995[277] TOHP, 1997[278] Trials of Hypertension Prevention Phase II Good	**Design:** RCT **Location:** 9 clinical centers, US **Recruitment Setting:** Mass mailings, sometimes tailored; community screenings through worksite health fairs, churches, shopping centers, and other community settings; blood collection agencies; newspaper, radio, and television advertising; referrals from medical providers **Self-selected:** Mixed (primarily self-selected)	**Inclusion:** Aged 30-54 years; nonmedicated DBP 83-89 mmHg and SBP <140 mmHg; BMI 26.1-37.4 for men and 24.4-37.4 for women (110-165% of ideal body weight) **Exclusion:** Current treatment with medications that might affect BP; clinical or laboratory evidence of CVD; DM; renal insufficiency (serum creatine concentration ≥150 mmol/L for men and ≥132 mmol/L for women); current or planned pregnancy; alcohol intake > 21 drinks/wk; current or planned pregnancy	**N recruited or assessed for eligibility:** 18,326 **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 1191 (does not include sodium and sodium + weight loss groups) IG: 595 CG: 596 **Followup (36 mo), n (%):** Total: 1101 (92.4) (calc) IG: 547 (calc) (92) CG: 554 (calc) (93) **Cluster information:** NA	**Age (mean):** 43.3 **Sex (% female):** 34.3 (calc) **Race/Ethnicity:** White: 78.8% Black: 17.5% **SES (income, education):** *% College graduate:* 50.8 **% Hypertension:** 0 **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems (list):** Elevated (but sub-clinical) DBP
Svetkey, 2008[170] Weight Loss Maintenance Trial PROTOCOL, 2008[279] WLM Good	**Design:** RCT **Location:** 4 clinical centers, US **Recruitment Setting:** Mass mailings, advertisements in local papers and radio, screening events, physician referral **Self-selected:** Yes	**Inclusion:** Age 25+, BMI 25-45 at start of Phase I; taking medication for hypertension, and/or dyslipidemia; no active CVD (with a positive Rose angina questionnaire or a CVD event >12 months before study entry and a negative stress test could join with permission from physician); access to a telephone and Internet; keep a 5-day food diary during the screening; weight loss of 4+ kg during Phase I **Exclusion:** Medication-treated DM; recent cardiovascular event, angina, cancer or other medical or psychiatric conditions that would preclude full participation; weight loss >9 kg in the last 3 months; recent use of weight loss medications or surgery; member of a household with a randomized participant or staff of WLM; use of meds for wt loss, psychosis or bipolar; pregnant, nursing or planning pregnancy; >21 drinks/wk	**N recruited or assessed for eligibility:** 3178 after pre-screening, 2402 attended in-person screening **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 1032 IG1 (interactive technology): 348 IG2 (personal contact): 342 CG: 342 Followup (12 mo), n (%): Total: 985 (95.4 (calc)) IG1: 333 (95.7 (calc)) IG2: 328 (95.9 (calc)) CG: 324 (94.7 (calc)) **Followup (30 mo), n (%):** Total: 964 (93.4) (calc) IG1: 323 (92.8 (calc)) IG2: 321 (93.9 (calc)) CG: 320 (93.6 (calc)) **Cluster information:** NA	**Age (mean):** 55.6 **Sex (% female):** 63.4 **Race/Ethnicity:** *% African American:* 37.6 *% Non- African American:* 62.4 **SES (income, education):** *Household income/y* <$60,000: 42.6% ≥$60,000: 57.4% *Education* ≤Some college: 38.4% College degree: 61.6% **% Hypertension:** 87% HTN meds **% Diabetes:** 0% DM meds **% Dyslipidemia:** 40% lipid meds **Other health problems (list):** NR

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
ter Bogt, 2009[171] Fair	**Design:** RCT **Location:** The Netherlands **Recruitment Setting:** General practices **Self-selected:** No (200-250 patients/provider invited to screening visit)	**Inclusion:** Aged 40-70 years; BMI between 25 and 40; hypertension (SBP ≥140 mmHg and DBP ≥90 mmHg based on 2 measurements on at least 2 different visits) and/or dyslipidemia (total serum cholesterol >5.5 mmol/L; HDL for men <0.9 and HDL for women <1.1 mmol/L; ratio of total-HDL cholesterol >6; or current use of cholesterol-lowering medication) **Exclusion:** Diabetes; hypothyroidism, pregnancy, liver or kidney disease; current treatment for malignancy; shortened life expectancy; mental illness; addiction to alcohol or drugs	**N recruited or assessed for eligibility:** 1378 **N eligible:** 825 **N excluded:** 381 **N refused or other reason:** 540 **N randomized:** Total: 457 IG: 225 CG: 232 **Followup (12 mo), n (%):** Total: 416 (91.0) IG: 201 (89.3) CG: 215 (92.7) **Cluster information:** (No cluster randomization, but analysis did adjust for nested data) Analysis Adjusted for Clustering: Y (for nested data) Number of clusters: 11 Average cluster size: 42 Inter-cluster correlation: NR	**Age (mean):** 56.1 (calc) **Sex (% female):** 51.9 (calc) **Race/Ethnicity:** NR **SES (income, education):** *% Low education:* 32.2 (calc, for 429 participants) **% Hypertension:** 61.7 (calc) **% Diabetes:** 0 **% Dyslipidemia:** 39.2 (calc) **Other health problems (list):** Metabolic syndrome; using medication for hypertension; using medication for dyslipidemia; current smokers; SCORE (Systematic Coronary Risk Evaluation; 10-year risk of fatal cardiovascular disease)
Tuomilehto, 2001[172] Eriksson, 1999[280] Lindstrom, 2003[281] Uusitupa, 2009[282] Finnish Diabetes Prevention Study Good	**Design:** RCT **Location:** Finland **Recruitment Setting:** Five participating centers recruited through epidemiological surveys, opportunistic population screenings with special emphasis on the high-risk groups such as obese subjects and first-degree relatives of Type II diabetic patients, and advertising in local papers **Self-selected:** Mixed	**Inclusion:** BMI >25; aged 40-64 years; 2-hour plasma glucose 7.8-11.0 mmol/L (OGTT 75 g) with a non-diabetic fasting glucose concentration, i.e. plasma glucose <7.8 mmol/L **Exclusion:** Persons with a previous diagnosis of DM other than gestational DM; involved regularly in a vigorous exercise program; receiving treatment to lower blood glucose other than routine dietary and health advice; any chronic disease making a 6-year survival improbable; other medical characteristics likely to interfere with participation in the study; unbalanced clinical conditions such as thyroid and liver diseases which could interfere with glucose metabolism	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 523, 1 excluded at baseline IG: 265 CG: 257 **Followup (12 mo), n (%) (calc):** Total: 507 (96.9) IG: 256 (96.6) CG: 250 (97.3) *Note: 1 subject did not undergo testing at 1 year but remained in the study, group NR* **Cluster information:** NA	**Age (mean):** 55 **Sex (% female):** 67.0 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** *On anti-hypertension meds:* IG: 30 CG: 31 **% Diabetes:** 0 **% Dyslipidemia:** *On meds of dyslipidemia:* IG: 4.3% CG: 6.1% **Other health problems (list):** Impaired glucose tolerance 8% DVC at baseline

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Villareal, 2008[173] Villareal, 2006[283] Villareal, 2006[284] Fair	**Design:** RCT **Location:** Missouri, US **Recruitment Setting:** Local advertisements **Self-selected:** Yes	**Inclusion:** Aged ≥65 years; BMI ≥30 kg/m^2; did not participate in regular exercise >2x/wk; stable body weight (±2 kg) in the previous year; treatment with medications was unchanged for at least 6 months before enrollment; moderate frailty by at least 2 of the following criteria: 1) physical performance test score of 18-32, 2) peak O_2 consumption of 11-18 ml/kg-min, 3) difficulty or need for assistance in 2 IADLs or 1 ADL **Exclusion:** Severe cardiopulmonary disease; neuromuscular impairments that preclude exercise training; visual, hearing, or cognitive impairments; history of malignant neoplasm; treatment with bone-acting drugs during the previous year	**N recruited or assessed for eligibility:** 40 **N eligible:** 27 **N excluded:** 13 **N refused or other reason:** 0 **N randomized:** Total: 27 IG: 17 CG: 10 **Followup (12 mo), n (%):** Total: 24 (88.9 (calc)) IG: 15 (88.2) (calc) CG: 9 (90.0) (calc) **Cluster information:** NA	**Age (mean):** 70.0 (calc) **Sex (% female):** 66.7 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** Moderate frailty
Werkman, 2010[174] Good	**Design:** RCT **Location:** The Netherlands **Recruitment Setting:** Pre-retirement workshops offered by employers to ~10% of the Dutch population **Self-selected:** No	**Inclusion:** Recent retirees (date of retirement maximum 6 months before or after baseline measurement); aged 55-65 years; not undergoing any medical treatment that might affect body composition **Exclusion:** NR	**N recruited:** ~1100 **N assessed for eligibility:** 443 **N eligible:** 415 **N excluded:** 28 **N refused or other reason:** 2 **N randomized:** Total: 413 (352 men) IG: 209 (174 men) CG: 204 (178 men) **Followup (12, 24 mo), n (%):** *12 mo (men only)* Total: 335 (95.2) IG: 166 (95.4) CG: 169 (94.9) *24 mo (men only)* Total: 301 (85.5) IG: 147 (84.5) CG: 154 (86.5) *(12 months after cessation of the intervention)* **Cluster information:** Analysis Adjusted for Clustering: Y (treatment effect), N (mean changes) Number of clusters: NR Average cluster size: NR Inter-cluster correlation: NR	**Age (mean):** 59.5 **Sex (% female):** 0 (women participants not included in the analysis) **Race/Ethnicity:** NR **SES (income, education):** *% Low educational level:* 24 **% Hypertension:** *% Hypertension drugs:* 16 **% Diabetes:** 3 **% Dyslipidemia:** *% Cholesterol-reducing drugs:* 12 **Other health problems (list):** Current smokers; perceived health

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Whelton, 1998[175] Appel, 1995[285] Chao, 2000[286] Kumanyika, 2002[287] Trial of Nonpharmacologic Interventions in the Elderly Good	**Design:** RCT **Location:** Four academic health centers, US **Recruitment Setting:** Mass mailings; radio, television, and newspaper advertisements; BP screenings; participants from prior research studies **Self-selected:** Mixed	**Inclusion:** Aged 60-80 years; average SBP<145 mmHg and DBP<85 mmHg (single antihypertensive medication or single combination regimen of a diuretic and nondiuretic agent); if taking 2 antihypertensive medications and weaned to 1 during screening; physician willing to participate; stable health; independent in ADLs; capacity to alter diet and PA **Exclusion:** History of a heart attack, stroke in previous 6 months; current angina pectoris; congestive heart failure; insulin-dependent DM; serious mental or physical illness; involuntary or unexplained weight loss ≥4.5 kg in the previous year; BMI<21 kg/m^2; BMI≥33 (men) or ≥37 (women) kg/m^2; inability to comply with the protocol; hypercreatinemia (>152 mmol/L); hyperglycemia (nonfasting level >14.4 mmol/L); anemia (hemoglobin level<110 g/L); hyperkalemia (>5.5 mmol/L)	**N recruited or assessed for eligibility:** 8787 **N eligible:** 995 **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 585; IG(WL) + IG(WL+Na); and IG(Na) + CG(UC) from overweight groups IG1 (WL) 147 IG2 (combined): 147 CG1 (UC): 147 CG2 (Na): 144 **Followup (15-36 mo, 29 median, end point known), n (%):** Total: NR IG1 (weight loss): 145 (99) IG2 (combined): 141 (96) CG1+ non-OW UC: 331 (97) (est 98% at 12-mo for OW sample) **Followup (15-36 mo, 29 median, last assessment done)** Total NR IG1 (weight loss): 137 (93) IG2 (combined): 131 (89) CG1+ non-OW UC: 314 (92) **Cluster information:** NA	**Age (mean):** 66 (calc) **Sex (% female):** 52.6 (calc) **Race/Ethnicity:** *% White:* 71.8 (calc) *% African American:* 27.9 (calc) **SES (income, education):** *% High school grad:* 87.5 (calc) **% Hypertension:** 100 **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR (Combining all 4 groups)
Wood, 1991[177] Kiernan, 2001[288] Fair	**Design:** RCT **Location:** California, US **Recruitment Setting:** NR **Self-selected:** Yes	**Inclusion:** Men with a BMI of 28-34 kg/m^2 and premenopausal women with a BMI of 24-30 kg/m^2; aged 25-49 years; non-smokers; sedentary (exercising not more than twice a week and for less than 30 minutes per time); consuming <4 alcoholic drinks per day on average; in generally good health; not taking medications known to affect blood pressure or lipid metabolism; resting blood pressure <160/95 mmHg; plasma total cholesterol <260 mg/dL; plasma triglyceride level <500 mg/dL **Exclusion:** Pregnant, lactating, or taking oral contraceptives in the previous 6 months (women); planning a pregnancy in the subsequent 2 years (women)	**N recruited or assessed for eligibility:** 1666 **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 264 IG1 (diet): 87 IG2 (diet + exercise): 90 CG: 87 **Followup (12 mo), n (%):** Total: 231 (87.5) IG1: 71 (81.6) IG2: 81 (90.0) CG: 79 (90.8) **Cluster information:** NA	**Age (mean):** 39.7 **Sex (% female):** 48.5 (calc) **Race/Ethnicity:** % White: 88.7 **SES (income, education):** Mean (SD) years of education: 16.5 (2.6) **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR *Note: Characteristics at baseline for completers (n=231)*

Appendix C Table 1a. Evidence Table of Behavioral Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Wood, 1988[176] Frey-Hewitt, 1990[150] Fair	**Design:** RCT **Location:** California, US **Recruitment Setting:** Solicitations through the media **Self-selected:** Yes	**Inclusion:** Men aged 30-59 years; 120-160 percent of "ideal" body weight; nonsmoker; consume <4 alcoholic drinks/day; not taking medications that might affect blood pressure or lipid metabolism, expected to reside in the Stanford area for at least 1 year; resting blood pressure <160/100 mmHg; plasma total cholesterol <8.28 mmol/L; triglycerides <5.65 mmol/L; weight stable (±5 lbs) over previous 1 year; sedentary **Exclusion:** Substantive electrocardiographic abnormalities during treadmill testing; BP >160/100; on medications known to affect lipids; plasma total cholesterol >300 mg/dl; triglycerides >500 mg/dl; exercising ≥3x/week	**N recruited or assessed for eligibility:** 750 **N eligible (per phone screen):** 334 **N excluded:** NR **N refused or other reason:** NR **N randomized:** Total: 155 IG1 (exercise only): 52 IG2 (diet only): 51 CG: 52 **Followup (12 mo), n (%):** Total: 131 (84.5) (calc) IG1: 47 (90.4 (calc)) IG2: 42 (82.4 (calc)) CG: 42 (80.8 (calc)) **Cluster information:** NA	**Age (mean):** 44.5 (calc) **Sex (% female):** 0 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** 0 (below 160/95) **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems (list):** NR
Woollard, 2003[178] Fair	**Design:** RCT **Location:** Australia **Recruitment Setting:** General practices **Self-selected:** No	**Inclusion:** Between 20-75 years of age; had hypertension (SBP>140 mmHg and DBP>90 mmHg or on antihypertensive drug therapy), non-insulin dependent diabetes mellitus, or coronary heart disease **Exclusion:** NR	**N recruited or assessed for eligibility:** NR **N eligible:** 591 **N excluded:** NR **N refused or other reason:** 379 **N randomized:** Total: 212 IG1 (low): 69 IG2 (high): 74 CG: 69 (1 missing at BL) **Followup (12, 18 mo), n (%):** *12 mo* Total: 150 (70.8) IG1: 49 (71.0) IG2: 48 (64.9) CG: 53 (76.8) *18 mo* Total: 163 (76.9) IG1: 52 (75.4) IG2: 54 (73.0) CG: 57 (82.6) **Cluster information:** Analysis Adjusted for Clustering: Y Number of clusters: 7 Average cluster size: 30 Inter-cluster correlation: NR	**Age (mean):** 60.2 (calc) **Sex (% female):** 50.7 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** % Treated hypertension: 84.8 (calc) **% Diabetes:** % Non-insulin dependent diabetes mellitus: 26.5 (calc) **% Dyslipidemia:** % Lipid-lowering drugs: 10.0 (calc) (only in IG2) **Other health problems (list):** 20% Coronary heart disease, 9.5% smokers

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Anderssen, 1995[144] ODES (Oslo Diet and Exercise Study) Fair	**Aim/theory:** *Diet* Decreased total calorie intake, increased intake of fish and fish products, reduced total and saturated fat intake, increased intake of vegetables, decrease intake of sugar, reduced salt intake (if elevated BP), reduction in body weight (usually 0.5-1.0 kg per month), advised against smoking *Exercise* Endurance exercise, advised against smoking	**Intervention description:** *Diet:* Focused on the aims. During counseling a target body weight reduction was agreed upon. At months 3 and 9 there was a followup of the dietary advice. 180-item food frequency questionnaire *Exercise:* Focused on the aims. Groups of 14-20 were offered a 1 hour supervised exercise program 3 times per week with intensity of 60-80% of each participant's peak heart rate. Additional physical activity was recorded in log books **Control description:** Told to not change their lifestyle and advised against smoking **Intervention Duration:** *Individual Sessions* Number: 3 (diet) (assumed) Length: NR Time period: 12 months *Group Sessions* Number: 156 (exercise) Length: 1 hour Time period: 12 months **Who administered intervention:** NR Providers: NR Training: NR **Intervention Setting:** Ullevaal Hospital (assumed) **Incentives:** NR
Burke, 2005[145] ADAPT Fair	**Aim/theory:** Aimed to decrease baseline weight by 5-10% over the 4-month period, larger goal to reduce need for hypertension meds	**Intervention Setting:** NR **Intervention description:** Individual sessions, interactive group workshops, and 5 handouts. Diet low in fat (<30% energy from total fat; <10% energy from saturated fat), salt, and sugar, high in fruits and vegetables, 4 fish meals/week. 30 min moderate activity most days and increased incidental activity. Alcohol intake ≤2 drinks per day. Printed handout and individual session on smoking. Social support from partners encouraged. Encouraged self-directed change in behavior focusing on barriers to change, costs/benefits of a healthy lifestyle, goal setting, and time management. Individual sessions addressed factors like diet, blood pressure, cholesterol, weight loss. Group session topics like food purchasing and prep (15-25/group) **Control description:** Information by the National Heart Foundation and the Health Department of Western Australia. Seminars at 2, 7, 12, 14 mo **Intervention Duration:** *Individual Sessions: (est 8 sessions in 12 mos)* Number: NR (6 weight/BP check and "regular" phone contact to monitor BP during followup) Length: NR Time period: 4 mo active, 12 mo followup *Group Sessions: (est 12 session in 12 mos)* Number: 6 active, 6 followup Length: 90 minutes Time period: 4 months **Who administered intervention:** Research staff Providers: NR Training: NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Christian, 2008[146] Fair	**Aim/theory:** Improve physical activity and diet, enhancing motivation to change	**Intervention Setting:** Outpatient clinic **Intervention description:** 10-min computer-based assessment of motivational readiness. Computer generated tailored report that addressed barriers to improving PA and diet. 30-page planning guide that provided supplemental information on diabetes and achieving a healthy lifestyle. A report was also generated for the patient's physician with findings from the assessment and counseling recommendations. During regularly scheduled visit, patients met with their physician and talked about the lifestyle change goals. Physicians used motivational interviewing. **Control description:** Packet of health education materials addressing diabetes, diet, and exercise. Completed regular clinic visits with physician **Intervention Duration:** *Individual Sessions* Number: 4 (baseline, 3,6,9 mo) Length: NR Time period: 9 months *Group Sessions* Number: NR Length: NR Time period: NR **Who administered intervention: Primary care staff** Providers: Patient's physician Training: 3-hour training session on brief motivational interviewing **Incentives:** NR
Cohen, 1991[147] Fair	**Aim/theory:** Reduce dietary caloric content	**Intervention Setting:** Family health center **Intervention description:** Physicians were taught about importance of weight reduction in managing hypertension and the effects of specific foods on body weight, caloric contents of foods, and strategies for changing dietary habits of their patients; patients were instructed about importance of blood pressure control at baseline; patients received consultations from their physicians about caloric content of various foods, suggestions regarding dietary changes, and short-term goal setting; participants' weight was recorded **Control description:** Instructed about importance of blood pressure control at baseline; usual care, physicians were free to refer their patients for dietary advice or therapy or to provide this themselves **Intervention Duration:** *Individual Sessions* Number: Presume 12 ("monthly") Length: NR Time period: Presume 12 months, length of study *Group Sessions* Number: NR Length: NR Time period: NR **Who administered intervention:** Primary care staff Providers: Primary care staff Training: Received education session conducted by behavioral psychologist **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Cussler, 2008[148] Fair	**Aim/theory:** Weight loss of 0.5 kg per week	**Intervention Setting:** NR **Intervention description:** Group sessions weekly. Encouraged to produce small but lasting changes in eating and PA patterns, leading to a daily energy deficit of 300-500 kcal. Individualized goals for energy intake and expenditure. Targeted physical activity, nutrition and healthy eating, social support, and the mind/body connection. After the 4 month intervention, the website hosted communication tools, progress monitoring tools, curriculum materials, dietary and PA information, links to other websites of interest. Participants were offered two 2-hour training sessions for the website **Control description:** Participated in the group sessions with the IG. After the 4 month intervention, self-directed participants had no further contact with the study staff except for testing **Intervention Duration:** *Individual Sessions* Number: NR Length: NR Time period: NR *Group Sessions* Number: 16 (weekly, wt-loss), 2 (maint) Length: 150 min (wt-loss), 2-hr (maint) Time period: 4 mo (wt-loss), 12 mo (maint) **Who administered intervention:** Research staff Providers: NR Training: NR **Incentives:** NR
Davis, 1992[149] Langford, 1991[260] Davis, 1989[261] TAIM Fair	**Aim/theory:** Reduction of 10% of baseline weight or 4.54 kg (whichever was greater)	**Intervention Setting:** NR **Intervention description:** Placebo med, standard program of diet counseling, nutrition education, and related activities aimed at weight loss **Control description:** Placebo med, No further nutritional counseling beyond the initial explanation of the allocation and general consultation provided to all participants **Control weighing frequency:** Monthly intervals for 6 months then quarterly **Intervention Duration:** *Individual Sessions* Number: Est 6 in 1st year (every 6 weeks after group phase ended), quarterly thereafter Length: NR Time period: For the duration *Group Sessions* Number: 10 Length: NR Time period: 30 months Session in 1st 12 mos: 16 **Who administered intervention:** NR *Providers:* NR *Training:* NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Diabetes Prevention Program Research Group, 1999[142] Diabetes Prevention Program Research Group, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2005[205] Diabetes Prevention Program Research Group, 2005[207] Ackermann, 2009[211] Diabetes Prevention Program Good	**Aim/theory:** Achieve and maintain weight reduction of at least 7% of initial body weight through healthy eating and physical activity. Achieve and maintain physical activity of 150 minutes/week through moderate activity.	**Intervention Setting:** NR **Intervention description:** *Standard:* Written info, 20-30 min individual session with case manager. Food Pyramid guidelines. Consume equivalent of National Cholesterol Education Program step 1 diet. Lose 5-10% of initial weight through diet and exercise, increase to 30 min of moderate activity 5 days/week, avoid excessive alcohol intake. Reviewed annually. *Intensive:* Training in diet, exercise, and behavior modification skills. Frequent support for behavior change. Flexible diet and exercise interventions. Common and individually tailored infor. Group courses focused on maintenance and topics related to exercise, weight loss, or behavioral issues. IG-L=Standard+Intensive **Control description:** Standard intervention. **Intervention Duration:** *Individual Sessions* Number: 1+16+12=29 Length: NR Time period: 24 weeks; 30 months *Group Sessions* Number: 12 Length: NR Time period: 30 months Est sessions in first 12 mos: 23 **Who administered intervention:** Research staff Providers: Case managers Training: In nutrition, exercise, or behavior modification **Incentives:** Rewards (by clinic judgment)
Fitzgibbon, 2010[204] ORBIT Fair	**Aim/theory:** Weight loss goal of 7% initial body weight for the first 6 mo, maintained for the next 12 mo	**Intervention Setting:** University campus **Intervention description:** *Weight-loss:* Group classes. Taught behavioral strategies like self-monitoring, stimulus and portion control. Encouraged to adopt low-fat high-fiber diet with increased fruit and vegetables and decreased caloric intake. Encouraged to increase physical activity (10,000 steps/day) and given a pedometer. Given feedback on self-monitoring logs. Motivational inter-viewing that addressed diet or physical activity *Maintenance:* Weight loss if goal not met during first 6 mo. Motivational interviewing and group sessions. Newsletters each month on general health and safety topics **Control description:** Weekly newsletters on general health and safety topics. Telephoned monthly for questions/concerns **Control weighing frequency:** BL, 6, 18 mo **Intervention Duration:** *Individual Sessions* Number: 18 Length: 20-30 minutes Time period: 18 mo *Group Sessions* Number: 117 Length: NR Time period: 18 mo Est contacts in first 12 mo: 116 **Who administered intervention:** Research staff Providers: Trained interventionists Training: "trained" **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Haapala, 2009[151] Fair	**Aim/theory:** Attitudes to teletechnology and perceptions of personal self-efficacy in dieting will influence contact and the use made of the program and affect weight loss	**Intervention Setting:** Over mobile phone **Intervention description:** Weight loss program called Weight Balance. Costs accrued due to the program were covered. Program calculated daily energy requirement and sent a text indicating percentage reached for the day's target weight; extent to which they had reached their daily weight goal; amount of food to be consumed in proportion to the subject's normal diet; and days remaining until target. Based only on text messages and initiated by participant. Advised to leave out foods high in sugar and/or fat and cut down on alcohol and increase physical activity. Website provided personal space for dietary records and tracking weight. Offered links to information on healthy nutrition and physical activity. Dieters were allowed to set target weight either as a short- or long-term goal and adjust as needed every 3 mo. Weight loss at 2 kg/mo (max of 4.8 kg/mo) **Control description:** Received no intervention (offered the intervention after 12 mo) **Control weighing frequency:** BL and 12 mo **Intervention Duration:** *Individual Sessions* Number: NA (text messages initiated by participant) Length: NR Time period: 12 mo *Group Sessions:* NR **Who administered intervention:** Research staff Providers: Text messages Training: NR **Incentives:** NR
Hypertension Prevention Trial Research Group, 1990[143] HPT Good	**Aim/theory:** Bring body weight to desirable body weight (individual); 5% reduction in mean body weight (group)	**Intervention Setting:** NR **Intervention description:** Counseling aimed at achieving and sustaining the desired dietary changes. Techniques included a mixture of didactic presentations and demonstrations, token incentives, telephone calls, and newsletters. **Control description:** "Passive" control with no dietary counseling. Appears that only control group contact is for assessment. (See p6S in Meintert et al) **Intervention Duration:** *Individual Sessions* Number: NR Length: NR Time period: NR *Group Sessions* Number: ~29 (calc) Length: NR Time period: 36 months (est 16 in 1st 12 mos) **Who administered intervention:** Research staff *Providers:* "Personnel trained and experienced in affecting behavior changes related to shopping, cooking, and eating practices." *Training:* NR **Incentives:** "Token incentives"

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Irwin, 2003[152] Frank, 2005[263] Mohanka, 2006[264] PATH Good	**Aim/theory:** Reduce by fat by at least 45 minutes of moderate-intensity exercise 5 days/week	**Intervention Setting:** Study facility and at home **Intervention description:** Exercise sessions at the study facilities including treadmill walking, stationary bicycling, and strength training; home exercises including walking, aerobics, and bicycling. Participants wore heart rate monitors at the exercise facilities and were encouraged to at home. Received weekly telephone calls to promote adherence; exercise behavior-change education classes; individual meetings at BL and every 3 months to outline goals and provide feedback on progress; quarterly newsletters; group activities such as hikes. Participants were asked to maintain their usual diet **Control description:** Stretching sessions; asked to maintain their usual diet and exercise habits **Intervention Duration:** *Individual Sessions* Number: 4 in-person + 52 phone calls Length: 0 Time period: 0 *Group Sessions* Number: 72 Length: 45 minutes Time period: 12 mo **Who administered intervention:** Providers: NR Training: NR **Incentives:** Stated that incentives were given, no further detail
Jeffery, 1993[153] Jeffery, 1995[289] Trial of Food Provision and Monitary Incentives Fair	**Aim/theory:** Behavioral therapy, food provision (antecedents) and financial incentives (consequences), alone or in combination, to reduce and maintain weight	**Intervention Setting:** NR **Intervention description:** IG1: Behavioral intervention program with weigh-in, presentation of information, group discussion, review of progress. Calorie goal of 1000 or 1500/day and weight loss goal of 14, 18, or 23 kg. Walk/bike 5 days/week working to a goal of burning 1000 calories/week. Food and exercise diaries for 20 weeks and 1 week/month after IG2: IG1 + 5 breakfasts and 5 dinners/week for 18 mo; meal plan; lunch recommendations IG3: IG1 + cash related to weight loss ($25/ week if met and maintained goal, $2.50/week if didn't gain, $12.50 when reached 50% of goal) IG4: IG1 + IG2 + IG3 **Control description:** No intervention. **Control weighing frequency:** BL, 6, 12, 18, and 30 months **Intervention Duration:** *Individual Sessions* Number: NA Length: NA Time period: NA *Group Sessions* (est 27 in first 12 mo) Number: 33 Length: NR Time period: 18 months **Who administered intervention:** Research staff Providers: Advanced degrees in nutrition or behavioral sciences Training: 2-day training session **Incentives:** Cash for IG3 and IG4

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Jones, 1999[154] Hansson, 1994[265] The HOT Study Group, 1993[266] Hypertension Optimal Treatment (HOT) Substudy Fair	**Aim/theory:** Caloric restriction and reduced fat intake	**Intervention Setting:** NR **Intervention description:** Counseled on food selection and preparation, weight reduction goals; blood pressure titrated to the target DBP as specified by the HOT protocol (by medication) **Control description:** Told by research nurses that they should lose weight **Control weighing frequency:** Every 6 months (plus additional weigh-in at 3 mos) **Intervention Duration:** *Individual Sessions* Number: 2 Length: NR Time period: 3-5 weeks *Group Sessions* Number: NR (2x/month for first 3 months, every 3-6 months thereafter) Length: NR Time period: 30 months (est 10 in first 12 mo) **Who administered intervention:** Research staff or primary care staff Providers: Registered dietician Training: NR **Incentives:** NR
Kastarinen, 2002[155] LIHEF Study (Lifestyle Intervention against Hypertension in Eastern Finland) Fair	**Aim/theory:** Achieve normal weight (BMI<25); daily NaCl intake <5g; alcohol <2 drinks/day; moderate intensity exercise 3+times/week at 30 mins; stop smoking	**Intervention Setting:** 10 municipal primary health care centers in eastern Finland **Intervention description:** Simple counseling and behavioral modification methods in four individual visits the first year and three visits the second year, as well as two 2-hour group sessions at 6 and 18 months **Control description:** Usual care, no further detail **Intervention Duration:** *Individual Sessions* Number: 7 Length: NR Time period: 2 years *Group Sessions* Number: 2 Length: 2 hours Time period: 18 months **Who administered intervention:** Research staff or primary care staff Providers: Public health nurses trained by the study physician and a nutritionist Training: Y **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Kulzer, 2009[156] Fair	**Aim/theory:** Lifestyle modification based on self-management theory to achieve 5% weight loss, change of unhealthy eating habits, and increase physical activity to >150 minutes per week.	**Intervention description:** Eight core lessons focusing on lifestyle modification and 4 booster lessons were given. The lessons were conducted in small groups (median size 7 people). Each participant received an exercise book containing information about diabetes prevention and resources such as a table of caloric values and worksheets for each lesson. **Control description:** Written information about diabetes prevention. **Intervention Duration:** *Individual Sessions* Number: 0 Length: NA Time period: NA *Group Sessions* Number: 12 Length: 90 minutes Time period: 8 lessons in 8 weeks, 4 booster lessons in 10 months **Who administered intervention:** Research staff *Providers:* Diabetes educators or psychologists *Training:* Qualified in group education and skills in the fields of nutrition and physical activity **Intervention Setting:** NR **Incentives:** NR
Langford, 1985[157] Wassertheil-Smoller, 1985[267] DISH Fair	**Aim/theory:** Reduce body weight to ideal weight or achieve a 20% reduction	**Intervention Setting:** NR **Intervention description:** Goal setting, behavior change techniques, and self-monitoring. Dietary change was approached as a gradual process and educational efforts were focused on such areas as diet attitudes, beliefs, knowledge, skills, behaviors, and environmental situations. Urged to keep food records, become aware and monitor their eating behavior, and score caloric intake **Control description:** Discontinue meds with no further intervention **Duration:** *Individual Sessions* Number: 15 Length: NR Time period: 11 months *Group Sessions* Number: 8 Length: NR Time period: 8 weeks (est 18 in 12 mo) **Who administered intervention:** Research staff *Providers:* Nutritionist (individual), NR (group) *Training:* NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Martin, 2008[158] Martin, 2006[268] Fair	**Aim/theory:** Gradual increases in physical activity with the goal of 150 minutes per week, decreased consumption of energy-dense foods, increased consumption of fruits and vegetables	**Intervention Setting:** Primary care physician office visits **Intervention description:** Physicians received 2 hours of instruction on general obesity treatment and 5 hours on assessment of stage of change, motivational interviewing, and techniques for behavioral treatment. Given instruction on appropriate dietary recommendations. Participants had monthly office visits with their physician (weight loss, ways to decrease dietary fat, ways to increase physical activity, dealing with barriers to weight loss, healthy eating, maintaining motivation). Personalized verbal recommendations and handouts summarizing the focus of each visit. **Control description:** Physicians providing standard care received training on current guidelines for the treatment of obesity, no specific weight loss protocol. Usual obesity management **Intervention Duration:** *Individual Sessions* Number: 6 Length: 15 minutes Time period: 6 months *Group Sessions*: NR **Who administered intervention:** Primary care staff Providers: Primary care physician Training: 7 hours on obesity treatment. **Incentives:** $35 per visit for assessments; $10 for IG monthly visits
Mayer-Davis, 2004[159] POWER Fair	**Aim/theory:** Achieving and maintaining 1 10% weight loss over 12 months	**Intervention Setting:** Primary health care centers **Intervention description:** IG1&2: Reduction in fat/calorie intake (25% of calories from dietary fat), increased activity (minimum of moderate intensity 150 minutes per week), frequent contact with a nutritionist (group and individual), self-monitoring, and other strategies for sustained behavior change. IG1: Re-imbursable lifestyle: 4 1-hour sessions over 12 mos, consistent with Medicare reimbursement rules IG2: Intensive Intervention: similar as year 1 of DPP, with added group sessions **Control description:** One meeting with the nutritionist over the 12-month period **Intervention Duration:** *Individual Sessions* Number: 8 (IG2), 4 (IG1) Length: 1 hour (IG1&2) Time period: 12 months (IG1&2) *Group Sessions* Number: 22 (IG2), 0 (IG1) Length: 1 hour Time period: 12 months **Who administered intervention:** Research staff (but integrated into primary health care center operations) Providers: Nutritionist Training: NR **Incentives:** $10 gift certificate to a local grocery store after screening visit 1; $25 after randomization; additional incentives with each followup (range $20-$25 gift cards plus gift)

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Mensink, 2003[160] Mensink, 2003[269] Fair	**Aim/theory:** Body weight loss of 5-7% and increasing physical activity to at least 30 minutes of moderate activity 5 days per week	**Intervention Setting:** NR **Intervention description:** Dietary recommendations based on Dutch guidelines for a healthy diet (Energy intake: 55% from carbohydrates, <30-35% from fat, <10% saturated fatty acids, protein 10-15%; Cholesterol intake <33mg/MJ; dietary fiber intake 3 g/MJ). Participants encouraged to stop smoking and reduce alcohol intake. Dietary advice given at regular intervals by a skilled dietician on an individual basis (considering 3-day food record). If no weight loss in first year, mild energy restriction proposed. Encouraged to increase levels of physical activity. Individual advice given on how to increase daily activity and goals are set. Encouraged to participate in a study exercise program. **Control description:** Verbal and written info about the beneficial effects of a health diet, weight loss, and physical activity. **Intervention Duration:** *Individual Sessions* Number: 9 Length: NR Time period: 24 months *Group Sessions* Number: NR Length: NR Time period: 24 months (est 4 in first 12 mos) **Who administered intervention:** Research staff Providers: Dieticians (for diet); NR (exercise) Training: NR **Incentives:** NR
Mitsui, 2008[161] Fair	**Aim/theory:** Walking and self-weight resistance training combined with dietary counseling	**Intervention Setting:** NR **Intervention description:** Participants attended lectures at a city gym on nutrition, cooking, exercise, and preventive medicine. Training consisted of walking 20-30 min and 2-3 self-weight resistance exercises for 10 min. Time was provided for warm-up and cool-down. Participants were advised to perform self-training 30-40 min/day initially 2-3 times per week; later they were asked to exercise more than 5 days per week **Control description:** NR **Intervention Duration:** *Individual Sessions* Number: NR Length: NR Time period: NR *Group Sessions* Number: 24 Length: NR Time period: 12 months **Who administered intervention:** Research staff *Providers:* NR *Training:* NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Moore, 2003[162] Fair	**Aim/theory:** Treating obesity through lifestyle modification	**Intervention Setting:** Primary care offices **Intervention description:** 3 90-minute training sessions over a max of 4 weeks. General practitioners and nurses were asked to attend. Four dietitians delivered the training. The training covered clinical benefit of weight loss and effective treatment options, including reduced dietary energy intake, increased physical activity, and pharmaceuticals. Practitioners saw patients ~every 2 weeks until they lost 10% of their original body weight and then every 1-2 months. Current weight, target weight, dietary and activity targets were recorded in the patients' records. Prescription of 500 kcal deficit was advocated. Diet sheets and supporting written resources were given to patients. Each practice devised individualized weight management protocols to implement with their patients **Control description:** Control practices were asked to provide usual care to their patients **Intervention Duration:** *Individual Sessions*: NR *Group Sessions*: NR **Who administered intervention:** Primary care staff Providers: General practitioners, practice nurses Training: Three 90-minute training sessions **Incentives:** NR
Narayan, 1998[163] Fair	**Aim/theory:** Increase energy expenditure over baseline by 700-1000 kcal per week through physical activity; reduce fat and alcohol and increase fiber intake	**Intervention Setting:** NR **Intervention description:** Choice of physical activities (walking, water aerobics, softball, volleyball, community farming/gardening, cleaning local cemetery) with a group or on their own. Maintained PA log. Advised by a dietitian, in keeping with the recommendations of the American Diabetics Association. Weekly group meetings, reinforced by home visits as needed. Behavioral techniques. Classes consisted of modeling and role-playing, group problem-solving, food prep demonstrations, food tasting, and grocery store tours **Control description:** Self-directed learning, facilitated by an appreciation of Pima culture. Small groups facilitated by community member once/month to discuss current lifestyles in the community, local speakers on Pima culture and history. Basic printed information on health eating and exercise habits. Pima Pride newsletters. Interviewed on their perceptions about health and lifestyle **Intervention Duration:** *Individual Sessions*: NR *Group Sessions* Number: 52 (weekly) Length: NR Time period: 12 months (assumed) **Who administered intervention:** Research staff Providers: Dietitian (dietary advice), NR (other) Training: NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Parikh, 2010[208] Project HEED Fair	**Aim/theory:** Promoting weight loss among overweight adults through a low-cost, peer-led lifestyle intervention	**Intervention Setting:** Community sites **Intervention description:** Lay leaders presented curriculum in a workshop consisting of eight 1.5 hour sessions over 10 weeks; topics included diabetes prevention, finding and affording healthy foods, meal planning, physical activity, label reading, and portion control **Control description**: Delayed intervention, 1 year *Individual Sessions*: NR *Group Sessions:* Number: 8 Length: 1.5 hours Time period: 10 weeks **Who administered intervention:** Providers: Community leaders / peers Training: NR **Incentives**: NR, but perhaps monetary compensation of some kind (participant response during interview "I don't do it for the money but for my health"
Perri, 1988[164] Fair	**Aim/theory:** Maintain weight loss over long-term (24 mos).	**Intervention Setting:** NR **Intervention description:** Conducted in groups. IG1 (BC): Received behavior therapy (CG) plus a maintenance program consisting of 26 biweekly therapist contacts. Maintenance program sessions consisted of weigh-ins, reviews of self-monitoring data, and therapist-led problem solving of difficulties in maintaining habit changes IG2 (BCS): IG1 plus a multifaceted program of social influence strategies designed to enhance motivation and to provide incentives for continued weight-loss. Monetary group contingencies for program adherence and continued weight loss. Active client participation in preparing and delivering lectures on maintaining weight loss. Instructions on how to provide peer support for weight loss through ongoing telephone contacts and peer group meetings IG3 (BCA): IG1 plus aerobic exercise maintenance program consisting of a new set of exercise goals for the posttreatment period and therapist-led bouts during the biweekly treatment sessions. Physical activity increased to 180 minutes per week after the first 6 months IG4 (BCAS): Received all interventions **Control description** (B): Behavior therapy. Participants taught self-control procedures including self-monitoring, stimulus control strategies, self-reinforcement, cognitive restructuring and procedures to slow the pace of eating. Provided with a regimen of aerobic exercise. Aerobic training included written instructions, therapist-led demonstrations, and practice of the exercise. Target of 80 minutes of aerobic exercise per week. Treatment was 20 weeks. **Control weighing frequency:** 2 post-tx *Individual Sessions (maintenance phase only)* Number: 26? unclear if main therapist contacts are in group context, or social contingency activities separate Length: NR Time period: 1 yr *Group Sessions (for maintenance phase only)* Number: 26? unclear if main therapist contacts are in group context, or social contingency activities separate Length: NR Time period: 1 yr Number of sessions in 1st 12 months: 26 **Who administered intervention:** Research staff Providers: Clinical psychologist paired with either a physician or a nurse practitioner Training: Provided with manuals and weekly training sessions **Incentives:** Monetary group contingencies for program adherence and continued weight loss (BCS and BCAS only)

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Pritchard, 1999[165] Fair	**Aim/theory:** Restriction of total dietary energy, reduction of the fat component to no more than 30%, with carbohydrate contributing 50% or more and protein the balance	**Intervention Setting:** General practice **Intervention description:** IG1: Individual counseling sessions focusing on principles of good nutrition and exercise. Dietitian identified lifestyle and dietary problem areas. Advice on food shopping and cooking methods, food selection, meal planning, and exercise programs. Dietary changes in aim. Smoking was discouraged and alcohol consumption ≤2 drinks/day (women) and ≤4 (men) with ≥2 alcohol free days/week. IG2: IG1+ Patients saw their general practitioner on 2 occasions to get encouragement and their progress monitored. **Control description:** Results of the initial measurements and if they had queries were advised to discuss with the doctor. Usual care. **Control weighing frequency:** BL and 12 mo **Intervention Duration:** *Individual Sessions* Number: 6 (IG2, + 2 appt with doctor) Length: 45 minutes for 1 session; 15 minutes for the remaining 5 (IG2, doctor devoted +5 minutes) Time period: 12 months *Group Sessions:* NR **Who administered intervention:** Primary care staff Providers: Dietitian (IG1 and IG2) and general practitioner (IG2 only) Training: NR **Incentives:** NR
Silva, 2009[166] Silva, 2008[270] Teixeira, 2009[271] Fair	**Aim/theory:** Self-determination theory	**Intervention Setting:** University **Intervention description:** 30 intervention sessions covering PA, eating/nutrition, body image, and more occurred weekly or bimonthly. Team promoted a sense of ownership over behavior so it would stem from an internal perceived locus of causality. Built sustainable knowledge that supported informed choices, encouraged choice and self-initiation, provided a menu of options and variety of avenues for behavior change, supported the presentation of tasks and choices with a clear rationale to adopt specific behavior, encouraged building and exploring congruence between values and goals and lifestyles **Control description:** 29 sessions, general health education curriculum based on several 3-6 week long education topics (nutrition, stress management, self-care, communication skills) **Control weighing frequency:** BL, 4 mo, 12 mo **Intervention Duration:** *Individual Sessions* Number: NR Length: NR Time period: NR *Group Sessions* Number: 30 Length: 120 minutes Time period: 12 months **Who administered intervention:** Research staff Providers: NR Training: NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Simkin-Silverman, 2003[167] Simkin-Silverman, 1998[272] Kuller, 2001[273] Park, 2007[274] Women's Healthy Lifestyle Project (WHLP) Good	**Aim/theory:** Reduction in weight by 5 lbs (BMI ≤24 kg/m2), 10 lbs (BMI 25-26 kg/m2), or 15 lbs (BMI ≥27 kg/m2); lower dietary fat to 25% of daily calories, saturated fat to 7%, and cholesterol to 100 mg/day; increase physical activity	**Intervention Setting:** NR **Intervention description:** 1300-1500 kcal meal plan for first 4 weeks, modified after; calcium supplement; 7-day pocket diaries for food monitoring; education and guidance to increase PA in a stepwise manner to expend 1000 kcals/week (1500 kcals/week if already active); self-monitored daily PA for first 6 months. Employed variety of behavioral mgmt techniques. **Control description:** Assessment only **Control weighing frequency:** BL, 6, 18, 30, 42, and 54 months **Intervention Duration:** *Individual Sessions* Number: NR Length: NR Time period: 54 months *Group Sessions* Number: 15 (Phase I), 6+ (Phase II) Length: NR Time period: 5 months (Phase I), 48 months (Phase II) (est 20 in first 12 mos) **Who administered intervention:** Research staff Providers: Behavioral psychologists and nutritionists Training: NR **Incentives:** "Healthy lifestyle prizes" to enhance attendance and the return of self-monitoring diaries
Stevens, 1993[168] Whelton, 1992[275] The Trials of Hypertension Prevention Collaborative Research Group, 1992[276] Trials of Hypertension Prevention Phase I Good	**Aim/theory:** Achieve weight loss of at least 4.5 kg during the first 6 months and maintain the weight loss for the remaining 12 months through reducing energy intake and increasing physical activity and using behavioral self-management techniques	**Intervention Setting:** NR **Intervention description:** Weigh-ins; information on basic nutrition and ways to reduce total energy consumption by reducing fat, sugar, and alcohol intake; food diaries for the first 14 weeks; asked to walk 20 minutes 3 days/week; later asked to exercise 30-45 mins 4-5 days/week at an intensity of 40-55% of heart rate reserve; received general exercise guidelines; exercise demonstrations; supervised exercise periods; short-term goal setting and plans of action; reinforcement and social support; record-keeping to assess progress; problem-solving; relapse prevention **Control description:** Usual care **Control weighing frequency:** BL, 3, 6, 12, and 18 months **Intervention Duration:** *Individual Sessions* Number: 1 Length: NR Time period: Initially *Group Sessions* Number: 29 Length: 90 minutes Time period: 18 months (weekly for 14 weeks, monthly thereafter) (est 23 in first year) **Who administered intervention:** Research staff Providers: Registered dietitian and psychologist or exercise psychologist Training: NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Stevens, 2001[169] Hollis, 1995[277] TOHP, 1997[278] Trials of Hypertension Prevention Phase II Good	**Aim/theory:** Lose ≥4.5 kg during the first 6 months and maintain the weight loss for the remainder of the trial. Reduce caloric intake; 30-45 mins of moderate PA 4-5 days/week. Achieve goal(s) in first 6 months and maintenance thereafter	**Intervention Setting:** NR **Intervention description:** Behavioral self-management, nutrition education, information on PA, social support, self-monitoring (food diaries and graphs of PA), goal-setting with action plans, strategies for situations that trigger problem eating **Control description:** NR **Control weighing frequency:** Every 6 mo to end of followup at 36, 42, or 48 mo, depending on randomization date **Intervention Duration:** *Individual Sessions* Number: 1+ Length: NR Time period: Beginning of the trial, optional after month 18 *Group Sessions* Number: 50+ (add'l optional) Length: NR Time period: 36 months (est 32 sessions in first 12 mos) **Who administered intervention:** Research staff or primary care staff *Providers:* Dieticians and Health Educators *Training:* NR **Incentives:** NR
Svetkey, 2008[170] Weight Loss Maintenance Trial PROTOCOL, 2008[279] WLM Good	**Aim/theory:** Maintenance of Phase I weight loss or additional loss if desired; moderate PA at least 225 mins/week; reduce caloric intake and adopt the DASH diet	**Intervention Setting:** NR **Intervention description:** IG1: Interactive website (goal-setting, graphing data over time, problem-solving and motivation, bulletin board for social support, and self-monitoring caloric intake and physical activity). Encouraged to log in at least 1x/week. IG2: Person-to-person guidance and support mostly via phone and in person every 4th month (self-reported weight, progress review, # of days food diary was kept, frequency of weighing, average minutes of exercise, progress on additional goals and action plans, problem-solving) **Control description:** Printed lifestyle guidelines with diet and physical activity recommendations; met with study interventionist at 12 mo **Control weighing frequency:** Every 6 months for 30 months **Intervention Duration:** *Individual Sessions* Number: IG1: 0, IG2: 30, (+ 20 6 mo phase 1) Length: IG1: NA, IG2: 5-15 mins x 23, 7 x 45-60 mins Time period: 30 months, (+6 months phase 1) *Group Sessions* Number: 0 (est 12 in first 12 mos) Length: NA Time period: NA **Who administered intervention:** Research staff Providers: IG1: NA, IG2: "Health counselor" Training: NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
ter Bogt, 2009[171] Fair	**Aim/theory:** NR	**Intervention Setting:** Primary Care **Intervention description:** 4 individual visits and one telephone session. NP was guided by standardized computer software. Visit 1 consisted of information on healthy lifestyle, stimulating awareness of lifestyle and body weight, conversation on history of slimming and motivation to change lifestyle/lose weight and first step in the development of the treatment plan. Visit 2 included feedback on lifestyle by critiquing food diary, physical activity, and BL questionnaire; finished treatment plan. Visit 3 evaluated goals, changed treatment plan if needed and referred to dietitian. Visit 4 and call evaluated and supported changes in lifestyle and if necessary, changed individual goals **Control description:** One visit with GP (~10 minutes) to discuss results from the initial screening and thereafter usual GP care **Control weighing frequency:** BL and 12 mo **Intervention Duration:** *Individual Sessions* Number: 4 (in person) + 1 (phone) Length: 35 minutes (Visits 1 and 2), 25 minutes (Visit 3), otherwise NR Time period: 12 mo *Group Sessions:* NR **Who administered intervention:** Primary care staff Providers: Nurse practitioners Training: Specially developed training program (4 4-hour sessions) and individual instruction about the software program **Incentives:** NR
Tuomilehto, 2001[172] Eriksson, 1999[280] Lindstrom, 2003[281] Uusitupa, 2009[282] Finnish Diabetes Prevention Study Good	**Aim/theory:** Reduction in weight ≥5%, in total intake of fat to <30% of energy consumed, and in intake of saturated fat to <10% of energy consumed; an increase in fiber intake to ≥15 g per 1000 kcal; and moderate exercise for ≥30 minutes/day	**Intervention Setting:** 5 participating centers, appear to be primarily research and university settings **Intervention description:** Individual dietary and physical activity counseling. Supervised, progressive, individually tailored circuit-type resistance training sessions were also offered **Control description:** General oral and written information about diet and exercise (2-page leaflet) **Intervention Duration:** *Individual Sessions* Number: 11 (counseling) + NR (circuit training) Length: NR Time period: 2 years *Group Sessions* Number: NR, but do have some Length: 0 Time period: 0 **Who administered intervention:** Research staff or primary care staff *Providers:* Nutritionist, presume research staff *Training:* NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Villareal, 2008[173] Villareal, 2006[283] Villareal, 2006[284] Fair	**Aim/theory:** Achieve 10% weight loss at 6 months and maintain 6 additional months through calorie deficit and exercise	**Intervention Setting:** University-based research center **Intervention description:** Energy deficit of 500-750 kcal/day; 30% of energy as fat, 50% as carbohydrate, and 20% as protein; behavior therapy; daily multivitamin; counseled to consume adequate dietary calcium and vitamin D; group exercise focusing on flexibility, endurance, strength training, and balance **Control description:** Instructed to maintain usual diet and activities, asked not to participate in any weight-loss or exercise programs **Control weighing frequency:** Baseline, 6, and 12 months **Intervention Duration:** *Individual Sessions* Number: 0 Length: NA Time period: NA *Group Sessions* Number: 52 with dietician, 156 exercise Length: NR with dietician, 90 mins exercise Time period: 52 weeks **Who administered intervention:** Research staff *Providers:* Dietician experienced in group behavioral therapy *Training:* NR **Incentives:** NR
Werkman, 2010[174] Good	**Aim/theory:** Small and sustained adaptations in physical activity and/or diet	**Intervention Setting:** Computer-based **Intervention description:** Choice of 5 modules. 1 included information leaflet and several energy balance tools. 2 was a CD-ROM providing individually tailored feedback on BMI, health consequences and energy balance behavior. 3 had computer-tailored feedback regarding physical activity, fiber consumption, portion sizes of energy dense foods and fat consumption. In 4, participants could find out information about diet and physical activity behavior, participate in a forum and use links to other sites. 5 was written tailored advice on reported body weight, a food frequency questionnaire, and a physical activity questionnaire. Newsletters every 2-3 months. **Control description:** Newsletters with general information about the study and information about art exhibitions and city trips for instance. **Control weighing frequency:** BL, 12, 24 mo **Intervention Duration:** *Individual Sessions* Number: NR (computer-based) Length: NR Time period: 12 mo *Group Sessions: NA* **Who administered intervention:** Research staff Providers: Computer-based Training: NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Whelton, 1998[175] Appel, 1995[285] Chao, 2000[286] Kumanyika, 2002[287] Trial of Nonpharmacologic Interventions in the Elderly Good	**Aim/theory:** Achieve and maintain a weight loss goal ≥4.5 kg, dietary sodium intake of ≤80 mmol (only sodium reduction arms), and withdrawal of antihypertensive medication through diet, calorie deficit and increasing PA	**Intervention Setting:** NR **Intervention description:** Information and motivation around calorie control, basics of a sound diet, how to increase activity, exercise precautions, self-efficacy and commitment to the trial, self-monitoring of calories, eating behaviors and pulse rate, management of eating behaviors and situations, relapse prevention, hands-on food preparation and group exercise, overcoming barriers, food and PA records with feedback **Control description:** Quarterly group sessions on topics unrelated to the goals of the trial **Control weighing frequency:** Quarterly for 15-36 months (median 29 months) **Intervention Duration:** *Individual Sessions* Number: 4 Length: NR Time period: 4 months *Group Sessions* Number: 26-47 (median 40) Length: NR Time period: 15-36 months (median 29 months) **Who administered intervention:** NR *Providers:* Nutritionists and exercise counselors with expertise in lifestyle change techniques *Training:* NR **Incentives:** Adherence-related incentives
Wood, 1991[177] Kiernan, 2001[288] Fair	**Aim/theory:** Lowered caloric intake for IG1; Lowered caloric intake and increased PA for IG2	**Intervention Setting:** NR **Intervention description:** IG1: Prudent diet with concomitant caloric reduction and no change in exercise level. Dietary recommendations presented by registered dietitians (approximately 55% of total energy was from carbohydrates, 30% from fat, ≤10% from saturated fat, dietary cholesterol below 300 mg/day) IG2: IG1 combined with increased physical activity. Supervised in a program of aerobic exercise (primarily brisk walking and jogging) that met 3 days a week. Instructed to work at 60-80% of maximal heart rate for at least 25 minutes initially, and to increase to at least 45 minutes by the 4th month **Control description:** Instructed to maintain their usual diet and exercise patterns **Control weighing frequency:** BL and 12 mo **Intervention Duration:** *Individual Sessions* Number: NR Length: NR Time period: NR *Group Sessions* Number: 25 Length: NR Time period: 12 mo **Who administered intervention:** Research staff Providers: Dietitians (NR for physical activity) Training: NR **Incentives:** NR

Appendix C Table 1b. Evidence Table of Behavioral Trials: Intervention Details

Study Reference Quality Rating	Intervention Aim/Theory	Description of Intervention and Control
Wood, 1988[176] Frey-Hewitt, 1990[150] Fair	**Aim/theory:** Exercise to reduce total body fat by 1/3 for IG1 (without changing diet); diet to reduce total body fat by 1/3 for IG2 (without changing exercise habits)	**Intervention Setting:** NR **Intervention description:** IG1: Supervised exercise program with individual prescriptions; diet prescription (reduce by 300-500 kcal/day); record body weight; behavioral strategies; 24-hour food log. Running diaries collected at monthly intervals. Exercise level adjusted to keep weight stable during final 6-weeks IG2: Individualized diet (reduction of 32.3 MJ = loss of 1 kg adipose tissue). Food intake adjusted to keep weight stable during final 6-weeks. Exercise prescription (treadmill test with VO2 max); supervised exercise class 1-3 mo of fast walking and gradually jogging; 2 additional days/week walking or jogging at 6 mo; miles run, exercise heart rate, and total duration recorded; no change in eating habits **Control description:** Usual diet and exercise patterns (offered weight-loss program at end) **Control weighing frequency:** BL, 7 and 12 mo **Intervention Duration:** *Individual Sessions* Number: 0 (IG1), NR (IG2) Length: NA (IG1), NR (IG2) Time period: 10.5 months (IG2) *Group Sessions* Number: NR Length: NR Time period: 10.5 months **Who administered intervention:** Research staff Providers: "Training staff" (1), nutritionists (2) Training: NR **Incentives:** NR
Woollard, 2003[178] Fair	**Aim/theory:** Control weight, increase physical activity, reduce fat and sodium intake, increase fiber consumption, moderate alcohol intake, and achieve cessation of smoking	**Intervention Setting:** NR **Intervention description:** IG1: UC + 1 face-to-face counseling session and 10-15 min phone consultations every month for 12 mo. Personalized education manual supporting cognitive behavioral approach. Counseling focused on enhancing patients' cognitive, affective and psychomotor skills IG2: Same as IG1 except individual counseling sessions up to 60 min every mo for 12 mo instead of phone consultations. **Control description:** Heart Foundation health promotion literature and remained under care of general practitioner **Control weighing frequency:** BL, 12, 18 mo **Intervention Duration:** *Individual Sessions* Number: 13 (IG1), 12 (IG2) Length: 60 minutes for 1 session (assumed), 10-15 minutes for remaining 12 sessions (IG1); 60 minutes (IG2) Time period: 12 months (IG1 and IG2) *Group Sessions:* NR **Who administered intervention:** Primary care staff Providers: Practice nurses Training: 170-hour program based on the principles of adult learning theories with emphasis on transtheoretical model **Incentives:** NR

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Anderssen, 1995[144] ODES (Oslo Diet and Exercise Study) Fair	Mean (SE) at BL, Mean change (SE) at 12 mo **BL 12 mo** **Weight/Relative weight:** *BMI, kg/height^2* BL DBP>91 mmHg **IG1** 29.9 (0.7) -1.7 (0.4)* **IG2** 29.5 (0.8) -0.4 (0.3) **IG3** 29.6 (0.9) -2.2 (0.2)* **CG** 30.0 (1.3) 0.2 (0.3) BL DBP 84-91 mmHg **IG1** 30.9 (1.2) -1.4 (0.5)* **IG2** 28.4 (0.7) 0.0 (0.3) **IG3** 27.9 (0.6) -2.0 (0.3)* **CG** 27.9 (0.6) 0.4 (0.2) BL DBP<84 mmHg **IG1** 28.0 (0.7) -0.7 (0.2)* **IG2** 27.4 (0.7 -0.5 (0.4)* **IG3** 28.0 (0.6) -1.2 (0.4)* **CG** 27.4 (0.5) 0.4 (0.1) **Central adiposity:** NR **Overall adiposity:** NR **p<0.05 for IG compared with CG* **IG1 n analyzed:** 16 (DBP>91), 17 (DBP 84-91), 19 (DBP<84) **IG2 n analyzed:** 20 (DBP>91), 16 (DBP 84-91), 13 (DBP<84) **IG3 n analyzed**: 24 (DBP>91), 20 (DBP 84-91), 21 (DBP<84) **CG n analyzed:** 12 (DBP>91), 16 (DBP 84-91), 15 (DBP<84)	Net difference versus CG (95% CI) **BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* BL DBP>91 mmHg **IG1** -- -0.11 (-0.61, 0.39) **IG2** -- -0.21 (-0.66, 0.24) **IG3** -- -0.14 (-0.64, 0.36) BL DBP 84-91 mmHg **IG1** -- -0.38 (-0.80, 0.04) **IG2** -- -0.06 (-0.39, 0.27) **IG3** -- -0.54 (-1.00, -0.08)* BL DBP<84 mmHg **IG1** -- 0.26 (-0.14, 0.66) **IG2** -- 0.24 (-0.23, 0.71) **IG3** -- -0.28 (-0.74, 0.18) *HDL cholesterol, mmol/L* BL DBP>91 mmHg **IG1** -- 0.09 (0.01, 0.10)* **IG2** -- 0.03 (-0.04, 0.10) **IG3** -- 0.13 (0.05, 0.21)* BL DBP 84-91 mmHg **IG1** -- -0.07 (-0.13, -0.01)* **IG2** -- -0.02 (-0.11, 0.07) **IG3** -- 0.08 (0.01, 0.15)* BL DBP<84 mmHg **IG1** -- 0.09 (0.02, 0.16)* **IG2** -- 0.08 (-0.03, 0.19) **IG3** -- 0.14 (0.06, 0.22)* *Triglycerides, mmol/L* BL DBP>91 mmHg **IG1** -- -1.00 (-1.75, -0.25)* **IG2** -- -0.79 (-1.34, -0.24)* **IG3** -- -0.96 (-1.55, -0.37)* BL DBP 84-91 mmHg **IG1** -- -0.02 (-0.52, 0.48) **IG2** -- -0.03 (-0.60, 0.54) **IG3** -- -0.46 (-1.08, 0.16) BL DBP<84 mmHg **IG1** -- -0.30 (-1.00, 0.40) **IG2** -- -0.46 (-1.13, 0.21) **IG3** -- -0.94 (-1.57, -0.31)*

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
(continued) Anderssen, 1995[144] ODES (Oslo Diet and Exercise Study) Fair		Mean (SE) at BL, Mean change (SE) at 12 mo **Blood pressure:** *Systolic Blood Pressure, mmHg* **IG1** -- -6.4 (1.4)* **IG2** -- -2.2 (1.1) **IG3** -- -5.9 (1.1)* **CG** -- -0.5 (1.7) BL DBP>91 mmHg **IG1** 144.5 (4.5) -8.4 (3.3)* **IG2** 139.5 (2.0) -4.1 (1.8) **IG3** 142.8 (2.4) -8.3 (2.1)* **CG** 137.5 (2.5) 2.9 (4.4) BL DBP 84-91 mmHg **IG1** 133.6 (2.2) -8.2 (1.9) **IG2** 130.6 (2.2) -1.6 (1.4) **IG3** 129.2 (--) -6.1 (1.3) **CG** 129.6 (1.9) -1.7 (2.9) BL DBP<84 mmHg **IG1** 122.2 (2.0) -3.2 (1.9) **IG2** 122.7 (2.7) 0.2 (2.3) **IG3** 121.9 (1.5) -3.0 (1.7) **CG** 120.8 (1.3) -1.9 (1.8) *Diastolic Blood Pressure, mmHg* **IG1** -- -3.4 (1.0) **IG2** -- -2.7 (1.0) **IG3** -- -5.2 (0.9)* **CG** -- -0.7 (1.3) BL DBP>91 mmHg **IG1** 97.3 (1.3) -7.1 (1.8) **IG2** 96.4 (1.1) -5.5 (1.7) **IG3** 97.0 (0.9) -7.1 (1.3)* **CG** 95.6 (1.1) -0.4 (3.6) BL DBP 84-91 mmHg **IG1** 88.1 (0.5 -4.5 (1.3) **IG2** 88.2 (0.6) -2.4 (1.4) **IG3** 86.6 (0.5) -6.4 (1.2) **CG** 88.0 (0.5) -2.2 (1.9) BL DBP<84 mmHg **IG1** 78.6 (1.2) 0.8 (1.5) **IG2** 79.4 (0.9) 1.2 (2.0) **IG3** 79.0 (0.7) -1.8 (1.7) **CG** 79.1 (1.3) 0.8 (1.5) **Glucose tolerance: NR** *p<0.05 for IG compared with CG **IG1 n analyzed:** 16 (DBP>91), 17 (DBP 84-91), 19 (DBP<84), 55 (total) **IG2 n analyzed**: 20 (DBP>91), 16 (DBP 84-91), 13 (DBP<84), 54 (total) **IG3 n analyzed:** 24 (DBP>91), 20 (DBP 84-91), 21 (DBP<84), 67 (total) **CG n analyzed:** 12 (DBP>91), 16 (DBP 84-91), 15 (DBP<84), 43 (total)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Burke, 2005[145] ADAPT Fair	**BL 4 mo 16 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 30.4 (2.9) -- -- **CG** 29.7 (2.5) -- -- *Weight, kg* **IG** 86.7 (1.2) 82.0 (1.2)* 82.8 (1.2)* **CG** 84.2 (1.1) 82.8 (1.1)* 82.8 (1.2)* *No group differences in weight loss for either participants aged <60 or those 60 and older* **Central adiposity:** *Waist circumference, cm* **IG** 96.6 (0.9) 91.6 (0.8)* 91.6 (0.9)* **CG** 93.7 (0.9) 92.0 (0.9)* 91.8 (1.0)* **p<0.001 for difference between IG and CG, adjusted for BL values* **Overall adiposity:** NR **IG n analyzed:** 106 **CG n analyzed:** 98	Mean (SE) **BL 4 mo 16 mo** **Lipids: (figure only): groups diffs in LDL at 16-mo, but no diffs in TC, HDL at 16-mo** **Blood pressure:** *Systolic Blood Pressure, mmHg* **IG** 128 (1) 122 (1)* 130 (1) **CG** 126 (1) 124 (1) 130 (1) *Diastolic Blood Pressure, mmHg* **IG** 77 (1) 75 (1)* 77 (1) **CG** 76 (1) 76 (1) 78 (1) *No group diffs in proportion with meds withdrawn, reduced, or unchanged at 4- or 16-mo* ** p<0.01 for difference between IG and CG, adjusted for BL values* **Glucose tolerance:** (figure only): no group diffs in glucose at 16-mo **IG n analyzed:** 106 **CG n analyzed:** 98
Christian, 2008[146] Fair	Mean (SD) at BL, Mean change (SD) at 12 mo **BL 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 35.4 (6.62) -- **CG** 34.8 (7.11) -- *Weight, pounds* **IG** 207.0 (47.3) -0.18 (10.92) **CG** 200.2 (44.7) 1.39 (10.60) *Lost ≥5% body weight, n* **IG** -- 30/141* **CG** -- 14/132 **Central adiposity:** *Waist circumference, cm* **IG** 118.1 (14.95) -1.764 (7.045) **CG** 116.6 (15.23) -0.543 (6.498) **Overall adiposity:** NR ** p=0.02* **IG n analyzed:** 155 (BL), 141 (12 mo) **CG n analyzed:** 155 (BL), 132 (12 mo)	Mean (SD) at BL, Mean change (SD) at 12 mo **BL 12 mo** **Lipids:** *Total cholesterol, mg/dL* **IG** 191.16 (46.33) -15.84 (44.76)* **CG** 189.61 (54.72) -3.93 (45.15) *HDL cholesterol, mg/dL* **IG** 42.04 (12.67) -0.43 (17.10) **CG** 44.29 (18.44) 1.56 (11.60) *LDL cholesterol, mg/dL* **IG** 100.18 (32.10) -14.62 (38.52)* **CG** 105.82 (38.81) -3.81 (38.51) *Triglycerides, mg/dL* **IG** 178.67 (103.71) -13.60 (97.06) **CG** 185.72 (112.25) -9.48 (95.67) **Blood pressure:** *Systolic Blood Pressure, mmHg* **IG** 131.80 (17.02) -2.55 (20.37) **CG** 132.26 (17.43) -4.66 (20.81) *Diastolic Blood Pressure, mmHg* **IG** 76.56 (10.53) -2.60 (13.79) **CG** 77.83 (9.58) -2.54 (11.63) **Glucose tolerance:** *Hemoglobin A1c, percent* **IG** 8.08 (2.02) -0.141 (1.76) **CG** 8.29 (1.93) -0.46 (1.63) *List other measurement instruments: NR* ** p<0.05 for difference between IG and CG* **IG n analyzed:** 155 (BL), 141 (12 mo) **CG n analyzed:** 155 (BL), 132 (12 mo)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Cohen, 1991[147] Fair	Mean (SD) at BL, Mean change (SD) at 6 and 12 mo **BL 6 mo 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 34.2 -- -- **CG** 34.0 -- -- *Weight, kg* **IG** 91.8 -1.8 (3.4)* -0.88 (4.0)** **CG** 91.7 0.56 (2.5) 1.3 (3.0) **Central adiposity:** NR **Overall adiposity:** NR **p=0.04 for IG vs CG* ***p<0.10 for IG vs CG* **IG n analyzed:** 15 **CG n analyzed:** 15	Mean change (SD) at 6 and 12 months **BL 6 mo 12 mo** **Lipids:** NR **Blood pressure:** *Mean arterial pressure, mmHg* **IG** -- 1.2 (13.7) 3.0 (14.2) **CG** -- -2.3 (7.5) -0.7 (11.3) (NS.) No group difference in number of anti-HTN meds **Glucose tolerance:** NR **IG n analyzed:** 15 **CG n analyzed:** 15
Cussler, 2008[148] Fair	Mean (SD) at BL, Mean change (SD) at 16 mo (12-mo since end of wt loss phase) **BL 16 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 30.6 (3.9) -2.1 (1.4) **CG** 30.1 (3.4) -1.9 (1.5) *Weight, kg* **IG** 84.4 (12.6) 0.7 (5.4) **CG** 82.0 (10.8) 1.0 (4.6) **Central adiposity:** NR **Overall adiposity:** *Percent fat at BL, Fat-free mass at time 2, Total body fat at time 2 (all measured with dual energy X-ray absorptiometry)* **IG n analyzed:** 52 (BL, 16 mo) **CG n analyzed:** 59 (BL, 16 mo)	NR

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Davis, 1992[149] Langford, 1991[260] Davis, 1989[261] TAIM Fair	Mean (SE) at BL, Mean change (SE) at 6, 12, 18, 24 mo **BL 6 mo 12 mo 18 mo 24 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** -- -- -- -- -- **CG** -- -- -- -- -- *Weight, lb at BL, kg at 6 mo* **IG** 198.6 (--) -4.4 (0.7) -- -- -- **CG** 189.8 (--) -0.7 (0.4) -- -- -- **IG n analyzed:** 100 (BL), 89 (6 mo) **CG n analyzed:** 100 (BL), 90 (6 mo) *Weight, kg (for those with complete data at all time points)* **IG** 89.1 (2.5) -4.7 (0.9) -3.7 (0.9) -2.7 (1.0) -1.9 (1.0) **CG** 84.6 (1.5) -0.5 (0.3) -0.5 (0.4) -1.0 (0.4) -0.4 (0.5) (Note: Attrition is too high, cannot use this data) **IG n analyzed:** 57 **CG n analyzed:** 61 Figures using ITT data show differences between weight loss and usual care groups through 2.5 years for	**Lipids:** NR Mean at BL, Mean change (SD) at 6 mo **BL 6 mo** **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 143.2 -11.49 (--) **CG** 144.5 -10.34 (--) **Total SD at 6 mo:** 4.67 *Diastolic blood pressure, mmHg* **IG** 94.0 -8.78 (10.97) **CG** 93.7 -7.96 (8.63) **IG n analyzed:** 90 **CG n analyzed:** 90 Figures show few differences between weight loss and usual care groups in DBP change from 12-months on for any medication group, but differences between weight loss and usual care seen through 12 months for 3 of the 4 medication groups. (p<0.05) **Glucose tolerance:** NR
Diabetes Prevention Program Research Group, 1999[142] Diabetes Prevention Program Research Group, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2005[205] Diabetes Prevention Program Research Group, 2005[207] Ackermann, 2009[211] Diabetes Prevention Program Good	Mean (SD) at BL, Mean change (SE) from BL at 6, 12, 30 mo and 2.8 yrs **BL 6 mo 12 mo 30 mo 2** **Weight/Relative weight:** *BMI, kg/m²* **IG** 33.9 (6.8) 2.41 (0.05) -2.42 (0.06)* -- -- **C** 34.2 (6.7) -0.12 (0.05) -0.15 (0.06) -- -- *Weight, kg* **IG** 94.1 (20.8) -6.73 (0.14) -6.76 (0.17)* -4.43 (7.3) -5 **CG** 94.3 (20.2) -0.32 (0.14) -0.42 (0.17) -- - 0.1 (--) **Central adiposity:** *Waist circumference, cm* **IG** 105.1 (14.8) -- -6.36 (0.19)* -- -- **CG** 105.2 (14.3) -- -0.69 (0.19) -- -- **Overall adiposity:** *Body fat measurement (visceral L2-L3, visceral L4-L5, subcutaneous L2-L3, subcutaneous L4-L5) (for subsample, n=758, 68.5%, #2496)* **p<0.001 IG vs CG* **IG n analyzed:** 1079, 1026 (12 mo), 962 (weight, 30 mo) **CG n analyzed:** 1	Mean (SD) at BL, Mean change (SE) from BL at 6, 12, 24, 36 mo **BL 6 mo 12 mo 24 mo 36 mo** **Lipids:** NR **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 123.7 (14.8) -- -3.4 (0.4)* -3.4 (0.4)* -3.27 (0.5)* **CG** 123.5 (14.4) -- -0.90 (0.4) -0.52 (0.4) -0.57 (0.5) *Diastolic blood pressure, mmHg* **IG** 78.6 (9.2) -- -3.6 (0.2)* -3.33 (0.2)* -3.82 (0.3)* **CG** 78.0 (9.2) -- -0.89 (0.2) -1.07 (0.2) -1.88 (0.3) **Glucose tolerance:** *Fasting glucose, mg/dL* **IG** 106.3 (8.1) -4.66 (0.30) -4.94 (0.36) -- -- **CG** 106.7 (8.4) 0.20 (0.30) 0.63 (0.36) -- -- ** p<0.001 versus CG for changes in mean over time (NR for fasting glucose)* **IG n analyzed:** 1079 (BL), 1026 (12-mo), 1000 (24-mo), 638 (36-mo) **CG n analyzed:** 1082 (BL), 1027 (12-mo), 1015 (24-mo), 657 (36-mo)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Fitzgibbon, 2010[204] ORBIT Fair	Mean (SD) at BL, Mean change (SD) at 18 mo **BL** **18 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 38.9 (5.5) -0.86 (2.79) **CG** 39.7 (5.9) 0.22 (2.07) **Diff between groups in adjusted mean change at followup (95% CI):** -1.13 (-1.83, -0.43)** *Weight, kg* **IG** 104.6 (15.8) -2.26 (7.42) **CG** 105.6 (18.1) 0.51 (5.69) **Diff between groups in adjusted mean change at followup (95% CI):** -2.83 (-4.71, -0.95)** n (percent) *≥5% below baseline weight* **IG** -- 22 (24)* **CG** -- 12 (12) **Central adiposity:** NR **Overall adiposity:** NR ** *p<0.01 for adjusted difference between IG and CG* * *p<0.05 for IG versus CG* **IG n analyzed:** 93 **CG n analyzed:** 97, 94 (≥5% weight loss)	**Lipids:** NR **Blood pressure:** NR **Glucose tolerance:** NR
Haapala, 2009[151] Fair	Mean (SD) **BL** **BLc†** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 30.6 (2.7) -- -- **CG** 30.4 (2.8) -- -- *Weight, kg* **IG** 87.5 (12.6) 86.6 (12.7) 82.1 (14.1)* **CG** 86.4 (12.5) 85.1 (12.5) 84.0 (13.2) **Central adiposity:** *Waist circumference, cm* **IG** 98.5 (10.3) 97.6 (10.5) 91.3 (11.7)* **CG** 96.6 (10.4) 95.7 (10.9) 93.3 (11.1) **Overall adiposity:** NR * *p<0.001 for time by group interaction* † BL data for completers **IG n analyzed:** 62 (BL), 42 (BLc, 12 mo) **CG n analyzed:** 62 (BL), 40 (BLc, 12 mo)	**Lipids:** NR **Blood pressure:** NR **Glucose tolerance:** NR

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Hypertension Prevention Trial Research Group, 1990[143] HPT Good	Mean at BL, Mean change (SE) at 6, 36 mo **BL 6 mo 36 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 29 -- -- **CG** 28 -- -- *Weight, kg* **IG** 87.4 -5.58 (0.27) -1.63 (0.41)* **CG** 83.4 0.18 (0.27) 1.86 (0.41) * *p<0.001 at 36 mo* **Central adiposity:** NR **Overall adiposity:** NR **IG n analyzed:** 125 (BL), 112 (6 mo), 117 (36 mo) **CG n analyzed:** 126 (BL), 119 (6 mo), 113 (36 mo)	Mean at BL, Mean change (SE) at 6, 36 mo **Lipids:** NR **BL 6 mo 36 mo** **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 125.3 -6.9 (0.7) -5.0 (0.9)* **CG** 124.7 -1.8 (0.7) -2.6 (0.9) *Diastolic blood pressure, mmHg* **IG** 83.0 -5.3 (0.7) -4.2 (0.8)* **CG** 83.3 -2.5 (0.7) -2.4 (0.8) *p<0.05 **Glucose tolerance:** NR **IG n analyzed:** 125 (BL), 112 (6 mo), 117 (36 mo) **CG n analyzed:** 126 (BL), 121 (6 mo), 115 (36 mo)
Irwin, 2003[152] Frank, 2005[263] Mohanka, 2006[264] PATH Good	Mean (95% CI) at BL, mean change (95%CI) at 12 months **BL 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 30.5 (29.6, 31.4) -0.3 (-0.6, -0.1)* **CG** 30.6 (29.8, 31.4) 0.3 (0.0, 0.6) *Weight, kg* **IG** 81.6 (78.4, 84.7) -1.3 (-2.0, -0.5)* **CG** 81.7 (79.1, 84.3) 0.1 (-0.6, 0.8) **Central adiposity:** *Waist circumference, cm* **IG** 93.1 (90.6, 95.6) -1.0 (-1.8, -0.1) **CG** 93.5 (91.3, 95.8) 0.1 (-0.8, 0.9) **Overall adiposity:** *Subcutaneous fat with CT, total % and total kg body fat by DXA* * *p≤0.05 for IG vs CG at 12 months and over time* **IG n analyzed:** 87 **CG n analyzed:** 86 *Note: Group differences did not differ by age*	Mean (95% CI) at BL, 12 mo **BL 12 mo** **Lipids:** *Total cholesterol, mg/dL* **IG** 230.7 (222, 239) 225.2 (216, 233)* **CG** 232.4 (223, 241) 225.1 (216, 233) *HDL cholesterol, mg/dL* **IG** 51.9 (49, 54) 52.2 (49, 55)** **CG** 52.6 (49, 55) 51.4 (48, 54) *LDL cholesterol, mg/dL* **IG** 152.3 (144, 160) 146.6 (139, 154)† **CG** 152.5 (143, 161) 147.1 (138, 155) *Triglycerides, mg/dL* IG 133.6 (121, 146) 129.6 (117, 142) CG 136.4 (121, 151) 132.9 (117, 148) *Note: TG values differ between Mohanka and Frank articles. Author could not clarify. Only Mohanka data used.* **Blood pressure:** NR **Glucose tolerance:** *Fasting glucose, mg/dL* **IG** 97.8 (81.4, 117.4) 98.9 (81.8, 119.5)§ **CG** 97.4 (82.5, 115.1) 98.4 (83.5, 115.9) *Note: Data reported only in Frank article, but SDs approximately 10 times larger than other comparable SDs. Do not use CIs/SDs* ** p=0.83 for IG vs CG* ***p=0.28 for IG vs CG* *†p=0.43 for IG vs CG* *‡p=0.95 for IG vs CG* *§p=0.99 for IG vs CG* **IG n analyzed:** 85 for total cholesterol, 87 for all other outcomes **CG n analyzed:** 86 *Note: Group differences did not differ by age*

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Jeffery, 1993[153] Jeffery, 1995[289] Trial of Food Provision and Monitary Incentives Fair	Mean at BL, 6, 12, 18, and 30 months (BMI), mean at BL (weight), mean change at 6, 12, and 18 months (weight), mean change (SD) at 30 months (weight) **BL** / **6 mo** / **12 mo** / **18 mo** / **30** **Weight/Relative weight:** *BMI, kg/m²* **IG1** 30.85 / 28.15 / 28.90 / 29.10 / -- **IG2** 30.66 / 26.86 / 27.46 / 28.17 / -- **IG3** 30.77 / 27.94 / 28.92 / 29.28 / -- **IG4** 31.26 / 27.39 / 28.29 / 28.95 / -- **CG** 30.88 / 30.48 / 30.38 / 30.67 / -- time*treatment effect p<0.001 *Weight, kg* **IG1** 89.4 / -7.7 / -4.5 / -4.1** / -1.4 (7.2) **IG2** 88.1 / -10.1 / -9.1 / -6.4* / -2.2 (6.6) **IG3** 92.3 / -7.7 / -4.5 / -4.1** / -1.6 (5.5) **IG4** 91.1 / -10.1 / -9.1 / -6.4* / -1.6 (6.3) **CG** 88.2 / -- / -- / -- / 0.6 (5.3) ** weight changes for IG2 and IG4 are for combined group IG2+IG4* *** weight changes for IG1 and IG3 are for combined group IG1+IG3*	NR
Jones, 1999[154] Hansson, 1994[265] The HOT Study Group, 1993[266] Hypertension Optimal Treatment (HOT) Substudy Fair	Mean (SD) at BL, mean change (SD) at 3 and 6 mo, mean change estimated from figure at 12 mo **BL** / **3 mo** / **6 mo** / **12 mo** **Weight/Relative weight:** *BMI* **IG** 34 (6) / -- / -- / -- **CG** 34 (6) / -- / -- / -- *Weight, kg* **IG** 97 (18) / -2.7 (3.4 / -3.2 (4.3)* / -0.7 **CG** 92 (18) / -1.7 (2.3) / -1.8 (2.7) / -0.5 **Central adiposity:** NR **Overall adiposity:** NR ** p=0.05 for IG vs CG* **IG n analyzed:** 51 **CG n analyzed:** 51 *Note: Weight changes for 6, 12, 18, 24, and 30 months shown in a figure*	**Blood pressure:** no group differences in % achieving target DBP at any time interval (3-30 mos), no group differences in average change in SBP or DBP

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Kastarinen, 2002[155] LIHEF Study (Lifestyle Intervention against Hypertension in Eastern Finland) Fair	Mean (SD) at BL, Mean change at 12, 24 mo **BL** **12 mo** **24 mo** **Weight/Relative weight:** *BMI, kg/m2* **IG** 28.9 (4.6) -- -- **CG** 28.5 (4.5) -- -- *Weight, kg* **IG** 81.1 (15.7 -1.5* -1.5* **CG** 80.0 (14.8) -0.2 -0.3 **Central adiposity:** *Waist circumference, cm* **IG** 97.2 (13.1) -1.2* -1.2* **CG** 95.8 (12.8) 0.3 0.2 **Overall adiposity:** NR ** p<0.05 for difference in change, IG versus CG (stats for diff in change provided)* **IG n analyzed:** 360 (BL), 317 (12 mo), 304 (24 mo) **CG n analyzed:** 355 (BL), 275 (12 mo), 283 (24 mo)	Mean at BL, Mean change at 12, 24 mo **BL** **12 mo** **24 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.66 (0.91) -0.05 -0.03* **CG** 5.59 (0.93) -0.03 0.07 *LDL cholesterol, mmol/L* **IG** 3.64 (0.81) -0.06 -0.11* **CG** 3.56 (0.79) -0.01 0.04 *HDL cholesterol, mmol/L* **IG** 1.32 (0.33) 0.02 0.10 **CG** 1.36 (0.38) 0.01 0.07 *Triglycerides, mmol/L* **IG** 1.56 (1.01) -0.03 -0.06 **CG** 1.49 (1.00) -0.06 -0.06 **Blood Pressure:** *Systolic Blood Pressure, mmHg* **IG** 149 (16) -4.7 -6.2 **CG** 148 (16) -3.4 -4.2 *Diastolic Blood Pressure, mmHg* **IG** 91(9) -4.0* -4.3 **CG** 91 (8) -2.4 -3.2 **Glucose Tolerance:** *Serum insulin, IU/l* **IG** 12.2 (6.8) -0.8 -1.1 **CG** 11.6 (6.3) -0.2 -0.5 ** p<0.05 for difference in change, IG versus CG* **IG n analyzed:** 360 (BL), 317 (12 mo), 304 (24 mo) **CG n analyzed:** 355 (BL), 275 (12 mo), 283 (24 mo)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Kulzer, 2009[156] Fair	Mean (SD) **BL 12 mo 12 mo change** **Weight/Relative weight:** *BMI, kg/m²* **IG** 31.0 (4.7) 29.7 (4.7)* -1.3 (1.7)* **CG** 32.0 (5.7) 31.5 (5.8)-0.5 (1.4) *Weight, kg* **IG** 92.1 (16.5) 88.3 (15.9)* -3.8 (5.2)* **CG** 93.6 (19.3) 92.2 (19.4) -1.4 (4.0) **Central Adiposity:** *Waist circumference, cm* **IG** 106.8 (13.7) 102.7 (12.5)* -4.1 (6.0)* **CG** 106.3 (13.7) 105.9 (14.1) -0.4 (6.2) **Overall Adiposity:** NR ** p<0.05 for between-group difference* **IG n analyzed:** 91 (assumed) **CG n analyzed:** 91 (assumed)	Mean (SD) **BL 12 m 12 mo change** **Lipids:** *Total cholesterol, mg/dL* **IG** 212.2 (43.8) 201.9 (35.6) -10.3 (35.9) **CG** 209.9 (36.6) 207.9 (36.8) -2.0 (35.1) *HDL cholesterol, mg/dL* **IG** 55.9 (14.1) 54.6 (14.9) -1.3 (6.9) **CG** 53.5 (13.2) 51.3 (14.5) -2.2 (9.4) *Triglycerides, mg/dL* **IG** 156.2 (151.0) 120.6 (65.5) -35.6 (136.8) **CG** 144.1 (102.1) 141.6 (99.5) -2.5 (100.3) **Blood Pressure:** *Systolic Blood Pressure, mmHg* **IG** 141.8 (18.6) 137.2 (17.1) -4.6 (19.1) **CG** 139.1 (15.9) 138.1 (15.3) -1.0 (16.7) *Diastolic Blood Pressure, mmHg* **IG** 88.5 (10.5) 84.1 (10.4) -4.4 (11.7) **CG** 87.3 (9.7) 85.2 (12.3) -2.1 (12.6) **Glucose Tolerance:** *Fasting glucose, mg/dL* **IG** 105.7 (12.4) 101.4 (11.3)* -4.3 (11.3)* **CG** 105.5 (12.4) 107.3 (14.3) 1.8 (13.1) *2-hour postprandial OGTT, mg/dL* **IG** 133.1 (36.2) 125.8 (41.3) -7.3 (30.8) **CG** 138.5 (34.9) 130.3 (36.1) -8.2 (36.9) *A1C, percent* **IG** 5.7 (0.5) 5.7 (0.4) 0.0 (0.3) **CG** 5.7 (0.6) 5.8 (0.5) 0.1 (0.4) ** p<0.05 for between-group difference* **IG n analyzed:** 91 (assumed) **CG n analyzed:** 91 (assumed)
Langford, 1985[157] Wassertheil-Smoller, 1985[267] DISH Fair	Mean (SD) at BL, Mean change (SD) at 13 mo **BL 13 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** -- -- **CG** -- -- *Weight, kg* **IG** 86.0 (17.3) -4.0 (5.0)* **CG** 89.8 (17.8) -0.46 (3.6) *≥5% weight loss, percent* **IG** -- 46.3* **CG** -- 11.7 **Central adiposity:** NR **Overall adiposity:** NR **p<0.05 for difference between IG and CG* **IG n analyzed:** 87 (BL), 67 (13 mo) **CG n analyzed:** 89 (BL), 77 (13 mo)	**Lipids:** NR **Blood pressure:** *Not taking anti-HTN meds at 56 wks, percent* **IG** 59.5 (calc n=52)* **CG** 35.3 (calc n=31) *No sex differences in likelihood of requiring a return to HTN meds. Treatment*sex effect was not tested.* *Black participants were almost twice as likely to require a return to HTN meds than white participants. Treatment*race effect was not tested.* **Glucose tolerance:** NR ** p<0.0015* **IG n analyzed:** 87 **CG n analyzed:** 89

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Martin, 2008[158] Martin, 2006[268] Fair	Mean (SD) at BL, Mean change (SD) at 9, 12, 18 mo **BL** **9 mo** **12 mo** **18 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 38.3 (7.5) -- -- -- **CG** 39.8 (7.8) -- -- -- *Weight, kg* **IG** 101.2 (20.6) -1.52 (3.72)* -1.38 (3.69) -0.49 (3.33) **CG** 103.4 (18.0) 0.61 (3.37) -0.16 (3.63) 0.07 (3.75) *≥5% weight loss, percent (calc n)* **IG** -- 13 (9) 10 (7) 7 (5) **CG** -- 7 (5 11 (8) 12 (8) **Central adiposity:** NR **Overall adiposity:** NR ** p<0.05 for difference between IG and CG* **IG n analyzed:** 68; **CG n analyzed:** 69	**Lipids:** NR **Blood pressure:** NR **Glucose tolerance:** NR
Mayer-Davis, 2004[159] POWER Fair	Mean (SD) at BL, Mean change (SE) at 6, 12 mo **BL** **6 mo** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG1** 37.5 (6.7) -0.296 (--) -- **IG2** 37.6 (6.5) -0.974 (--)* -- **CG** 35.2 (7.5) -0.161(--) -- *Weight, kg* **IG1** 100.0 (19.8) -- -- **IG2** 99.5 (17.1) -- -2.2 (--) **CG** 93.0 (20.3) -- -0.3 (--) *Note: At 12-mo IG2 diff from CG, IG1 did not differ from either group* **Central adiposity:** NR **Overall adiposity:** NR ** p<0.01 for IG versus CG* **IG1 n analyzed:** 47 **IG2 n analyzed:** 49 **CG n analyzed:** 56	Mean (SD) at BL, Mean change at 6 mo **BL** **6 mo (cannot use in MA)** **Lipids:** *Total cholesterol, mg/dL* **IG1** 198.9 (39.6) -0.03 **IG2** 198.6 (47.4) -0.09 **CG** 217.3 (57.9) -6.32 *HDL cholesterol, mg/dL* **IG1** 51.7 (15.6) 1.58 **IG2** 48.4 (10.4) 0.73 **CG** 52.4 (16.2) -1.12 *LDL cholesterol, mg/dL* **IG1** 115.1 (37.3) -1.44 **IG2** 119.0 (41.0) -3.37 **CG** 129.1 (48.6) -7.07 *Triglycerides, mg/dL* **IG1** 134.3 (1.8) 0.83 **IG2** 125.2 (1.6) 0.87 **CG** 134.3 (1.8) 0.91 **Blood pressure:** *Systolic blood pressure, mmHg* **IG1** 136.9 (15.9) -4.26 **IG2** 139.7 (14.6) -3.31 **CG** 143.2 (17.9 -9.52 *Diastolic blood pressure, mmHg* **IG1** 81.2 (8.3) -0.07 **IG2** 83.0 (8.7) -0.49 **CG** 81.0 (13.1) -2.65 **Glucose tolerance:** *Hemoglobin A1c, percent* **IG1** 9.7 (3.1) -0.843 **IG2** 10.2 (2.5) -1.56 **CG** 9.6 (2.9) -1.12 **IG1 n analyzed:** 47; **IG2 n analyzed:** 49; **CG n analyzed:** 56

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Mensink, 2003[160] Mensink, 2003[269] Fair	Mean (SE) at BL, Mean change (SE) at 12, 24 mo **BL** **12 mo** **24 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 29.8 (0.5) -1.1 (0.2)** -0.8 (0.2)** **CG** 29.3 (0.4) -0.1 (0.2) 0.0 (0.2) *Weight, kg* **IG** 86 (1.9) -3.1 (0.6)* -2.4 (0.7)** **CG** 83.7 (1.5) -0.2 (0.5) -0.1 (0.5) **Central adiposity:** *Waist circumference, cm* **IG** 102.4 (1.5) -3.8 (0.6)** -1.9 (0.7) **CG** 102.3 (1.1) -1.2 (0.6) -0.6 (0.6) **Overall adiposity:** *Percent body fat (skinfold measurements)* ** *p<0.01 between groups* **IG n analyzed:** 55 (BL), 40 (12, 24 mo) **CG n analyzed:** 59 (BL), 48 (12, 24 mo)	Mean (SE) at BL, Mean change (SE) at 12, 24 mo **BL** **12 mo** **24 mo** **Lipids:** *Total cholesterol, mM* **IG** 5.1 (0.1) 0.0 (0.1) 0.3 (0.1) **CG** 5.2 (0.1) 0.2 (0.1) 0.4 (0.1) *HDL cholesterol, mM* **IG** 1.16 (0.04) -0.04 (0.02) 0.06 (0.03) **CG** 1.10 (0.03) -0.03 (0.02) 0.05 (0.02) *LDL cholesterol, mM* **IG** 3.30 (0.10) 0.01 (0.08) 0.32 (0.11) **CG** 3.44 (0.10) 0.16 (0.06) 0.32 (0.09) *Triglycerides, mM* **IG** 1.59 (0.18) -0.01 (0.08) -0.30 (0.12)** **CG** 1.46 (0.11) 0.19 (0.11) 0.25 (0.11) **Blood pressure:** NR **Glucose tolerance:** *Hemoglobin A1c, percent* **IG** 5.9 (0.1) -0.2 (0.1) 0.0 (0.1) **CG** 5.9 (0.1) -0.2 (0.1) -0.1 (0.1) *Fasting Glucose* **IG** 5.9 (0.1) -0.1 (0.1) 0.2 (0.1) **CG** 5.8 (0.1) 0.1 (0.1) 0.5 (0.1) *Other measurement instruments: 2-hr glucose, HOMA index for insulin resistance, fast insulin* ** *p<0.01 between groups* **IG n analyzed:** 55 (BL), 40 (12, 24 mo); **CG n analyzed:** 59 (BL), 48 (12, 24 mo)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Mitsui, 2008[161] Fair	Mean (SD) **BL** **3 mo** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 24.8 (2.2) 24.0 (2.2) 23.7 (2.4) **CG** 25.6 (2.5) 25.5 (2.6 25.5 (2.6) *Weight, kg* **IG** 64.0 (8.9) -- -- **CG** 67.4 (10.6) -- -- **Central adiposity:** *Waist circumference, cm* **IG** 92.7 (5.1) 89.9 (5.4)* 89.8 (6.1)* **CG** 94.9 (6.2) 95.0 (6.9) 95.7 (7.3) **Overall adiposity:** NR ** p<0.05 for IG versus CG* **IG n analyzed:** 22 **CG n analyzed:** 21	Mean (SD) **BL** **3 mo** **12 mo** **Lipids:** *Total cholesterol, mg/dL* **IG** 225.4 (34.0) 215.5 (26.8) 220.6 (30.9) **CG** 230.9 (23.8) 225.9 (30.7) 236.8 (30.3) *HDL cholesterol, mg/dL* **IG** 51.6 (9.2) 51.8 (12.1) 54.4 (11.9) **CG** 50.7 (12.1) 52.6 (11.1) 52.0 (11.8) Median (range) *Triacylglycerol, mg/dL* **IG** 120.0 (57, 232) 100.0 (54, 249) 112.5 (48, 316) **CG** 146.0 (25, 326) 138.0 (72, 274)* 155.0 (69, 392) Mean (SD) **Blood pressure:** *Systolic Blood Pressure, mmHg* **IG** 139.3 (22.2) 130.7 (19.3) 129.3 (17.5) **CG** 129.0 (12.4) 128.0 (13.7) 127.8 (13.6) *Diastolic Blood Pressure, mmHg* **IG** 81.4 (13.0) 75.9 (12.2) 74.7 (11.5) **CG** 78.1 (11.1) 76.5 (9.6) 75.7 (10.9) **Glucose tolerance:** *Blood glucose, mg/dL* **IG** 96.3 (12.4) 92.6 (10.7) 91.1 (11.8) **CG** 97.6 (15.7) 96.4 (10.2) 98.5 (12.7) *List other measurement instruments: NR* ** p<0.05 for IG versus CG* **IG n analyzed:** 22; **CG n analyzed:** 21
Moore, 2003[162] Fair	Mean (SD) **BL** **12 mo** **18 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 37.0 (5.7) 36.9 (--) 37.1 (--) **CG** 36.9 (5.8) 36.8 (--) 36.9 (--) **Diff between IG and CG (95 %CI), 12 mo:** 0 (-1.0, 1.0) **Diff between IG and CG (95% CI), 18 mo:** 0.1 (-1.0, 1.1) *Weight, kg* **IG** 100.8 (18.1) 100.3 (--) 100.8 (--) **CG** 100.2 (17.4) 99.3 (--) 99.5 (--) **Diff between IG and CG (95% CI), 12 mo:** 1.0 (-1.9, 3.9) **Diff between IG and CG (95% CI), 18 mo:** 1.3 (-1.8, 4.4) **Central adiposity:** NR **Overall adiposity:** NR **IG n analyzed:** 415 (BL), 279 (12 mo, weight), 256 (18 mo, weight) **CG n analyzed:** 428 (BL), 286 (12 mo, weight), 275 (18 mo, weight) **Total n analyzed:** 564 (12 mo, BMI), 530 (18 mo, BMI)* ** Note: One patient missing height data; not reported if this was in the IG or CG.*	**Lipids:** NR **Blood pressure:** NR **Glucose tolerance:** NR

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Narayan, 1998[163] Fair	Median (range) at BL, Median change at 6, 12 mo **BL** **6 mo** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 36.5 (24.1, 59.9) 0.3 0.9 **CG** 33.2 (20.2, 55.8) 0.2 0.5 Regression: IG greater increase in BMI than CG (p=0.05) *Weight, kg* **IG** 96.4 (59.4, 159.1) 1.0 2.5 **CG** 89.3 (59.2, 184.8) 0.5 0.8 Regression: IG greater increase in weight than CG (p=0.03) **Central adiposity:** *Waist circumference, cm* **IG** 116 (87, 161) 0.1 0.1 **CG** 110 (85, 163) -1.5 -2.1 **Overall adiposity:** NR **IG n analyzed:** 48 (BL), NR (6, 12 mo) **CG n analyzed:** 47 (BL), NR (6, 12 mo)	Median (range) at BL, Median change at 6, 12 mo **BL** **6 mo** **12 mo** **Lipids:** *Total cholesterol, mM* **IG** 4.5 (2.1, 6.1) 0.0 0.2 **CG** 4.5 (3.2, 6.2) -0.1 0.1 **P** 0.83 *Triglycerides, mM* **IG** 1.4 (0.3, 3.6) -10.0 0.5 **CG** 1.3 (0.6, 1.4) 2.1 7.2 **P** 0.31 0.27 0.78 **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 116 (90, 146) 2.5 6.0 **CG** 116 (92, 176) 5.2 4.1 **P** 0.39 0.79 0.18 *Diastolic blood pressure, mmHg* **IG** 70 (48, 90) 2.5 1.1 **CG** 72 (53, 98) 0.1 -1.0 **P** 0.15 0.2 0.07 **Glucose tolerance:** *Fasting glucose, mM* **IG** 5.4 (4.5, 6.5) 0.1 0.1 **CG** 5.1 (4.2, 6.1) 0.1 0.1 **P** 0.03 0.94 0.96 *Other measurement instruments: 2-hour plasma glucose, fasting and 2-hour insulin* **IG n analyzed:** 48 (BL), NR (6, 12 mo); **CG n analyzed:** 47 (BL), NR (6, 12 mo)
Parikh, 2010[208] Project HEED Fair	Median (range) at BL, Mean (SD) change at 12 mo **BL** **12 mo (completers)** **12 mo (LOCF)** **Weight/Relative weight:** *BMI, kg/m²* **IG** 32.0 (4.0) -- **CG** 31.0 (5.0) -- *Weight, lb* **IG** 174.0 (39.0) -7.2 (7.3)* -5.5 (--)* **CG** 162.0 (27.0) -2.4 (8.1) -2.3 (--) *≥5% weight loss, percent (n)* **IG** -- 34* (16) -- **CG** -- 14 (6) -- **Central adiposity:** *Waist circumference, in* **IG** 40.0 (4.0) -1.3 (2.6)* -- **CG** 39.0 (4.0) 0.1 (3.4) -- **Overall adiposity:** NR ** p<0.05 for IG versus CG* **IG n analyzed:** 50 (BL), 35 (12 mo), 47 (≥5% weight loss, 12 mo, calc) **CG n analyzed:** 49 (BL), 37 (12 mo), 43 (≥5% weight loss, 12 mo, calc)	Mean (SD) at BL, Mean change (SD) at 12 mo **BL** **12 mo** **Lipids:** *LDL cholesterol, mg/dl* **IG** 109 (32) -1 (35) **CG** 103 (33) 4 (29) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 112 (13) -1 (13) **CG** 119 (25) -7 (17) *Diastolic blood pressure, mmHg* **IG** 70 (7) -2 (9) **CG** 73 (10) -4 (8) **Glucose tolerance:** *Fasting glucose, mg/dL* **IG** 104 (9.6) 10 (13) **CG** 102 (9.5) 11 (11) *Hemoglobin A1c, percent* **IG** 5.6 (0.3) -0.3 (0.2) **CG** 5.6 (0.2) -0.3 (0.2) *Other measurement instruments:* 2-hr plasma glucose, isolated impaired fasting, impaired tolerance, and impaired fasting/tolerance **IG n analyzed:** 50 (BL), 35 (12 mo); **CG n analyzed:** 49 (BL), 37 (12 mo)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Perri, 1988[164] Fair	Mean at BL, Mean change (SD) at 6, 12, 18, 24 months (6 mo=end of initial wt loss phase, 18 mo=12 mo into maintenance phase) **BL 6 mo 12 mo 18 mo 24** **Weight/Relative weight:** *Weight, kg* **IG1** 97.37 -13.17 (5.35) -15.79 (11.77) -12.88 (12.44) -11.41 (12.13) **IG2** 96.94 -11.34 (3.07) -13.54 (6.17) -13.35 (7.37) -8.43 (7.47) **IG3** 95.21 -13.05 (4.83) -15.19 (6.21) -12.97 (7.63) -9.14 (6.41) **IG4** 97.40 -13.67 (5.85) -17.75 (11.66) -15.70 (14.29) -13.54 (15.16) **CG** 89.03 -10.80 (7.60) -8.94 (8.76)* -5.67 (6.90)* -3.60 (6.18)* *IGs had greater wt loss than CG, exact p NR* **Central adiposity:** NR **Overall adiposity:** NR ** p<0.01 for significant differences between CG and all other IG's* **IG1 n analyzed:** 19 **IG2 n analyzed:** 19 **IG3 n analyzed:** 18 **IG4 n analyzed:** 19 **CG n analyzed:** 16	**Lipids:** NR **Blood pressure:** NR **Glucose tolerance:** NR
Pritchard, 1999[165] Fair	Mean **BL 12 mo (ITT) 12 mo (completers)** **Weight/Relative weight:** *BMI, kg/m^2* **IG** -- -- -- **CG** -- -- -- *Weight, kg* **IG1** 85.5 80.4 76.6 **IG2** 91.7 85.5 82.7 **CG** 89.1 89.7 91.7 *Note: IG1 and IG2 lost greater percent of weight than CG (p<0.05)* **Central adiposity:** NR **Overall adiposity:** NR **IG1 n analyzed:** 88 (BL, 12 mo ITT), 48 (12 mo completers) **IG2 n analyzed:** 92 (BL, 12 mo ITT), 65 (12 mo completers) **CG n analyzed:** 90 (BL, 12 mo ITT), 64 (12 mo completers) *Note: Results abstracted for overweight subsample only.*	**Lipids:** NR **Blood pressure:** NR **Glucose tolerance:** NR

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Silva, 2009[166] Silva, 2008[270] Teixeira, 2009[271] Fair	Mean (SD) at BL, Mean change at 12 mo (SD, assumed) **BL 12 mo 24 mo** **Weight/Relative weight:** *BMI, kg/m^2* **IG** 31.7 (4.24) -2.3 (1.9)* -- **CG** 31.3 (4.00) 0.7 (1.9) -- *Weight, kg* **IG** 82.1 (11.9) -- -- **CG** 81.5 (12.1) -- -- *Mean difference in weight loss between IG and CG at end of the intervention was about 6%* **IG n analyzed:** 123 **CG n analyzed:** 116 Percent *≥5% weight loss (calc n/N)* **IG** -- 65 (69/106)* 50 (52/103)* **CG** -- 20 (18/88) 28 (22/80) *≥10% weight loss* **IG** -- 32 (34/106)* 18 (19/103)* **CG** -- 7 (6/88) 12 (11/88) **IG n analyzed:** 106 (12 mo), 103 (24 mo) **CG n analyzed:** 88 (12 mo), 80 (24 mo) **Central adiposity:** NR **Overall adiposity:** *Body fat %, lean mass, fat mass (all "lab-measured") (IG lost more body fat, fat mass p<0.001)* ** p<0.001 for IG versus CG*	**Lipids:** NR **Blood pressure:** NR **Glucose tolerance:** NR

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Simkin-Silverman, 2003[167] Simkin-Silverman, 1998[272] Kuller, 2001[273] Park, 2007[274] Women's Healthy Lifestyle Project (WHLP) Good	Mean (SD) at BL, 6, 18 mo, Mean change (SD) at 30, 42, 54 mo **BL 6 mo 18 mo 30 mo 42 mo 54** **Weight/Relative weight:** *BMI, kg/m²* **IG** 24.9 (3.2) 23.1 (3.1)*23.8 (3.2)* -0.67 (1.8)** -0.34 (1.9)**0.05 **CG** 25.1 (3.3) 25.0 (3.3) 25.2 (3.4) 0.44 (1.6) 0.67 (1.7) 0.96 time*group p<0.001 through 18 mo *Weight, lb* **IG**148.0 (21.3)137.1 (20.5)*141.3 (20.7)* -- -- - **CG**147.6 (21.9)146.8 (21.8)148.2 (22.2) -- -- - time*group p<0.001 **Central adiposity:** NR **Overall adiposity:** *% body fat (group differences statistically significant at 30, 42, and 54 months)* ** p<0.05 for IG vs CG* *** p<0.001 for IG vs CG* **IG n analyzed:** 236 (BL, 6 mo, 18 mo), NR	Mean (SD) at BL, 6, 18 mo **BL 6 mo 18 mo** **Lipids:** *Total cholesterol, mg/dl* **IG** 189.7 (24.5) 175.9 (28.0)* 188.1 (28.3)** **CG** 189.6 (24.3) 190.5 (26.4) 197.4 (28.0) *HDL cholesterol, mg/dl* **IG** 59.7 (13.0) 57.3 (12.0)* 60.7 (11.8)** **CG** 58.4 (12.1) 58.2 (11.9) 61.3 (13.2) *LDL cholesterol, mg/dl* **IG** 114.7 (21.8) 103.4 (24.3)* 110.5 (24.2)** **CG** 116.3 (21.8) 116.2 (23.9) 119.0 (25.7) *Triglycerides, mg/dl* **IG** 82.2 (38.2) 77.7 (35.5)* 84.6 (41.3)† **CG** 78.2 (42.4) 83.7 (56.3) 85.6 (51.3) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 110.0 (12.5) 106.6 (10.7)* 107.3 (13.2)** **CG** 110.1 (13.0) 108.7 (11.9) 109.6 (12.3) *Diastolic blood pressure, mmHg* **IG** 68.5 (7.6) 66.0 (7.0)* 69.9 (8.1)† **CG** 67.9 (8.5) 67.6 (8.0) 69.9 (8.1) **Glucose tolerance:** Fasting glucose **IG** 98.1 (8.0) 97.1 (7.8)* 99.4 (9.1)** **CG** 97.8 (8.3) 98.7 (8.0) 100.6 (9.6) ** p<0.05 for IG vs CG compared to BL **p<0.05 for IG vs CG compared to BL; p<0.05 for Time (0, 6, 18) x Group †p<0.05 for Time (0, 6, 18) x Group* **IG n analyzed:** 236; **CG n analyzed:** 253
Stevens, 1993[168] Whelton, 1992[275] The Trials of Hypertension Prevention Collaborative Research Group, 1992[276] Trials of Hypertension Prevention Phase I Good	Mean (SD) at BL, Mean change (SD) at 6, 18 mo **BL 6 months 18 months** *Weight, kg* **IG** 90.2 (13.3) -5.68 (5.74)* -3.83 (6.12)* **CG** 89.3 (13.0) -0.01 (3.24) 0.07 (4.01) **p<0.01 for IG vs CG* *Adults who met 4.5 kg weight loss goal, % (calc n/N)* *Men* **IG** -- -- 45 (95/212) **C** -- -- 12 (18/151) *Women* **IG** -- -- 26 (22/83) **CG** -- -- 18 (15/85) **Central adiposity:** NR **Overall adiposity:** NR **IG n analyzed:** 308 (BL), 294 (6 mo), 293 (18 mo) **CG n analyzed:** 256 (BL), 237 (6 mo), 235 (18 mo) *The treatment*baseline BMI interaction was statistically significant; the estimated difference in weight loss between IG and CG was 2.2 kg for those who were below the median baseline weight of 89.4 kg, and 5.5 kg for those above the median.*	Mean (SD) at BL, mean change (SE) at 6, 12 and 18 months Lipids: NR **BL 6 months 12 month 18 months** **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 124.3 (8.4) -6.5 (0.5)* -5.4 (0.5)* -5.3 (0.4)* **CG** 124.6 (8.1) -2.7 (0.5) -3.1 (0.5) -2.3 (0.5) *Diastolic blood pressure, mmHg* **IG** 83.7 (2.6) -6.3 (0.4)** -5.8 (0.4)** -6.2 (0.4)** **CG** 84.0 (3.0) -3.7 (0.4) -3.8 (0.4) -3.8 (0.4) *The treatment*sex interaction was not significant for blood pressure. Also, there were no difference between men and women in the effect of weight change on blood pressure.* **p=0.001 for IG vs CG* *** p<0.001 for IG vs CG* **IG n analyzed**: 308 (BL), 294 (6 mo), 293 (18 mo) **CG n analyzed:** 256 (BL), 237 (6 mo), 235 (18 mo)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Stevens, 2001[169] Hollis, 1995[277] TOHP, 1997[278] Trials of Hypertension Prevention Phase II Good	Mean at BL (SD), Mean change (95% CI) at 6, 18, 36 mo **BL 6 mo 18 mo 36 mo** **Weight/Relative weight:** *Weight, kg* **IG** 93.4 (14.1) -4.4 (-4.8, -3.9)* -2.0 (-2.5, -1.5)* -0.2 (-0.7, 0.3)* **CG** 93.6 (13.5) 0.1 (-0.1, 0.4) 0.7 (0.4, 1.6) 1.8 (1.3, 2.2) **Central adiposity:** NR **Overall adiposity:** NR **p<0.001 for IG vs CG* **IG n analyzed:** 595 (BL), 565 (6 mo), 545 (18 mo), 547 (36 mo) **CG n analyzed:** 596 (BL), 561 (6 mo), 551 (18 mo), 554 (36 mo) *Note: Age was associated with greater weight loss at 36 months (but not 18 months). Treatment*age interaction not reported.* *Note: In the IG, white participants had greater net weight loss than black participants by 1.8 kg at 18 months but differences were not significant at 36 months.*	Mean (SD) at BL, Mean (SD) change from baseline at 6, 18, and 36 mo **BL 6 mo 18 mo 36 mo** **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 127.6 (6.1) -6.0 (8.1)* -3.6 (7.9)* -0.8 (8.7)** **CG** 127.3 (6.4) -2.2 (8.1) -1.8 (7.0) -0.6 (8.5) *Diastolic blood pressure, mmHg* **IG** 86.0 (1.9) -5.5 (6.9)* -4.5 (6.1)* -3.2 (6.5)† **CG** 85.8 (1.9) -2.8 (6.1) -3.2 (5.8) -2.4 (7.0) **p<0.001 for CG vs IG* *** p=0.01 for CG vs IG* *† p<0.05 for CG vs IG* **IG n analyzed:** 595 (BL), 561 (6 mo), 533 (18 mo), 527 (36 mo) **CG n analyzed:** 596 (BL),538 (6mo), 525 (18 mo), 514 (36 mo)
Svetkey, 2008[170] Weight Loss Maintenance Trial PROTOCOL, 2008[279] WLM Good	Mean (SD) at BL, Adjusted* mean change (SE) at 30 mo post-rand (from randomization and from BL) **BL Start of Phase II 30 mo (rand) 30-mo (BL)** **Weight/Relative weight:** *Weight, kg* **IG1** 97.2 (16.2) 88.6 15.4) 5.2 (0.3) -3.3 (0.4) **IG2** 97.1 (17.5) 88.7 (16.9) 4.0 (0.3) -4.2 (0.4) **CG** 95.9 (16.2) 87.4 (15.3) 5.5 (0.3) -2.9 (0.4) IG1 (p=0.005) and IG2 (p<0.001) greater wt loss from baseline than CG at 12-mo in adjusted model *≥5% weight loss, percent (n/N)* **IG1** -- -- 35.3 (122/347) **IG2** -- -- 42.2 (144/341) **CG** -- -- 33.9 (116/341) *IG2>CG, p=0.02* **Central adiposity:** NR **Overall adiposity:** NR ** Adjusted for entry weight, site, age, race, sex, race-by-gender interaction, and change in weight in Phase I* *** p<0.001 for change within treatment group* **IG1 n analyzed:** 347 **IG2 n analyzed:** 341 **CG n analyzed:** 341 *No significant treatment*age interaction*	NR

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
ter Bogt, 2009[171] Fair	Mean (SD) at BL, Mean change (SD) at 12 mo **BL** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 29.5 (3.1) -- **CG** 29.6 (3.6) -- *Weight, kg* Men **IG** -- -2.1 (4.8)* **CG** -- 0.0 (3.9) Women **IG** -- -1.5 (4.1) **CG** -- -1.4 (4.9) *Adjusted % change in body weight, mean (95% CI)* IG -- -1.9 (-2.5, -1.2)* CG -- -0.9 (-1.5, -0.2) (adjusted for sex, age, baseline BMI, weight change between screening and baseline) **Central adiposity:** *Waist circumference, cm* **IG** -- -2.4 (7.1) **CG** -- -1.2 (5.9) Men **IG** 104 (7.8 -2.8 (6.2)* **CG** 105 (9.5 -0.9 (4.5) Women **IG** 97 (9.8) -2.0 (7.8) **CG** 97 (11.8) -1.5 (6.8) **Overall adiposity:** NR ** p<0.05 for IG versus CG after adjustment for BL values* **IG n analyzed:** 225 (BL), 103 (Women, 12 mo), 98 (Men, 12 mo) **CG n analyzed:** 232 (BL), 114 (Women, 12 mo), 101 (Men, 12 mo) *Note: Significant group*sex interaction (p=0.03). Men in IG showed greater weight loss (-2.1 vs 0.0 kg) and reduction in WC (-2.8 vs -0.9 cm) than CG, but there were no group differences for women for either measure (wt: IG=-1.5, CG=-1.4; WC: IG=-2.0, CG=-1.5)* *Note: No group differences in weight loss for either participants aged <60 or those 60 and older or for either participants with BMI<30 and those with BMI 30+*	Mean (SD) at BL, Mean change (SD) at 12 mo **BL** **12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.66 (1.0) -- **CG** 5.56 (1.0) -- Men **IG** -- -0.18 (0.6) **CG** -- 0.03 (0.7) Women **IG** -- 0.02 (0.8) **CG** -- -0.06 (0.8) *HDL cholesterol, mmol/L* **IG** 1.44 (0.4) -- **CG** 1.43 (0.4) -- Men **IG** -- -0.06 (0.2) **CG** -- -0.05 (0.2) Women **IG** -- -0.11 (0.2) **CG** -- -0.12 (0.2) *LDL cholesterol, mmol/L* **IG** 3.5 (0.9) -- **CG** 3.43 (0.9) -- Men **IG** -- -0.04 (0.6) **CG** -- 0.12 (0.6) Women **IG** -- 0.15 (0.7) **CG** -- 0.02 (0.7) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 146 (18.5 -- **CG** 145 (15.5) -- Men **IG** -- -8.5 (16.8) **CG** -- -5.3 (12.7) Women **IG** -- -5.3 (20.1) **CG** -- -2.2 (16.5) *Diastolic blood pressure, mmHg* **IG** 87 (9.6) -- **CG** 86 (8.2) -- Men **IG** -- -2.6 (11.2) **CG** -- -1.3 (7.8) Women **IG** -- -0.3 (9.6) **CG** -- 0.2 (8.4)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
(continued) ter Bogt, 2009[171] Fair		**Glucose tolerance:** *Fasting glucose, mmol/L* **IG** 5.20 (0.5) -- **CG** 5.25 (0.7) -- Men **IG** -- -0.03 (0.6) **CG** -- -0.05 (0.8) Women **IG** -- -0.08 (0.6) **CG** -- -0.11 (0.5) **Other measurement instruments:** NR **IG n analyzed:** 225 (BL), 103 (Women, 12 mo), 98 (Men, 12 mo) **CG n analyzed:** 232 (BL), 114 (Women, 12 mo), 101 (Men, 12 mo)
Tuomilehto, 2001[172] Eriksson, 1999[280] Lindstrom, 2003[281] Uusitupa, 2009[282] Finnish Diabetes Prevention Study Good	Mean (SD) at BL, Mean change (SD) at 12, 24 mo **BL 12 mo 24 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 31.3 (4.6) -- -- **CG** 31.0 (4.5) -- -- *Weight, kg* **IG** -- -4.2 (5.1)* -3.5 (5.5)* **CG** -- -0.8 (3.7) -0.8 (4.4) Weight reduction >5% (calc n) IG -- 43% (110) CG -- 13% (32) **Central adiposity:** *Waist circumference, cm* **IG** 102.0 (11.0) -4.4 (5.2)* -4.2 (5.2)* **CG** 100.5 (10.9) -1.3 (4.8) -1.3 (5.4) **Overall adiposity:** NR **p<0.001 for IG vs CG* **IG n analyzed:** 265 (BL), 256 (12 and 24 mo) **CG n analyzed:** 257 (BL), 250 (12 and 24mo)	Mean (SD) at baseline, Mean change (SD) at 12, 24 mo **BL 12 mo 24 mo** **Lipids:** *Total cholesterol, mg/dl* **IG** 215 (37) -5 (28) -4 (31) **CG** 215 (35) -4 (28) 0 (27) *HDL cholesterol, mg/dl* **IG** 46 (12) 2 (7) 4 (7) **CG** 47 (11) 1 (6) 3 (7) *Triglycerides, mg/dl* **IG** 154 (72) -18 (51)* -18 (53)** **CG** 158 (69) -1 (60) 0 (75) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 140 (18)*** -5 (14)† -5 (14)†† **CG** 136 (17) -1 (15) 0 (15) *Diastolic blood pressure, mmHg* **IG** 86 (9) -5 (9)‡ -5 (9)‡‡ **CG** 86 (10) -3 (9) -3 (9) **Glucose tolerance:** *Fasting glucose, mg/dl* **IG** 109 (14) -4 (12)‡ -2 (12)§ **CG** 110 (13) 1 (12) 4 (14) *Other measurement instruments:* Plasma glucose 2 hours after oral glucose challenge **p=0.001 for IG vs CG* ***p=0.0026 for IG vs CG* **** p=0.03 for IG vs CG* *†p=0.007 for IG vs CG* *††p=0.0005 for IG vs CG*

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Villareal, 2008[173] Villareal, 2006[283] Villareal, 2006[284] Fair	Mean (SD) at BL, Mean change (SD) at 6 mo **BL** **6 mo** **12 mo** **Weight/Relative weight:** *Weight, kg* **IG** 99.7 (13.6) -8.2 (5.7)* -- **CG** 103.2 (19.8) 0.7 (2.7) -- *Weight lost, percent* **IG** -- -- -10.1 (2.0) **CG** -- -- 1.2 (1.3) **Central adiposity:** *Waist circumference, cm* **IG** 115 (15) -10 (10)** -- **CG** 115 (16) 1 (8) -- **Overall adiposity:** *Fat mass and fat-free mass in kg (dual-energy x-ray absorptiometry) only at 6 mo* ** p<0.001 for IG vs CG* *** p<0.05 for IG vs CG* **IG n analyzed:** 17 **CG n analyzed:** 10	Mean (SD) at BL, Mean change (SD) at 6 mo **BL** **6 months** **Lipids:** *HDL cholesterol, mg/dL* **IG** 48 (9) -1 (4) **CG** 43 (5) -1 (2) *LDL cholesterol, mg/dL* **IG** 110 (33) -5 (22) **CG** 119 (21) 4 (30) *Triglycerides, mg/dL* **IG** 180 (87) -45 (63)* **CG** 133 (39) 0 (36) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 139 (9) -14 (9)** **CG** 139 (10) -3 (11) *Diastolic blood pressure, mmHg* **IG** 79 (8) -7 (7)* **CG** 78 (4) -1 (7) **Glucose tolerance:** *Fasting glucose, mg/dL* **IG** 100 (10) -4 (7)** **CG** 99 (10) 4 (11) *Other measurement instruments: NR* ** p<0.05 for IG vs CG* *** p<0.01 for IG vs CG* **IG n analyzed:** 17 **CG n analyzed:** 10
Werkman, 2010[174] Good	Mean (SD) at BL, Mean change (SD) at 12, 24 mo **BL** **12 mo** **24 mo** **Weight/Relative weight:** *BMI, kg/m^2* **IG** 26.7 (3.6) -0.49 (1.01) -1.47 (3.66) **CG** 27.3 (3.1) -0.43 (0.98 -1.58 (3.96) *Weight, kg* **IG** 85.1 (11.9) -1.86 (3.08) -0.37 (1.12) **CG** 86.1 (11.4) -1.62 (3.03) -0.40 (1.29) **Central adiposity:** *Waist circumference, cm* **IG** 99.2 (9.5) -2.32 (3.24) -1.06 (3.48) **CG** 100.4 (9.2) -1.9 (3.06) -1.08 (3.60) **Overall adiposity:** *Total body fat (single frequency, tetra polar, body impedance analyzer was used to estimate total body water that was used to calculate total body fat)* *Note: 24 mo data is 12 mon after cessation of the intervention.* **IG n analyzed:** 174 (BL), 166 (12 mo), 147 (24 mo) **CG n analyzed:** 178 (BL), 169 (12 mo), 154 (24 mo)	**Lipids:** NR Mean (SD) at BL, Mean change (SD) at 12, 24 mo **BL** **12 mo** **24 mo** **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 142.7 (16.8) -6.50 (9.93) -4.19 (12.03) **CG** 145.6 (17.9) -4.59 (12.45) -4.57 (14.68) *Diastolic blood pressure, mmHg* **IG** 86.1 (10.1) -4.03 (6.62) -2.89 (7.86) **CG** 86.1 (8.9) -2.79 (7.23) -2.54 (7.21) **Glucose tolerance:** NR *Note: 24 month data is 12 months after cessation of the intervention.* **IG n analyzed:** 174 (BL), 166 (12 mo), 147 (24 mo) **CG n analyzed:** 178 (BL), 169 (12 mo), 154 (24 mo)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Whelton, 1998[175] Appel, 1995[285] Chao, 2000[286] Kumanyika, 2002[287] Trial of Nonpharmacologic Interventions in the Elderly Good	Mean at BL, Mean change (95% CI) at 9, 18, 30 mo **BL 9 mo 12 mo 18 mo 30 mo** *Weight, kg* **IG1 (WL)** 87 (10) -- -- -- -- **IG2 (WL+Na)** 86 (10) -- -- -- -- **IG1+IG2** -- -5.0 (--) -4.7 (--) -4.4 (--) -4.7 (--) **CG1 (UC)** 86 (10) -- -- -- -- **CG2 (SR)** 88 (11) -- -- -- -- **CG1+CG2** -- -1.2 (--) -1.1 (--) -0.8 (--) -0.9 (--) **IG1+IG2 vs** **CG1+CG2:** -3.8 (3.1, 4.5)** -- -3.6 (2.8, 4.3)** -3.9 (2.7, 5.1)** *One site only 48-mo weight, lb (n=94 of 141 rand)* **IG1+IG2** -9.7 (11.4) (n=50)** **CG1+CG2** -3.3 (10.8) (n=44) *Percent meeting 4.5kg weight reduction goal (~5.2%), %, calc n (statistical significance NR)* **IG1+IG2** -- 47 (129/275) -- 42(--/--) 44(--/--) **CG1+CG2** -- 13 (34/260) -- 11(--/--) 13(--/--) **IG1+IG2 n analyzed:** 294 (BL), NR (9, 18, and 30 months) **CG1+CG2 n analyzed:** 291 (BL), NR (9, 18, and 30 months) Mean (SE) at BL, Adjusted weight change at 27 mo **BL 27 mo** *Weight, kg* Black **IG1+IG2** 88.5 (1.0) -3.3 (0.5)* **CG1+CG2** 87.3 (1.0) -1.4 (0.4) White **IG1+IG2** 87.6 (0.7) -4.2 (0.4)** **CG1+CG2** 87.4 (0.6) -0.9 (0.4) ** p<0.01* *** p<0.001* *Note: Whites lost more weight than Blacks (p<0.01)* **IG1+IG2 n analyzed:** 294 **CG1+CG2 analyzed:** 291	Mean (SD) at BL and mean change (95% SE) at last visit prior to attempted med withdrawal (median 3.2 mos) **BL Last visit** **Blood pressure:** *Systolic blood pressure, mmHg* **IG1 (WL)** 128.6 (10.8) -4.0 (1.3) **CG*** 127.7 (12.1) -0.8 (0.8) *Diastolic blood pressure, mmHg* **IG1 (WL)** 70.7 (9.6) -1.1 (0.8) **CG*** 71.5 (8.5) -0.8 (0.5) (See health outcomes for combined outcome, including BP meds) **Glucose tolerance:** NR ** CG is both overweight and non-overweight usual care groups* **IG n analyzed:** 147 (BL), 144 (last visit) **CG n analyzed:** 341 (BL), 333 (last visit)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Wood, 1991[177] Kiernan, 2001[288] Fair	Mean (SD) at BL, Mean change (SD) at 12 mo **BL** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* Men **IG1** 30.4 (2.1) -1.6 (1.7)* **IG2** 30.7 (2.1 -2.7 (1.8)* **CG** 30.7 (2.2) 0.5 (1.5) Women **IG1** 28.0 (2.1) -1.5 (2.0)* **IG2** 28.0 (2.4) -1.9 (1.9)* **CG** 28.1 (2.4) 0.5 (2.0) *Weight, kg* Men **IG1** 97.7 (9.8) -5.1 (5.8)** **IG2** 98.5 (10.6) -8.7 (5.7)** **CG** 98.9 (8.9) 1.7 (4.8) Women **IG1** 74.8 (6.1) -4.1 (5.5)** **IG2** 74.9 (8.2) -5.1 (5.3)** **CG** 75.1 (8.1) 1.3 (5.2) **Central adiposity:** NR **Overall adiposity:** *Fat weight (calculated based on an equation by Siri)* ** p<0.01 for difference between IG1 and IG2 versus CG* *** p<0.001 for difference between IG and CG* **IG1 n analyzed:** 40 (men), 31 (women) **IG2 n analyzed:** 39 (men), 42 (women) **CG n analyzed:** 40 (men), 39 (women)	Mean change (SD) at 12 mo **BL** **12 mo** **Lipids:** *Total cholesterol, mmol/L* Men **IG1** -- -0.42 (0.51) **IG2** -- -0.38 (0.87) **CG** -- -0.14 (0.64) Women **IG1** -- -0.39 (0.61)** **IG2** -- -0.28 (0.52)* **CG** -- -0.03 (0.47) *HDL cholesterol, mmol/L* Men **IG1** -- 0.02 (0.17) **IG2** -- 0.14 (0.18)*** **CG** -- -0.05 (0.15) Women **IG1** -- -0.15 (0.26) **IG2** -- 0.02 (0.18) **CG** -- -0.05 (0.24) *LDL cholesterol, mmol/L* Men **IG1** -- -0.39 (0.48) **IG2** -- -0.27 (0.78) **CG** -- -0.20 (0.59) Women **IG1** -- -0.28 (0.63)* **IG2** -- -0.29 (0.46)* **CG** -- -0.03 (0.41) *Triglycerides, mmol/L* Men **IG1** -- -0.12 (0.59) **IG2** -- -0.48 (0.75)*** **CG** -- 0.18 (0.67) Women **IG1** -- 0.09 (0.36) **IG2** -- -0.02 (0.26)* **CG** -- 0.13 (0.37) **Blood pressure:** *Systolic blood pressure, mmHg* Men **IG1** -- -4.1 (8.1)* **IG2** -- -5.4 (8.3)** **CG** -- 0.1 (7.7) Women **IG1** -- -4.1 (6.0)* **IG2** -- -3.6 (7.7)* **CG** -- -0.2 (6.6)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
(continued) Wood, 1991[177] Kiernan, 2001[288] Fair		*Diastolic blood pressure, mmHg* Men **IG1** -- -2.4 (6.6)*** **IG2** -- -4.9 (5.7)*** **CG** -- 2.1 (5.0) Women **IG** -- -2.2 (5.1)** **IG2** -- -2.0 (4.1)** **CG** -- 0.9 (5.3) **Glucose tolerance:** Other measurement instruments: Apolipoproteins A-I and B ** p<0.05 for difference between IG and CG* *** p<0.01 for difference between IG and CG* **** p<0.001 for difference between IG and CG* **IG1 n analyzed:** 40 (men), 31 (women) **IG2 n analyzed:** 39 (men), 42 (women) **CG n analyzed:** 40 (men), 39 (women)
Wood, 1988[176] Frey-Hewitt, 1990[150] Fair	Mean (SD) at BL, Mean change (SD) at 7 and 12 mo **BL** **7 mo** **12 mo** **Weight/Relative weight:** *Weight, kg* **IG1** 94.1 (8.6) -3.0 (2.8)* -4.0 (3.9)* **IG2** 93.0 (8.8) -7.6 (3.9)* -7.2 (3.7)* **CG** 95.4 (10.6) 0.2 (2.5) 0.6 (3.7) **Central adiposity:** NR **Overall adiposity:** *Fat free mass (kg), fat mass (kg), % body fat (underwater weighing)* *(IG1 & IG2 had greater reductions in fat mass, %body fat than CG (p≤0.01)* ** p<0.001 for IG vs CG* **IG1 n analyzed:** 47 **IG2 n analyzed:** 42 **CG n analyzed:** 42	Mean (SD) at BL, Mean change (SD) at 7 and 12 mo **BL** **7 mo** **12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG1** 5.64 (1.11) -0.21 (0.63) -0.25 (0.64) **IG2** 5.71 (0.99) -0.40 (0.55)† -0.36 (0.56) **CG** 5.70 (0.84) -0.21 (0.48) -0.23 (0.65) *HDL cholesterol, mmol/L* **IG1** 1.06 (0.23) 0.09 (0.21)* 0.11 (0.15)* **IG2** 1.10 (0.23) 0.06 (0.14)* 0.12 (0.16)** **CG** 1.05 (0.23) 0.00 (0.10) -0.02 (0.11) *LDL cholesterol, mmol/L* **IG1** 3.83 (0.93) -0.11 (0.54) -0.25 (0.61) **IG2** 3.84 (0.90) -0.27 (0.59) -0.31 (0.64) **CG** 3.93 (0.82) -0.15 (0.46) -0.21 (0.67) *Triglycerides, mmol/L* **IG1** 1.52 (0.68) -0.25 (0.61)† -0.16 (0.53)† **IG2** 1.59 (0.82) -0.40 (0.61)* -0.27 (0.72)† **CG** 1.47 (0.71) -0.01 (0.51) 0.08 (0.60) **Blood pressure:** NR **Glucose tolerance:** NR ** p<0.01 for IG vs CG* *** p<0.001 for IG vs CG* *† p<0.05 for IG vs CG* **IG1 n analyzed:** 47 **IG2 n analyzed:** 41 (HDL at BL), 42 (all other outcomes and time points) **CG n analyzed:** 41 (HDL at BL), 42 (all other outcomes and time points)

Appendix C Table 1c. Evidence Table of Behavioral Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Woollard, 2003[178] Fair	Mean (SE) at BL, Mean change (SE) at 12, 18 months **BL** **12 mo** **18 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG1** 28.0 (0.6) -- -- **IG2** 30.3 (0.7) -- -- **CG** 29.8 (0.8) -- -- (outcomes data shown in figure only, NS) *Weight, kg* **IG1** -- 1.0 (0.7) 0.5 (0.6) **IG2** -- 0.5 (0.8) 1.2 (0.6) **CG** -- 2.0 (0.7) 1.7 (0.7) **Central adiposity:** NR **Overall adiposity:** NR **IG n analyzed:** 69 (BL), 49 (12 mo), 52 (18 mo) **IG2 n analyzed:** 74 (BL), 48 (12 mo), 54 (18 mo) **CG n analyzed:** 68 (BL), 53 (12 mo), 57 (18 mo)	**Lipids:** Total serum cholesterol, LDL, HDL, and triglycerides: group differences NS at both 12 and 18 mo (Data shown in a figure only) **Blood pressure:** NR **Glucose tolerance:** NR

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Anderssen, 1995[144] ODES (Oslo Diet and Exercise Study) Fair	NR	Mean change (SE) at 12 mo **BL 12 mo** *VO_2, mL-kg/minute* BL DBP>91 mmHg **IG1** -- -0.5(0.9) **IG2** -- 1.6 (1.2)* **IG3** -- 4.4 (0.7)* **CG** -- -2.3 (1.0) BL DBP 84-91 mmHg **IG1** -- -0.3 (1.0) **IG2** -- 2.5 (1.0)* **IG3** -- 4.9 (1.1)* **CG** -- -2.5 (0.8) BL DBP<84 mmHg **IG1** -- -0.1 (0.8) **IG2** -- 2.0 (1.5)* **IG3** -- 4.9 (0.8)* **CG** -- -1.3 (0.5) **p<0.05 for IG compared with CG* **IG1 n analyzed:** 16 (DBP>91), 17 (DBP 84-91), 19 (DBP<84) **IG2 n analyzed:** 20 (DBP>91), 16 (DBP 84-91), 13 (DBP<84) **IG3 n analyzed:** 24 (DBP>91), 20 (DBP 84-91), 21 (DBP<84) **CG n analyzed:** 12 (DBP>91), 16 (DBP 84-91), 15 (DBP<84)	NR	**Subgroup analyses:** Wt change in subset with metabolic syndrome provided in Anderssen 2007
Burke, 2005[145] ADAPT Fair	NR	NR	NR	**Subgroup analyses:** Sex **Other:** At 40 months, 64/118 (54.2%) completed the study in the CG and 76/123 (61.8%). Due to the high attrition, outcomes at 40 months were not abstracted (weight, waist circumference, SBP, DBP, total cholesterol, HDL, triacylglycerols, glucose, insulin).
Christian, 2008[146] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** NR

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Cohen, 1991[147] Fair	**QOL** Instrument used: NR Range: NR # of questions: NR Directionality (higher score=better or worse): NR **Disability** Instrument used: NR Range: NR # of questions: NR Directionality (higher score=better or worse): NR **Depression** Instrument used: NR Range: NR # of questions: NR Directionality (higher score=better or worse): NR	NR	NR	**Subgroup analyses:** Change in mean arterial pressure, change in number of medications, and visits to physician reported for gainers vs losers **Other:** Change in number of antihypertensive medications also reported Of the 18 physicians: 1 had 5 ppts (IG - slight avg weight loss) 1 had 4 ppts (CG-no change on avg) 1 had 3 ppts (CG-slight avg weight gain) 3 had 2 ppts ea 12 had 1 ppt each
Cussler, 2008[148] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** Analysis also available for baseline observation carried forward, not just completers **Maintenance trial**
Davis, 1992[149] Langford, 1991[260] Davis, 1989[261] TAIM Fair	**QOL** Instrument used: Life Satisfaction Scale, Physical Complaints Inventory, Symptom Check List Range: NR # of questions: NR Directionality (higher score = better or worse): NR	Relative Risk (N) **BL 6 mo** *Cardiovascular Risk* Blacks **IG** -- 1.01 (27) **CG** -- 1.00 (26) Whites **IG** -- 0.91 (57) **CG** -- 1.00 (53) Mean at BL, Mean change (SE) at 6 mo *Pulse rate, beats/minute* **IG** 79.1 -4.9 (1.0) **CG** 76.4 -1.8 (1.2) **IG n analyzed:** 90 (BL), 89 (6 mo); **CG n analyzed:** 90 (BL, 6 mo) In addition, specific subscales measured depression, anxiety, sleep disturb-ances, fatigue, and sexual complaints. There was significantly greater improvement in total physical complaints (p<0.002) and sexual problems (p<0.001) in weight reduction groups vs other diet group assignments. However, no diet/drug combo was better than any other or than placebo and usual diet.	NR	**Subgroup analyses:** NR **Other:** Phase II data not used due to how they randomized patients to the second phase and presentation of results (Davis, 1993, RM #8345)

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Diabetes Prevention Program Research Group, 1999[142] Diabetes Prevention Program Research Group, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2005[205] Diabetes Prevention Program Research Group, 2005[207] Ackermann, 2009[211] Diabetes Prevention Program Good	**Depression** Instrument used: Beck Depression Inventory or current use of antidepressants (BDI ≥11 threshold used for depression) Range: 0-63 # of questions: NR Directionality (higher score = better or worse): Higher score = worse **Anxiety** Instrument use: Beck Anxiety Inventory Range: 0-63 # of questions: NR Directionality: Higher score = worse **QOL** Instrument used: Medical Outcomes Study SF-36 Range: NR # of questions: 36 Directionality: Lower score = worse Instrument used: Quality of Well-Being Scale (QWB-SA) Range: NR # of questions: NR Directionality: Higher score = better	**BL 12 mo 24 mo 36 mo** *Depression (BDI>10 or antidepressant use), percent* Men **IG** 10.0 7.9 6.7 -- **CG** 9.1 7.5 8.9 -- Women **IG** 16.1 15.0 15.5 -- **CG** 18.1 17.1 19.6 -- **Men n analyzed*:** 1029 (BL), 948 (12 mo), 848 (24 mo) **Women n analyzed*:** 2158 (BL), 1980 (12 nmo), 1819 (24 mo) *Cardiovascular disease related deaths, n* **IG** -- -- -- 2 **CG** -- -- -- 4 *Nonfatal cardiovascular disease events, percent* **IG** -- -- -- 2.2 **CG** -- -- -- 1.7 *Incidence of nonfatal cardiovascular disease events, events/1000 patient-years* **IG** - -- -- 9.7 **CG** -- -- -- 7.3 *Note: The small, nonsignificant excess of events in IG consisted of CVD hospitalizations and revascularization procedures.* *Diabetes mellitus crude cumulative incidence, cases/100 p-y* IG -- -- -- 4.8 CG -- -- -- 11.0 *Diabetes Mellitus cumulative incidence, percent* IG 0 -- -- 14.4 CG 0 -- -- 28.9	**48 mo†** **Age: All 25-44 45-59 60-85** *Gastrointestinal symptoms (diarrhea, flatulence, nausea, vomiting), number of events/100 person-years* **IG** 12.9* 13.1 14.2 9.7 **CG** 30.7 32.4 30.8 27.8 *Musculoskeletal problems (mostly myalgia, arthritis, arthralgia), number of events/100 person-years* **IG** 24.1* 19.9 25.4 28.0 **CG** 21.1 16.1 21.9 26.7 *One or more hospital admissions, percent* **IG** 15.6 15.4 13.3 20.6 **CG** 16.1 11.1 16.9 21.9 *Rate of hospitalization, number of admissions/100 person-years* **IG** 8.0 7.5 6.4 12.3 **CG** 7.9 6.3 7.9 10.6 *Median hospital stay, days* **IG** 3 3 3 3 **CG** 3 3 3 4	**Subgroup analyses:** Weight and waist circumference at 36 mo by age (although >40% of participants were lost to followup by 36 mo); Subset of 758 participants who had measurements of body fat and body fat distribution by sex at 1 year; Fasting glucose, TG, HDL, BP, waist circumference, and BMI median percent change at 1 year stratified by % weight loss and then sex; Weight loss by race/ethnicity **Other:** 10-year unblinded followup results available (#8173). After removal of interaction terms, race (p<0.0001) and gender (p=0.0259) main effects were significant within lifestyle treatment. IG produced significantly larger percent weight

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Diabetes Prevention Program Research Group, 1999[142] Diabetes Prevention Program Research Group, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2005[205] Diabetes Prevention Program Research Group, 2005[207] Ackermann, 2009[211] Diabetes Prevention Program Good		**BL 12 mo 24 mo 36 mo** *Diabetes Mellitus incidence, percent lower from CG (95% CI)* **IG** 0 -- -- 58 (48, 66) *Diabetes incidence, cases/100 person-years* 25-44 years **IG -- -- --** 6.3 **CG** -- -- -- 11.0 45-59 years **IG** -- -- -- 4.9 **CG** -- -- -- 10.8 60-85 years **IG** -- -- -- 3.3 **CG** -- -- -- 10.3 **IG n analyzed:** 1079 **CG n analyzed:** 1082 **BL 12 mo** *Anxiety, Beck Anxiety Inventory* **IG** 3.19 (4.48) -0.89 (4.78) **CG** 3.78 (4.89) -0.25 (4.80) **IG n analyzed**: 1011 (BL), 998 (12 mos) **CG n analyzed**: 1012 (BL), 993 (12 mos) *SF-6D* **IG** 0.802 (0.106) 0.0004 (0.103) **CG** 0.788 (0.111) -0.013 (0.106) *SF-36 Physical Component Score* **IG** 50.6 (6.9) 1.33 (7.00) **CG** 50.4 (7.2) -0.04 (7.12) *SF-36 Mental Component Score* **IG** 53.7 (7.6) -0.70 (8.67) **CG** 54.0 (7.4) -1.16 (8.33) **IG n analyzed:** 1072 (BL), 1017 (12 mos) **CG n analyzed:** 1079 (BL), 1018 (12 mos) *Quality of Well-being* **IG** 0.710 (0.115) 0.022 (0.113) **CG** 0.700 (0.115) 0.013 (0.124) **IG n analyzed**: 679 (BL), 268 (12 mos) **CG n analyzed:** 702 (BL), 252 (12 mos) *In a fully adjusted model including both IG and weight change, assignment to either IG was not significantly associated with changes in SF-6D at 12 mo vs CG. After adjusting for IG, change in weight were associated with significant changes at 12 mo for SF-6D (p<0.001), PCS-36 (p<0.001), MCS-36 (p=0.04) for ever 5 kg loss; similar associations at 24 mo.* ** Not available by IG and CG. Ns are for both IGs (metformin and behavioral counseling) and CG.*	**48 mo†** **Age: AI 25-44 45-59 60-85** *Deaths, number/100 person-years* **IG** 0.10 0.1 0.0 0.31 **CG** 0.16 0.0 0.0 0.86 * p<0.05 for comparison with CG † 3.2 yrs for age groups **IG n analyzed:** 1073 (22-44 yrs: 318; 45-59 yrs: 541; 60-85 yrs: 214) **CG n analyzed:** 1092 (22-44 yrs: 324; 45-59 yrs: 557; 60-85 yrs: 201) The rate of musculoskeletal symptoms was highest in the IG-L. Hospital admissions were more common in the oldest age group, but did not differ by IG or CG.	loss than CG and achieved greater weight loss than the metformin group across the race-gender groups (all p<0.05). Weight loss, reduction in waist circumference, and percentage of participants who achieved the 7% weight loss goal all increased with increasing age. Association of weight loss and health utilities is reported which is independent of treatment group

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Fitzgibbon, 2010[204] ORBIT Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** NR
Haapala, 2009[151] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** NR
Hypertension Prevention Trial Research Group, 1990[143] HPT Good	NR	NR	NR	**Subgroup analyses:** NR **Other:** NR
Irwin, 2003[152] Frank, 2005[263] Mohanka, 2006[264] PATH Good	NR	NR	No injuries were reported as a result of the exercise program	**Subgroup analyses:** Weight and body fat measures stratified by age and BMI at baseline; lipoprotein measures stratified by change in body fat and change in VO2 max; glucose and triglycerides stratified by change in total fat mass and by minutes of exercise per week **Other:** NR
Jeffery, 1993[153] Jeffery, 1995[289] Trial of Food Provision and Monitary Incentives Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** NR
Jones, 1999[154] Hansson, 1994[265] The HOT Study Group, 1993[266] Hypertension Optimal Treatment (HOT) Substudy Fair	NR	NR	NR	**Subgroup analyses:** Mean (SEM) SBP by target DBP at 3, 6, 12, 18, 24, and 30 months; mean (SEM) DBP by target DBP at BL, 3, 6, 12, 18, 24, and 30 months **Other:** NR

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Kastarinen, 2002[155] LIHEF Study (Lifestyle Intervention against Hypertension in Eastern Finland) Fair	NR	NR	NR	**Subgroup analyses:** BP outcomes for those with and without HTN meds **Other:** NR
Kulzer, 2009[156] Fair	**QOL** Instrument used: World Health Organization-Five Well-Being Index (WHO-5) Range: NR # of questions: NR Directionality: Higher score = better **Depression** Instrument used: Center for Epidemiologic Studies Depression Scale (CES-D) Range: NR # of questions: NR Directionality: Higher score = worse	Mean (SD) **BL 12 mo 12 mo change** *Psychological well-being, WHO-5* **IG** 15.3 (5.1) 16.7 (4.8) 1.4 (3.9) **CG** 14.3 (4.9) 14.3 (5.1) 0.0 (4.2) *Depression, CES-D* **IG** 12.0 (9.5) 9.8 (7.5) -2.2 (7.7) **CG** 13.7 (8.2) 11.4 (7.8) -2.3 (6.8)	NR	**Subgroup analyses:** NR **Other:** NR
Langford, 1985[157] Wassertheil-Smoller, 1985[267] DISH Fair	NR	NR	NR	**Subgroup analyses:** Race **Other:** If a patient's drug therapy was restarted because of blood pressure rise as specified, or if drug therapy was restarted by physicians outside the study, this was considered a terminating event and the patient was counted as "withdrawal failure." Other terminating events were strokes, a new myocardial infarction, congestive heart failure, or an elevated creatine level
Martin, 2008[158] Martin, 2006[268] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** Weight change for completers also available; the results were not statistically significant

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Mayer-Davis, 2004[159] POWER Fair	NR	NR	NR	**Subgroup analyses:** High attenders **Other:** NR
Mensink, 2003[160] Mensink, 2003[269] Fair	NR	Mean (SE) at BL, Mean change (SE) at 12, 24 mo **BL 12 mo 24 mo** *VO_{2max}, L/minute* **IG** 2.15 (0.1) 0.11 (0.03)* 0.09 (0.04)* **CG** 2.13 (0.1) -0.01 (0.04) -0.03 (0.04) ** p<0.05 between groups* **IG n analyzed:** 55 (BL), 40 (12, 24 mo) **CG n analyzed:** 59 (BL), 48 (12, 24 mo)	No serious adverse events were observed in the IG during 2 years of followup	**Subgroup analyses:** NR **Other:** NR
Mitsui, 2008[161] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** Mean steps per day for IG and CG available in a figure
Moore, 2003[162] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** NR
Narayan, 1998[163] Fair	NR	n (percent) **BL 6 mo 12 mo** *Abnormal glucose tolerance, 2-hour PG ≥7.8 mM* **IG** 0 (0) 12 (27) 13 (29) **CG** 0 (0) 4 (9) 5 (11)	NR	**Subgroup analyses:** NR **Other:** Low attendance at intervention classes; authors note that weekly classes may have been too onerous
Parikh, 2010[208] Project HEED Fair	NR	*Incidence of diabetes, cases per person-year* **IG** 0.36 **CG** 0.33	NR	Subgroup analyses: NR Other: IG group reported very limited behavior changes in diet and exercise
Perri, 1988[164] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other: Maintenance trial**: each group received an intervention for 6 months, but after 6 months the treatment differed
Pritchard, 1999[165] Fair	NR	**BL 12 mo** *Daily dose of cardiovascular drug use, n (daily doses; 95% CI)* **IG1** -- 16 (1.8; 0.8, 2.8) **IG2** -- 21 (3.2; 1.9, 4.5) **CG** -- 19 (2.1; 1.4, 2.8) *Note: No significant differences in the daily doses of cardiovascular drug use.*	NR	**Subgroup analyses:** NR **Other:** Compared with CG, the cost of an extra kilogram of weight loss for IG1 was $9.76 and for IG1 it was $7.30.

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Silva, 2009[166] Silva, 2008[270] Teixeira, 2009[271] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** Moderate/vigorous and lifestyle PA associated with 12 mo change in most eating behavior variables (disinhibition, perceived hunger, emotional eating, external eating) and body weight change
Simkin-Silverman, 2003[167] Simkin-Silverman, 1998[272] Kuller, 2001[273] Park, 2007[274] Women's Healthy Lifestyle Project (WHLP) Good	NR	NR	IG lost more BMD than CG at total hip, femoral neck, but not at spine or whole body after controlling for age and baseline BMD. Differences disappeared after controlling for weight change. Combining treatment and control groups, women who lost weight showed greatest reductions in hip, neck, and trochanteric sites and women who gained weight showed smallest reductions	**Subgroup analyses:** HDL, LDL, TG, and glucose by hormone use (non- users saw greater increases in LDL and smaller increases in HDL than users in both treatment groups, no diffs in TG, glucose) **Other:** NR
Stevens, 1993[146] Whelton, 1992 TOHP Collaborative Research Group, 1992 Trials of Hypertension Prevention Phase I Good	NR	*Incidence of Hypertension at either 12- or 18-mo, percent (n/N)* **IG** 6.5 (20/308) **CG** 13.3 (34/256) *RR (95% CI):* 0.66 (0.46, 0.94)	NR	**Subgroup analyses:** Weight loss and BP presented by men and women: Group diffs in SBP and DBP seen at all followup time points for men, only SBP at 6-mo for women Linear regression showed smaller intervention effects for weight change and BP change for black than white participants **Other:** NR
Stevens, 2001[169] Hollis, 1995[277] TOHP, 1997[278] Trials of Hypertension Prevention Phase II Good	NR	Percent (n) and risk ratio **6 mo 18 mo 36 mo 48 mo** *Hypertension* **IG** 4.2 (25) 16.6 (97) 31.9 (185) 38.5 (211) **CG** 7.3 (43) 21.1 (124) 39.2 (229) 44.4 (248) *Risk ratio* 0.58* 0.78* 0.81** 0.87 ** p≤0.05 for CG vs IG* *** p<0.01* **IG n analyzed:** 595 (6 mo), 584 (18 mo), 582 (36 mo), 548 (48 mo) **CG n analyzed:** 589 (6 mo), 588 (18 mo), 577 (36 mo), 559 (48 mo)	NR	**Subgroup analyses:** Weight change by sex and race/ ethnicity (significant group diffs for white men and women through 18 mo, but not white women at 36 mo; black men and women through 6 mo, not at 18 and 36 mo for either black men or women); weight change by # of counseling sessions attend-ed, SBP and DBP by amount of weight lost. In IG, men had greater net wt loss than women by 1.2 kg at 18 mo and 1.7 kg at 36 mo. **Other:** NR

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Svetkey, 2008[170] Weight Loss Maintenance Trial PROTOCOL, 2008[279] WLM Good	NR	*Deaths* **IG1:** 1 **IG2:** 1 **CG:** 1	NR	**Subgroup analyses:** Report change at 30 mo within 4 race-sex subgroups: no sig interactions with age or sex, and magnitude of observed treatment effects was generally consistent across race-sex subgroups. Change in weight from study entry (Phase I, pre-randomization); maintenance of at least 4 kg weight loss relative to entry weight; no net weight gain from entry; at least 5% loss from entry; no more than 3% gain from randomization **Other:** NR
ter Bogt, 2009[171] Fair	NR	NR	NR	**Subgroup analyses:** % change in body weight by gender, age, education, BMI, attempts to lose weight during the past 5 years, visits to NP, treatment recommended **Other:** NR
Tuomilehto, 2001[172] Eriksson, 1999[280] Lindstrom, 2003[281] Uusitupa, 2009[282] Finnish Diabetes Prevention Study Good	NR	**BL 12 m 24 mo 72 mo** *Diabetes Mellitus, no. cases** **IG** -- 5 15(/265=5.7%) 27(/265=10.2%) **CG** -- 16 37(/257=14.4%) 59(/257=23.0%) ()=calc **BL 10.2 years 10.6 years** *Cardiovascular Disease events*** **IG** -- 57 -- **CG** -- 54 -- *Deaths**** **IG** -- -- 6 **CG** -- -- 10 ** Diffs in incidence of DM statistically significant after 2 years. Using all person-years accumulated, cumulative incidence in IG was 58% lower (hazard ratio 0.4, 95% CI 0.3-0.7, p<0.001)* ***Hazard ratio (95% CI) 1.04 (0.72-1.51), adjusted for age and sex* ****Hazard ratio (95% CI) 0.57 (0.21-1.58), adjusted for age and sex*	NR	**Subgroup analyses:** Incidence of DM by success of attaining intervention goals; Incidence of DM by leisure-time physical activity **Other:** NR

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Villareal, 2008[173] Villareal, 2006[283] Villareal, 2006[284] Fair	**QOL** Instrument used: SF-36* Range: NR # of questions: NR Directionality (higher score = better or worse): Higher score = better ** All 8 domains reported, data abstracted for the three with significant differences between groups*	Mean (SD) at BL, Mean change (SD) at 6 mo **BL 6 months** *SF-36 physical function domain* **IG** 60.0 (21.0) 23.2 (20.9)* **CG** 67.0 (15.1) 2.5 (26.4) *SF-36 role limitations, physical domain* **IG** 54.4 (43.5) 23.6 (35.9)* **CG** 62.5 (44.5) 5.0 (19.7) *SF-36 change in health domain* **IG** 38.2 (12.3) 25.3 (13.2)** **CG** 38.0 (6.3) 0.0 (9.4) *VO_{2peak} mL/kg per min* **IG** 16.4 (2.3) 1.7 (1.6)* **CG** 15.7 (3.0) 0.3 (1.1) * p<0.05 for IG vs CG ** p<0.001 for IG vs CG **IG n analyzed:** 17 **CG n analyzed:** 10	**% with adverse effect (calc)** **%falling during PA sessions:** **IG CG** Fell 5.9 (N/A) 0 experienced any a.e. in serum electrolyte concentrations or in renal or liver function test results at 6 mo Mean (SD) at BL, Percent change (NR) at 12 mo **BL 12 mo** *Total hip bone mineral density, g/cm2* **IG** 0.947 (0.115) -2.4 (2.5)* **CG** 0.993 (0.141) 0.1 (2.1) *Trochanter bone mineral density, g/cm2* **IG** 0.716 (0.107) -3.3 (3.1)* **CG** 0.747 (0.152) -0.2 (3.3) *Intertrochanter bone mineral density, g/cm2* **IG** 22.4 (7.0) -2.7 (3.0)* **CG** 24.8 (7.8) 0.3 (2.7) *Lumbar spine bone mineral density, g/cm2* **IG** 1.107 (0.127) 0.9 (3.1) **CG** 1.127 (0.132) 1.3 (5.8) *Whole body bone mineral density, g/cm2* **IG** 1.151 (0.127) -0.9 (1.7) **CG** 1.197 (0.138) 0.3 (2.1) *Spine bone mineral content, g* **IG** 65.5 (11.6) 2.1 (6.1) **CG** 67.7 (17.1) 2.1 (4.9) *Whole body bone mineral content, g* **IG** 2423 (474) -1.4 (2.5) **CG** 2606 (669) -1.7 (2.4)	**Subgroup analyses:** NR **Other:** Changes in body weight correlated directly with changes in BMD at the total hip, trochanter, and intertrochanter sites.
Werkman, 2010[174] Good	NR	NR	NR	**Subgroup analyses:** Men with low educational attainment (found group diffs in WC at 12-mo only, other outcomes NS) **Other:** Module 1 was used by 82%, Module 2 was used by 72%, Module 3 was used by 41%, Module 4 was used by 54%, and Module 5 was used by 16%

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Whelton, 1998[175] Appel, 1995[285] Chao, 2000[286] Kumanyika, 2002[287] Trial of Nonpharmacologic Interventions in the Elderly Good	NR	**12 mo 18 mo 30 mo** *% free of medication, hypertension, and CV events after initial med withdrawn* **IG1+IG2** 54.2 48.6 39.2 **CG1+CG2** 42.2 38.6 26.2 Hazard ratio (95% CI): 0.70 (0.57, 0.87) **IG1+IG2 n analyzed:** 291; **CG1+CG2 n analyzed:** 294 *% with cardiac event* **IG1 (WL) CG*** Stroke 0.0 0.6 TIA 0.0 2.3 MI 1.4 1.2 Angina 6.8 5.6 CHF 0.7 0.3 Arrhythmia 1.4 1.2 Other 4.1 5.6 Total CV 14.3 16.7 *CG is both overweight and nonoverweight usual care *p>0.05 for IG vs CG, limiting CG to overweight only*	**Subset of 67 overweight women** No differences in the magnitude of change of bone mineral density of the spine, femoral neck, or total body between the IGs at 12 months (all p>0.30) When groups were combined, for each pound of weight loss the average decrease of BMD at 6 and 12 months were 0.0006 g/cm, i.e., 0.05%. No sig relationship at distant sites suggesting effects were more pronounced at the spine and not evident at the femoral neck, indicating exercise may be a protective factor for the femoral neck	**Subgroup analyses:** BP for those who were off antihypertensive meds by the last visit; BMD among subset of 67 overweight postmenopausal women (Chao 2000, RM #8229), outcomes by race (Kumanyika 2002, RM #8206) **Other:** HR (95% CI) for freedom from HTN med, high BP, and CV events by trial end IG (WL, WL + Na) vs CG: 0.70 (0.57, 0.87), p=0.001
Wood, 1991[177] Kiernan, 2001[288] Fair	**Depression** Instrument used: Beck Depression Inventory Range: 0-63 # of questions: 21 Directionality (higher score = better or worse): worse	Mean (SD) at BL, Mean change (SD) at 12 mo **BL 12 mo** *Depression* Men **IG1** 4.3 (3.2) 1.1 (3.8) **IG2** 5.4 (5.0) -0.2 (4.9) **CG** 5.5 (4.7) -0.7 (2.9) Women **IG1** 5.8 (4.1) -1.4 (4.4) **IG2** 6.0 (4.9) -0.3 (5.8) **CG** 6.0 (5.9) 0.3 (5.4) *Aerobic Capacity, mL/kg/min* Men **IG1** 34.8 (5.3) 1.6 (5.0)** **IG2** 33.8 (5.3) 8.6 (5.7)** **CG** 33.6 (3.8) -0.2 (4.1) Women **IG1** 26.6 (4.2) 1.4 (4.1)** **IG2** 26.5 (4.8) 6.4 (4.8)** **CG** 27.7 (3.3) 0.0 (4.4) *Estimated 12-year CHD risk, events/1000 persons* Men **IG1** -- -12.9 (23.2)** **IG2** -- -21.8 (24.1)*** **CG** -- 0.6 (15.4) Women **IG1** -- -1.0 (4.6) **IG2** -- -3.5 (5.4)*** **CG** -- 1.3 (6.3) **p<0.01 for diff between IG and CG;***p<0.001	NR	**Subgroup analyses:** Sex **Other:** NR

Appendix C Table 1d. Evidence Table of Behavioral Trials: Health Outcomes and Adverse Effects

Study Reference Quality Rating	Health Outcome Instruments	Health Outcomes	Adverse Effects	Comments
Wood, 1988[176] Frey-Hewitt, 1990[150] Fair	NR	Mean (SD) at BL, mean change (SE) at 12 mo **BL** **12 mo** *Resting metabolic rate (kcal/hr)* **IG1** 77.14 (8.03) -6.21 (1.49)* **IG2** 75.30 (8.68) -0.95 (1.34) **CG** 73.33 (10.75) 1.13 (1.39) *VO2max* **IG1** 33.81 (4.05) -0.27 (2.97)* **IG2** 35.33 (4.88) 4.16 (6.04) **CG** 33.72 (4.48) -2.41 (3.24) ** p≤0.01 for IG vs CG*	NR	**Subgroup analyses:** NR **Other:** IG1 significantly different from CG at BL for RMR expressed as kcal/kg/hr, may have confused the interpretation of RMR changes for IG1
Woollard, 2003[178] Fair	NR	NR	NR	**Subgroup analyses:** NR **Other:** NR

Abbreviations: ACE=angiotensin-converting enzyme; ADAPT=Activity, Diet, and Blood Pressure Trial; ADL=activity of daily living; AE=adverse event; ASA=aspirin; BDI=Beck Depression Inventory; BL=baseline; BMD=bone mineral density; BMI=body mass index; BP=blood pressure; calc=calculated; CES-D=Center for Epidemiologic Studies Depression Scale; CG=control group; CHD=coronary heart disease; CHF=congestive heart failure; CI=confidence interval; Cl=chloride; CT=computed tomography; CV=cardiovascular; CVD=cardiovascular disease; DASH=Dietary Approaches to Stop Hypertension; DBP=diastolic blood pressure; diff=differ/difference; DISH=Dietary Intervention to Study Hypertension; DM=diabetes mellitus; DMV=Department of Motor Vehicles; DPP=Diabetes Prevention Program; DXA=dual-energy x-ray absorptiometry; ECG=electrocardiography; est=estimated; GP=general practitioner; H/O=history of; HDFP=Hypertension Detection and Followup Program; HDL=high-density lipoprotein; HOMA-IR=homostasis model of insulin resistance; HOT=Hypertension Optimal Treatment; HPT=Hypertension Prevention Trial; HTN=hypertension; IG=intervention group; IQR=interquartile range; ITT=intention to treat; LDL=low-density lipoprotein; med=medication; MI=myocardial infarction; N=no; n=number; NA=not applicable; Na=sodium; NR=not reported; NS=not significant; ODES=Oslo Diet and Exercise Study; OW=overweight; PA=physical activity; PATH=Physical Activity for Total Health; POWER=Pounds Off with Empowerment; PREDIAS=Prevention of Diabetes Self-Management Program; pt=patient; QOL=quality of life; RCT=randomized controlled trial; RMR=resting metabolic rate; SBP=systolic blood pressure; SCORE=Systematic Coronary Risk Evaluation; SDT=Self Determination Theory; SD=standard deviation; SE=standard error; SEM=standard error of the mean; SES=socioeconomic status; sig=significance; SR=sodium reduction; stat=statistics; TAIM=Trial of Antihypertensive Interventions and Management; TG=triglycerides; TIA=transient ischemic attack; TOHP=Trials of Hypertension Prevention; tx=treatment; UC=usual care; US=United States; VO2=maximal oxygen consumption; WC=waist circumference; WHLP=Women's Healthy Lifestyle Project; WHO=World Health Organization; WL=weight loss; WLM=Weight Loss Management; wt=weight; x=times; Y=yes.

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Orlistat Trials				
Berne, 2005[180] Fair	**Design:** RCT **Location:** Sweden **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Patients with type 2 diabetes receiving treatment with metformin alone or metformin and sulphonylurea; 30-75 years old; BMI 28-40 kg/m^2; hemoglobin A1c was 6.5-10% **Exclusion:** Treatment with insulin; recent myocardial infarction; other significant peripheral vascular, cardiac, respiratory, renal, neurological, gastrointestinal, or endocrine diseases; signs of fat soluble deficiencies; taking the following medications: drugs that influence appetite, resins, fish oil supplements, and retinoids	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial:** NR **N Randomized:** Total: 220 (221 randomized but 1 didn't ever receive drug) IG: 111 CG: 109 **Followup (12 mo), n (%):** Total: 190 (86.4) IG: 96 (86.5) CG: 94 (86.2) **Cluster information:** NR	**Age (mean):** 59.1 (calc) **Sex (% female):** 45.5 (calc) **Race/Ethnicity:** *% Caucasian:* 100 **SES (income, education):** NR **% Hypertension:** *% Antihypertensive drugs:* 45 **% Diabetes:** 100 **% Dyslipidemia:** *% Lipid-lowering drugs:* 14 **Other health problems:** NR
Broom, 2002[181] UK Multimorbidity Study Fair	**Design:** RCT **Location:** UK **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Men and nonpregnant women; aged 18-80 yrs; BMI ≥28 kg/m^2 (both at baseline and screening visits); at least one of the following obesity-associated CV risk factors: imapired glucose tolerance (serum glucose ≥8.0 mmol/L, 2 hrs after standard 75 g OGTT), dyslipidemia (total serum cholesterol ≥5.2 mmol/L or LDL cholesterol ≥4.2 mmol/L at screening); hypertension (sitting DBP 90-105 mmHg) **Exclusion:** Women of child-bearing age that were lactating or not using adequate contraception; MI; coronary artery bypass graft or percutaneous transluminal coronary angioplasty within 3 months before screening; gastrointestinal surgery for weight reduction; active gastrointestinal disorders; pancreatic disease; history of post-surgical adhesions; excessive alcohol intake; substance abuse; required any drug that might alter body weight or plasma lipids; administration of systemic steroids (other than hormone-replacement therapy); concomitant pharmacotherapy for type 2 diabetes, dyslipidemia or hypertension	**N recruited or assessed for eligibility:** 737 **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Single-blind placebo and mildly hypocaloric diet (600 kcal/day deficit) Required compliance: NR Length: 2 weeks N (%) retained after run-in: NR Compliance used as stratification variable **N Randomized:** Total: 531 IG: 265 CG: 266 **N ITT:** Total: 522 IG: 259 CG: 263 **Followup (12 mo), n (%):** Total: 347 (65) IG: 186 (70) CG: 161 (61) **Cluster information:** NR	**Age (mean):** 46.0 **Sex (% female):** 78.4 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension alone:** 21.6 **% Hypertension overall**: 43 **% Impaired glucose tolerance alone:** 5.0 **% Impaired glucose tolerance overall:** 17.0 **% Dyslipidemia alone:** 44.8 **% Dyslipidemia overall:** 72 **Other health problems:** Combinations of IGT, hypertension, and dyslipidemia *Note: Characteristics for N ITT.*

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Davidson, 1999[182] Fair	**Design:** RCT **Location:** Multiple states, US **Recruitment Setting:** Clinical research centers **Self-selected:** NR	**Inclusion:** Age older than 18 years; BMI 30-43 kg/m^2; adequate contraception in women of childbearing potential; absence of weight loss (>4 kg) in the previous 3 months **Exclusion:** Frequently changed smoking habits or had stopped smoking in the past 6 months; history or presence of substance abuse; excessive intake of alcohol; significant cardiac, renal, hepatic, gastrointestinal, psychiatric, or endocrine disorders; drug-treated type 2 diabetes mellitus; concomitant use of medications that alter appetite or lipid levels	**N recruited or assessed for eligibility:** NR **N eligible:** 1187 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Controlled-energy diet (30% intake as fat and energy, prescribed as 1.3 BMR − 2100 to 3360 kj/d), placebo capsules Required compliance: ≥75% placebo capsules taken Length: 4 weeks N (%) retained after run-in: 892 (75.1) **N Randomized:** Total: 892 IG: 668 CG: 224 **N ITT:** Total: 880 IG: 657 CG: 223 **Followup (12 mo), n (%):** Total: 591 (66.3) IG: 458 (68.6) CG: 133 (59.4) *24 mo data not given because high attrition* **Cluster information:** NR	**Age (mean):** 43.5 (calc) **Sex (% female):** 84.2 (calc) **Race/Ethnicity:** *% White:* 80.8 (calc) *% Black:* 14.0 (calc) *% Hispanic:* 4.2 (calc) *% Other:* 1.0 (calc) **SES (income, education):** NR **% Hypertension:** *% DBP>90 mmHg* *Untreated:* 5.9 (calc) *Treated:* 2.5 (calc) **% Diabetes:** 4.1 **% Dyslipidemia:** *% Abnormal LDL level (>129.9 mg/dL):* 33.1 (calc) *% Abnormal HDL level (<.9 mmol/L):* 14.4 (calc) *% Abnormal triglycerides level (>98.2 mg/dL):* 9.2 (calc) **Other health problems:** Impaired glucose tolerance * Characteristics for N ITT

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Derosa, 2003[183] Fair	**Design:** RCT **Location:** Italy **Recruitment Setting:** Database from the Clinica Medica II at the University of Pavia **Self-selected:** N	**Inclusion:** Obese (BMI>30 kg/m^2); aged >40 years; severe hypercholesterolemia (TC≥240 mg/dL); normotensive (SBP<140 mmHg and DBP<90 mmHg); nonsmokers; normal thyroid function; not taking diuretics or beta-blockers **Exclusion:** NR	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Controlled-energy diet (1500 kcal, 54% carbohydrates, 24% proteins, 22% lipids (6% saturated), 108 mg cholesterol, and 35 g fiber); placebo Required compliance: NR Length: 4 weeks N (%) retained after run-in: NR Degree of weight loss in compliance trial used for stratification **N Randomized:** Total: 99 IG-O: 27 IG-F: 24* IG-OF: 25* CG: 23 Total (IG-O + CG): 50 **Followup (12 mo), n (%):** Total (IG-O + CG): 48 (96.0) IG-O: 25 (92.6) CG: 23 (100) **Cluster information:** N/A *IG-F (fluvastatin) & IG-OF (orlistat + fluvastatin) are not included in remainder of abstraction.	**Age (mean):** 52.0 (calc) **Sex (% female):** 52 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR
Derosa, 2010[215] Good	**Design:** RCT **Location:** Italy **Recruitment Setting:** University medical centers **Self-selected:** N	**Inclusion:** Caucasian; type II diabetic patients; aged 18 years or older; BMI ≥30 kg/m^2; uncontrolled type II diabetes (glycated hemoglobin >8.0%) in therapy with different oral hypoglycemic agents or insulin **Exclusion:** History of ketoacidosis; unstable or rapidly progressive diabetic retinopathy, nephropathy, or neuropathy; impaired hepatic function; impaired renal function; severe anemia; serious cardiovascular disease or cerebrovascular conditions within 6 months before study enrollment; women pregnant or breastfeeding or of childbearing potential and not taking adequate contraceptive precautions	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial:** NR **N Randomized:** Total: 254 IG: 126 CG: 128 **Followup (12 mo), n (%):** Total: 234 (92.1) IG: 113 (89.7) CG: 121 (94.5) **Cluster information:** NR	**Age (mean):** 52.5 (calc) **Sex (% female):** 49.6 (calc) **Race/Ethnicity:** *% White:* 100 **SES (income, education):** NR **% Hypertension:** 71.7 **% Diabetes:** 100 **% Dyslipidemia:** *% Hypercholesterolemia:* 35.0 *% Hypertriglyceridemia:* 3.1 *% Combined dyslipidemia:* 17.3 **Other health problems:** NR

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Finer, 2000[184] James, 1997[290] Fair	**Design:** RCT **Location:** UK **Recruitment Setting:** Local advertisement or GP referral **Self-selected:** Mixed	**Inclusion:** Obese (BMI 30-43 kg/m^2); 18 years or older **Exclusion:** Weight loss of more than 4 kg in the 3 months before screening; history of any serious systemic disease, including diabetes; uncontrolled hypertension; previous gastrointestinal surgery for weight reduction; history of post-surgical adhesions; history or presence of cancer; psychiatric or neurological disorder requiring chronic medications or liable to prejudice patient compliance; evidence of alcohol or substance abuse; bulimia or evidence of laxative abuse; pregnancy or lactation (women of childbearing potential were allowed to enter the study if using adequate contraceptive precautions); post-menopausal women who had been amenorrhoeic for less than 1 year; taken drugs capable of influencing body weight, resins for lipid-lowering, anti-coagulants, digoxin or lipid-soluble vitamin supplements within the previous month	**N recruited or assessed for eligibility:** NR **N eligible:** 267 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Placebo and low-calorie diet Required compliance: Taking 75% of capsules Length: 4 weeks N (%) retained after run-in: 228 (85.4) Stratified by weight loss during run in **N Randomized:** Total: 228 IG: 114 CG: 114 **Followup (12 mo), n (%):** Total: 139 (61.0) IG: 66 (57.9) CG: 73 (64.0) **Cluster information:** NR	**Age (mean):** 41.5 (calc) **Sex (% female):** 88.5 (calc) **Race/Ethnicity:** *% White:* 94.9 *% Black:* 1.4 *% Other:* 3.7 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR
Hanefeld, 2002[187] Fair	**Design:** RCT **Location:** Germany **Recruitment Setting:** Centers (primary care physicians and outpatient clinics) **Self-selected:** NR	**Inclusion:** Aged 18-70 years; BMI ≥28 kg/m^2; HbA1c 6.5-11%; diagnosis of type 2 diabetes treated with sulphonylureas for at least two months before screening or were diagnosed with type 2 diabetes but not yet treated with antidiabetic medication **Exclusion:** Diabetes patients treated with drugs other than sulphonylureas; treated with medications known to effect body weight, serum lipids or vitamins; proliferative retinopathy or papilloedema; uncontrolled hypertension (DBP>120 mmHg); hypo- or hyper-thyroidism; secondary or type I diabetes; cardiac insufficiency (NYHA III/IV); presence or history of cancer or any significant appetite, renal, hepatic, gastrointestinal, psychiatric, immunological, or metabolic disorders; pregnant, lactating, or of childbearing potential and not taking adequate contraceptive measures	**N recruited or assessed for eligibility:** **N eligible:** 492 **N excluded:** **N refused or other reason:** **Pre-randomization compliance trial** Description: Placebo and diet Required compliance:NR Length: 4 weeks N (%) retained after run-in: 383 (77.8) **N Randomized:** Total: 383 IG: 195 CG: 188 **N ITT:** IG: 189 CG: 180 **Followup (12 mo), n (%):** Total: 264 (68.9) IG: 133 (68.2) CG: 131 (69.7) **Cluster information:** NR	**Age (mean):** 56.2 (calc) **Sex (% female):** 50.9 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 100 **% Dyslipidemia:** NR **Other health problems:** NR

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Hauptman, 2000[189] Fair	**Design:** RCT **Location:** Multiple states, US **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Obese (BMI 30-44 kg/m^2); aged >18 years **Exclusion:** Women who were pregnant, lactating, or of childbearing potential and not taking adequate contraceptive measures; weight loss of more than 4 kg during the previous 3 months; history of significant cardiac, renal, hepatic, or gastrointestinal disorders; uncontrolled hypertension or any other clinically significant condition; gastrointestinal surgery for weight-reducing purposes; bulimia or laxative and/or substance abuse; abnormal laboratory measures (values ≥10% greater than the reference value for the normal range sufficient to require medical followup by the study physician); changes in smoking habits in the previous 6 months; use of any drug that might influence body weight or food intake during the 8 weeks before screening	**N recruited or assessed for eligibility:** NR **N eligible:** 796 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Placebo and reduced-energy diet (same as in study) Required compliance: 75% compliance, determined by counting capsules returned Length: 4 weeks N (%) retained after run-in: 635 (79.8) **N Randomized:** Total: 635 IG1 (60 mg): 213 IG2 (120 mg): 210 CG: 212 (Use IG2 in MA) **Followup (12 mo), n (%):** Total: 427 (67.2) IG1: 154 (72.3) IG2: 151 (71.9) CG: 122 (57.5) **Cluster information:** NR	**Age (mean):** 42.5 (calc) **Sex (% female):** 78.3 **Race/Ethnicity:** % White: 90.9 % Black: 6.8 % American Indian: 0.2 % Hispanic: 1.9 % Other: 0.3 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR
Hill, 1999[190] Fair	**Design:** RCT **Location:** Multiple sites, US **Recruitment Setting:** Clinical research centers **Self-selected:** NR	**Inclusion:** Men and women aged ≥18 years; BMI 28-43 kg/m^{2,} had to lose ≥8% of their initial body weight in run in **Exclusion:** Ever had significant medical disorders; uncontrolled hypertension; recurrent nephrolithiasis; symptomatic cholelithiasis; active gastrointestinal disorders; type 2 diabetes; pancreatic disease; cancer; pregnant or lactating; history of presence of substance abuse; eating disorders; excessive alcohol intake; significantly abnormal laboratory test results; previous gastrointestinal surgery for weight reduction; history of postsurgical adhesions; had not taken any medications known to influence body weight, appetite, or lipid concentrations during the 8 weeks prior to screening	**N recruited or assessed for eligibility:** NR **N eligible:** 1313 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Hypoenergetic diet (deficit of 4180 kJ/day with goal 0.5-1.0 kg/wk; 30% fat, 50% carb, 20% protein) with no pharmacologic intervention. Included dietary counseling, 4 session behavioral modification (UM's Wise Weighs) program, and encouraged to increase physical activity (brisk walking 20-30 min 5 times/wk) Required compliance: Lose ≥8% of initial body wt Length: 6 months N (%) retained after run-in: 729 (55.5) **N Randomized:** Total: 729 IG1 (30 mg): 187 IG2 (60 mg): 173 IG3 (120 mg): 181 CG: 188 **Followup (12 mo), n (%):** Total: 537 (73.7) IG1: 140 (74.9) IG2: 133 (76.9) IG3: 126 (69.6) CG: 138 (73.4) **Cluster information:** NR	**Age (mean):** 46.3 (calc) **Sex (% female):** 84.0 (calc) **Race/Ethnicity:** % White: 88.3 (calc) % Black: 5.8 (calc) % Hispanic: 4.9 (calc) % Other: 1.0 (calc) **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR *Note: Characteristics captured at beginning of run-in period (-6 months), not at randomization. Also, 9 participants appear to be missing in the characteristics table (720 participants total, yet 729 completed the run-in period).*

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Hollander, 1998[191] Fair	**Design:** RCT **Location:** 12 centers, US **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Aged >18 years; drug compliance ≥70% during 5-week placebo run-in; HbA1c of 6.5-10%, fasting plasma glucose level of 5.6-12.2 mmol/l at the end of the 4th week of the run-in; blood levels of fat-soluble vitamin above the lower limit of the normal reference range; BMI 28-40 kg/m^2; were on oral hypoglycemic drug therapy for at least 6 months before the study; stable plasma glucose level on a second-generation sulfonylurea agent as the only hypoglycemic agent at entry **Exclusion:** Pregnant; lactating; of child-bearing potential and not using contraception; any clinically relevant condition that might affect study outcomes; complications associated with diabetes; weight loss of >4 kg during the previous 3 months; history of recurrent hephrolithiasis or symptomatic cholelithiasis; gastrointestinal surgery for weight reducing purposes; history of bulimia or laxative abuse; had taken any drug that might influence body weight or plasma lipids during the 8 weeks before the study initiation	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Placebo and mildly hypocaloric(-500 kcal) weight loss diet (~30% calories from fat, 50% from carbohydrate, and 20% from protein, with a maximum of 300 mg/day of cholesterol) Required compliance: ≥70% drug compliance Length: 5 weeks N (%) retained after run-in: 322 (82.4 (calc)) (322 of 391) **N Randomized:** Total: 322 IG: 163 CG: 159 **Followup (12 mo), n (%):** Total: 254 (79) IG: 139 (85) CG: 115 (73) **Cluster information:** NR	**Age (mean):** 55.1 (calc) **Sex (% female):** 48.9 (calc) **Race/Ethnicity (calc):** *% White:* 87.5 *% Black:* 6.9 *% Hispanic:* 3.1 *% Other:* 2.5 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR
Krempf, 2003[193] Fair	**Design:** RCT **Location:** France **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Aged 18-65 years; BMI ≥28 **Exclusion:** Serious eating disorders; type I or type II diabetes; pregnant or lactating; smoking ≥1 pack/day or intention to stop smoking during the trial; previous surgical treatment for obesity; known or suspected substance abuse; significant thyroid, renal, hepatic, gastrointestinal, or immune disorders; concomitant use of medications that alter body weight, appetite, or the absorption of food	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Placebo run-in, no further information Required compliance: NR Length: 15 days N (%) retained after run-in: 696 (87.4% (calc)) **N Randomized:** Total: 696 IG: 346 CG: 350 **Followup (18 mo), n (%):** Total: 425 (61.1) (calc) IG: 224 (64.7) (calc) CG: 201 (57.4) (calc) **Cluster information:** NR	**Age (mean):** 41 **Sex (% female):** 86.4 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems:** NR

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Lindgarde, 2000[194] Swedish Multimorbidity Study Fair	**Design:** RCT **Location:** Sweden **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Men and nonpregnant women; aged 18-75 yrs; BMI 28-38 kg/m^2; at least one of the following obesity-associated CHD risk factors: fasting serum glucose ≥6.7 mmol/L or confirmed type 2 diabetes treated with sulphonylurea or metformin but not insulin, total serum cholesterol ≥6.5 mmol/L and/or LDL cholesterol ≥4.2 mmol/L on at least 2 occasions or prescribed lipid-lowering med, DBP ≥90 mmHg on at least 2 occasions or confirmed hypertension treated with antihypertensive medication **Exclusion:** Women of child-bearing potential who were lactating or not using adequate contraception; MI within 3 mo prior to screening; gastrointenstinal surgery for weight reduction; active gastrointestinal disorders; pancreatic disease; history of postsurgical adhesions; excessive alcohol intake; substance abuse; required any drug that might alter body weight or plasma lipids; administration of systemic steroids (other than hormone replacement therapy) or insulin	**N recruited or assessed for eligibility:** NR **N eligible:** 382 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: single blind placebo and mildly hypocaloric diet (-600 kcal/day deficit); minimum diet 1200 kcal; 30% fat Required compliance: NR (weight loss used for stratification) Length: 2 weeks N (%) retained after run-in: 376 (98.4) **N Randomized:** Total: 376 IG: 190 CG: 186 **Followup (12 mo), n (%):** Total: 323 (85.9) IG: 159 (83.7) CG: 164 (88.2) **Cluster information:** NR	**Age (mean):** 53.5 **Sex (% female):** 63.6 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** 74.5 **% Diabetes:** 26.1 (type 2) **% Dyslipidemia:** 39.9 (hypercholesterolemia) **Other health problems:** Combinations of hypercholesterolemia, diabetes, and hypertension and with each condition alone
Miles, 2002[197] Fair	**Design:** RCT **Location:** US and Canada **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Patients with type 2 diabetes; 40-65 yrs; BMI 28-43 kg/m^2; maintained stable weight for ≥3 mo; HbA1c between 7.5 and 12.0%; received metformin treatment at 1000-2500 mg/day for at least 6 weeks (sulfonylurea therapy in combination with metformin was permitted as long as the sulfonylurea dose was stable for 12 weeks before study entry) **Exclusion:** Receiving insulin, thiazolidinediones, or α-glucosidase inhibitors; any clinical condition that might affect study end points, including renal, hepatic, or endocrine disorders; poorly controlled hypertension (SBP≥160 mmHg or DBP≥100 mmHg); active gastrointestinal disease; previous bariatric surgery; history of bulimia; substance abuse; use of any weight loss medications; women who were pregnant, lactating, or of child-bearing potential	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial:** NR **N Randomized:** Total: 516 IG: 255 CG: 261 **N ITT:** Total: 504 IG: 250 CG: 254 **Followup (12 mo), n (%):** Total: 311 (60) IG: 165 (65) CG: 146 (56) **Cluster information:** NR	**Age (mean):** 53.1 (calc) **Sex (% female):** 48 (calc) **Race/Ethnicity:** *% Caucasian:* 82 *% Black:* 12 *% Other:* 6 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 100 **% Dyslipidemia:** NR **Other health problems:** NR

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Richelsen, 2007[198] Fair	**Design:** RCT **Location:** Multiple sites, Scandinavia **Recruitment Setting:** Clinical research centers **Self-selected:** NR	**Inclusion:** Aged 18-65 years; BMI between 30-45 kg/m^2 and a waist circumference ≥102 cm (men) or ≥92 cm (women); one or more of the following risk factors: impaired fasting glucose (plasma glucose ≥6.1 mmol/L), diet-treated type 2 diabetes (plasma glucose ≥7.0 mmol/L) or dyslipidemia (HDL cholesterol ≤0.9 mmol/L for men, ≤1.1 mmol/L for women), and/or serum triglycerides ≥2.0 mmol/L but <10.0 mmol/L **Exclusion:** NR	**N recruited or assessed for eligibility:** NR **N eligible:** 383 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Very-low-energy diet of 600-800 kcal/day Required compliance: Body weight loss of ≥5% Length: 8 weeks N (%) retained after run-in: 309 (80.7) **N Randomized:** Total: 309 IG: 153 CG: 156 **Followup (36 mo), n (%):** Total: 200 (64.7) IG: 102 (66.7) CG: 98 (62.8) **Cluster information:** NR	**Age (mean):** 47.0 (calc) **Sex (% female):** 50.8 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 22.3 **% Dyslipidemia:** *% Low HDL (≤0.9/1.1 mmol/L):* 43.4 *% High triglycerides (>2.0 mmol/L):* 59.2 **Other health problems:** Impaired fasting glucose *Characteristics reported for -2 months*
Rossner, 2000[199] Fair	**Design:** RCT **Location:** 14 centers, Europe **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Aged ≥18 years; BMI 28-43 kg/m^2 **Exclusion:** Pregnant, lactating, or of childbearing potential but not taking adequate contraceptive measures; any clinically significant condition other than obesity that might affect the outcome of the study; lost >4 kg during the previous 6 months; undergone GI surgery for weight reducing purposes; had a history of post-surgical adhesions or of bulimia or laxative abuse; taken any drug that might influence body weight or serum lipids during 8 weeks before screening; uncontrolled hypertension, drug-treated DM, or history or presence of symptomatic cholelithiasis	**N recruited or assessed for eligibility:** NR **N eligible:** 783 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Placebo plus nutritionally balanced diet that was designed to cause a 600-kcal daily energy deficit and to supply about 30% of energy as fat Required compliance: 75% assessed by proportion of capsules taken Length: 4 weeks N (%) retained after run-in: 729 (93.1) (calc) **N Randomized:** Total: 729 (calc) IG1 (60 mg): 242 IG2 (120 mg): 244 CG: 243 **Followup (12, 24 mo), n (%):** *12 mo* Total: 524 (71.9) (calc) IG1: 185 (76.4) (calc) IG2: 181 (74.2) (calc) CG: 158 (65.0) *24 mo* Total: 435 (59.7) (calc) IG1: 140 (57.9) (calc) IG2: 159 (65.2) (calc) CG: 136 (56.0) **Cluster information:** NR	**Age (mean):** 44.2 (calc) **Sex (% female):** 82.3 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** % DBP ≥90 mmHg: 21.6 **% Diabetes:** NR **% Dyslipidemia:** % LDL cholesterol ≥3.362 mmol/L: 53.3 **Other health problems:** NR NOTE: Reported for 718 subjects only (assume that this excluded the subjects who had no followup assessments, n=11)

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Sjostrom, 1998[200] Fair	**Design:** RCT **Location:** Multi-center, Europe **Recruitment Setting:** Hospital waiting lists and local advertising **Self-selected:** Mixed	**Inclusion:** Obese (BMI 28-47 kg/m^2) men and women; aged 18 years and over; using adequate contraception (women of child-bearing age) **Exclusion:** Serious diseases, including uncontrolled hypertension and pharmacologically treated diabetes; weight loss of more than 4 kg in the 3 months before screening; surgery for weight reduction; history of post surgical adhesions, bulimia, or laxative abuse; use of any drug that might have influenced body weight or plasma lipids in the month before study entry; drug or alcohol abuse	**N recruited or assessed for eligibility:** 937 **N eligible:** 743 **N excluded:** 194 **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Placebo TID with meals and hypo-caloric diet with -600 kcal/day from total estimated energy expenditure (1.3 times BMR) (roughly 30% of energy from fat); minimum 1200 kcal/day Required compliance: 75% compliance calculated from number of capsules returned Length: 4 weeks **N (%) retained after run-in:** 688 (92.6) **N Randomized:** Total: 688 IG: 345 CG: 343 **N ITT:** Total: 683 IG: 343 CG: 340 **Followup (12 mo), n (%):** Total: 544 (79) IG: 284 (82) CG: 260 (76) (Not clear if randomly reassigned at 12 mo) **Cluster information:** NR	**Age (mean):** 44.8 (calc)* **Sex (% female):** 83.0 (calc)* **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR ** Characteristics from ITT participants*
Swinburn, 2005[201] Fair	**Design:** RCT **Location:** 8 clinical research centers, Australia and New Zealand **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** Aged 40-70 years, BMI 30-50 kg/m^2; One or more of the following conditions: hypercholesterolemia (serum total cholesterol >5.5mmol/l and/or LDL >3.5 mmol/L and clinically stable if on treatment), hypertension (systolic >140 mmHg and/or diastolic >90 mmHg and clinically stable if on treatment), and/or Type-2 diabetes treated with dietary modification or any oral hypoglycemic agent for 6+ months and clinically stable (glycated hemoglobin: 6.5-10%) **Exclusion:** History of significant cardiac, renal, hepatic, gastrointestinal, or endocrine disorders; uncontrolled hypertension; previous gastrointestinal surgery for weight reduction; history of post-surgical adhesions; smoking; history or presence of substance abuse, bulimia, type-1 diabetes, psychiatric disorders, or active gastrointestinal disease	**N recruited or assessed for eligibility:** 352 **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial:** Description: Single blind placebo lead-in period with advice on reducing dietary fat and increasing physical activity levels Required compliance: NR Length: 4 weeks N (%) retained after run-in: NR **N Randomized:** Total: 339 IG: 170 CG: 169 **Followup (12 mo), n (%):** Total: 269 (79.4) (calc) IG: 132 (77.6 (calc)) CG: 137 (81.1 (calc)) **Cluster information:** NR	**Age (mean):** 52.2 (calc) **Sex (% female):** 56.9 (calc), significantly greater in CG **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** 56.6 (calc) **% Diabetes:** *% Type 2 diabetes:* 26.8 (calc) **% Dyslipidemia:** *% Hypercholesterolemia:* 65.5 (calc) **Other health problems:** 10 year risk CV disease

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Torgerson, 2004[202] Torgerson, 2001[291] XENDOS Fair	**Design:** RCT **Location:** 22 medical centers, Sweden **Recruitment Setting:** Newspaper advertisements **Self-selected:** Y	**Inclusion:** Aged 30-60 years; BMI ≥30 kg/m^2; nondiabetic glucose tolerance (2-hour whole blood glucose <10.0 mmol/L and fasting whole blood glucose <6.7 mmol/L); IGT (fasting whole blood glucose <6.7 mmol/L and 2-hour whole blood glucose 6.7-10.0 mmol/L) **Exclusion:** Diabetes; ongoing and active cardiovascular and gastrointestinal disease; change in body weight >2 kg between screening and baseline examinations; SBP >165 mmHg or DBP >105 mmHg on the same 2 consecutive visits; MI within 6 months; symptomatic cholelithiasis; gastrointestinal surgery for weight reduction; peptic ulcer; active pancreatic disease; malignancy; significant psychiatric or neurologic disorder; abuse or previous participation in any trial of orlistat	**N recruited or assessed for eligibility:** 20,401 **N eligible:** 3373 **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial:** NR **N Randomized:** Total: 3305 IG: 1650 CG: 1655 **Followup, n (%):** *12 mo* Total: 2746 (83.1) (calc) IG: 1478 (calc) (89.6) CG: 1268 (calc) (76.6) *48 mo* Total: 1414 (42.8%) IG: 850 (52%) , ITT 1640 (99.4 (calc)) CG: 564 (34%), ITT 1637 (98.9 (calc)) **Cluster information:** NR	**Age (mean):** 43.3 (calc) **Sex (% female):** 55.2 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems:** NR
Metformin Trials				
Fontbonne, 1996[185] BIGPRO Fair	**Design:** RCT **Location:** France **Recruitment Setting:** NR **Self-selected:** NR	**Inclusion:** High waist-to-hip ratio (≥0.95 for men, ≥0.80 for women); men aged 35-60 years; women aged 40-65 years **Exclusion:** Ischemic cardiovascular disease (diagnosed before inclusion or detected by ECG required for inclusion; diabetes (diagnosed before inclusion or by OGTT at inclusion); heavy chronic medical treatment; serious life-threatening medical conditions; psychiatric disorders; impaired renal function (plasma creatinine ≥15 mg/dL)	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial:** NR **N Randomized:** Total: 457 IG: 227 CG: 230 **Followup (12 mo), n (%):** Total: 324 (70.9) IG: 164 (72.2) CG: 160 (69.6) **Cluster information:** NR	**Age (mean):** 49.5 **Sex (% female):** 66.7 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** *% With antihypertensive treatment:* 33.0 (calc) **% Diabetes:** *% Abnormal glucose tolerance:* 21.5 **% Dyslipidemia:** NR **Other health problems:** NR *Characteristics at baseline are for those for participants who complete study; Also present baseline characteristics of subjects present and absent at 12 months*

Appendix C Table 2a. Evidence Table of Medication Trials: Study Characteristics

Study Reference Quality Rating	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Gambineri, 2006[186] Fair	**Design:** RCT **Location:** Italy **Recruitment Setting:** Division of Endocrinology, S. Orsola-Malpighi Hospital **Self-selected:** Probably not but did not state that all PCOS were assessed so could have been some volunteer recruitment through fliers, etc.	**Inclusion:** Women with polycystic ovarian syndrome (Rotterdam consensus: (*need 2 of the following*)) 1. chronic anovulation or severe oligomenorrhea/amenorrhea, 2. hirsutism or total testosterone levels of at least 0.72 ng/mL, 3. polycystic ovarian morphology at ultrasound); aged 18-45 years; BMI of at least 28 kg/m^2; waist circumference of at least 88 cm; consistent with an abdominal fat distribution phenotype **Exclusion:** Use of any medication or a significant modification in body weight within the previous 3 months or dieting; hyperprolactinemia; Cushing's syndrome; late-onset congenital adrenal hyperplasia; thyroid dysfunction; diabetes; cardiovascular, renal, or liver diseases	**N recruited or assessed for eligibility:** 140 **N eligible:** 85 **N excluded:** 55 **N refused or other reason:** 5 **Pre-randomization compliance trial:** NR	**Age (mean):** 27.0 (calc) **Sex (% female):** 100 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** *% Impaired glucose tolerance and/or impaired fasting glucose:* 33 **% Dyslipidemia:** NR **Other health problems:** 100% Polycystic ovarian syndrome
Diabetes Prevention Program Research Group, 1999[142] Haffner, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2006[210] Ratner, 2005[207] Knowler, 2002[206] West, 2008[214] Rubin, 2005[205] Ackermann, 2009[211] Diabetes Prevention Program Good	**Design:** RCT **Location:** 27 clinical centers (research and community based), US **Recruitment Setting:** Mass media, mail, telephone contacts, and recruitment through employment or social groups or health care systems **Self-selected:** Assume mostly self-selected	**Inclusion:** Fasting plasma glucose 95-125 mg/dL (≤125 mg/dL in American Indian clinics); 2-hour postchallenge glucose 140-199 mg/dL after a 75 g glucose load; aged ≥25 years; BMI ≥24 kg/m^2 (≥22 kg/m^2 for Asian Americans) **Exclusion:** Diabetes at baseline; medical conditions likely to limit life span and/or increase risk of intervention; conditions or behaviors likely to affect conduct of the trial; medications and medical conditions likely to confound the assessment for diabetes	**N recruited or assessed for eligibility:** NR **N eligible:** NR **N excluded:** NR **N refused or other reason:** NR **Pre-randomization compliance trial** Description: Compliance with pill taking (placebo) and diet and exercises recordkeeping, no further detail Required compliance: NR Length: 3 weeks N (%) retained after run-in: NR **N Randomized:** Total: 3234 IG-Metformin: 1073 IG-Lifestyle: 1079 CG: 1082 **Followup (12 mo, 36 mo), n (%):** *12 mo* Total: 3070 (94.9) (calc) IG-M: 1017 (94.8 (calc)) IG-L: 1026 (95.1 (calc)) CG: 1027 (94.9 (calc)) *36 mo* Total: 1921 (59.4) (calc) IG-M: 626 (58.3 (calc)) IG-L: 638 (59.1 (calc)) CG: 657 (60.7 (calc)) **Cluster information:** NR	**Age (mean):** 50.6 **Sex (% female):** 67.7 **Race/Ethnicity:** *% White:* 54.7 *% African American:* 19.9 *% Hispanic:* 15.7 *% American Indian:* 5.3 *% Asian/Pacific Islanders:* 4.4 **SES (income, education):** NR **% Hypertension:** 29.6 **% Diabetes:** 0 **% Dyslipidemia:** 44.1% had elevated LDL or taking medication **Other health problems:** History of stroke, revascularization, MI, MI by ECG, elevated TG, metabolic syndrome

Appendix C Table 2b. Evidence Table of Medication Trials: Intervention Details

Study Reference Quality Rating	Medication Dose/Duration	Behavioral Components
Orlistat Trials		
Berne, 2005[180] Fair	**Intervention setting:** 16 primary care centers and 6 hospital-based diabetes clinics **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR (Assume not PCP) **Incentives:** NR	**Diet prescription:** Mildly reduced calorie diet (600 kcal per day deficit) containing 30% of calories from fat. **Exercise prescription:** Encouraged to increase their physical activity by a daily 30-minute walk **Behavioral intervention description:** Dietary counseling by nurse or dietician at every study visit. Self-management package given including leaflets and a food diary. **Control weighing frequency (after BL):** 4 times over 52 weeks
Broom, 2002[181] UK Multimorbidity Study Fair	**Intervention setting:** 54 GP surgeries and 12 hospital clinics **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Mildly hypocaloric diet (nutritionally balanced with approximately 30% of energy from fat; negative 600 kcal/day); at 6 months, the diet was reduced by a further 300 kcal/day **Exercise prescription:** NA **Behavioral Intervention description:** NR **Control weighing frequency (after BL):** 12 times over 12 months
Davidson, 1999[182] Fair	**Intervention setting:** Clinical research centers **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 12 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Controlled-energy diet (30% intake as fat and energy prescribed as 1.3 BMR minus 2100 to 3360 kj/d [500-800 kcal(calc]--est mid-point for MA: 650) **Exercise prescription:** Encouraged to walk briskly for 20-30 minutes 3-5 times per week **Behavioral intervention description:** Dietitians provided instructions on dietary intake recording as part of behavior modification program and used food diaries for counseling. 4 behavior modification session on weight loss strategies **Control weighing frequency (after BL):** 17 times in 1 year (including final)
Derosa, 2003[183] Fair	**Intervention setting:** NR **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 12 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Controlled-energy diet (1500 kcal, 54% carbohydrates, 24% proteins, 22% lipids (6% saturated), 108 mg cholesterol, and 35 g fiber) **Exercise prescription:** Standardized physical activity program of ≥30 minutes 4 days per week by bicycle **Behavioral intervention description:** Food diaries and discussion used to ensure dietary and exercise compliance; every 3 mo dieticians provided instruction on dietary intake-recording procedures as part of behavior-modification program; patient discussion and assessment to diaries used for counseling patients during study period **Control Weighing Frequency (after BL):** 2 times (including final)

Appendix C Table 2b. Evidence Table of Medication Trials: Intervention Details

Study Reference Quality Rating	Medication Dose/Duration	Behavioral Components
Derosa, 2010[215] Good	**Intervention setting:** University medical centers **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 12 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Controlled energy diet (near 600 kcal daily deficit) based on AHA recommendations, including 50% of calories from carbohydrates, 30% from fat (6% saturated), and 20% from proteins, with a maximum cholesterol content of 300 mg/day and 35 g/day of fiber. No vitamin or mineral preparations. Standard diet advice by dietitian who periodically provided instruction on dietary intake recording procedures and used food diaries for counseling **Exercise prescription:** Encouraged to increase physical activity by walking briskly for 20-30 min 3 times/week or by cycling **Behavioral intervention description:** NR **Control Weighing Frequency (after BL):** 4 times over 12 months
Finer, 2000[184] James, 1997[290] Fair	**Intervention setting:** 5 centers (authors from mix of research centers, medical schools, hospitals) **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 12 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Low-calorie diet with a 600 kcal deficit with a minimum of 1200 kcal/day (30% of energy derived from fat, alcohol limited to 150 g/week). After 24 weeks, another reduction of 300 kcal/day. Goal weight loss through diet of 0.25 to 0.5 kg/week **Exercise prescription:** NR **Behavioral intervention description:** NR **Control weighing frequency (after BL):** 15 times over 12 months
Hanefeld, 2002[187] Fair	**Intervention setting:** Not stated, but likely center (primary care physicians and outpatient clinics) where recruited **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 12 mo (48 weeks) **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Nutritionally balanced, mildly calorie-reduced diet (30% fat, 50% carbohydrates, 20% protein, and 300 mg of cholesterol maximum), based on estimates of maintenance needs less 600 kcal/day to promote weight loss of 0.25 to 0.50 kg/week by week 24, minimum of 1200 kcal/day **Exercise prescription:** NR **Behavioral intervention description:** Diet diary every 4 weeks for four days, at week 20, patients' diets examined and modified if necessary to provide appropriate caloric intake **Control weighing frequency (after BL):** 12 times over 48 weeks
Hauptman, 2000[189] Fair	**Intervention setting:** Primary care centers **Medication:** Orlistat **Dose:** IG1: 60 mg TID IG2: 120 mg TID **Duration:** 12 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Reduced-energy diet; nutritionally balanced; 30% energy as fat, 50% carbohydrate, 20% protein, maximum of 300 mg/day of cholesterol; alcohol limited to 10 drinks per week; 5020 kj/day for patients <90 kg, 6275 for patients ≥90 kg **Exercise prescription:** Encouraged to increase physical activity by walking briskly for 20-30 minutes 3-5 times per week **Behavioral intervention description:** Dietary guidance on desired energy intake from study physician only at start of placebo lead-in phase. Physicians did not receive any specific training in nutrition or weight management techniques beyond same instructional materials given to patients. No registered dieticians or behavioral psychologists were involved. At 4 points during first 52 weeks, patients viewed videos of behavior modification techniques for weight control. No group meetings or counseling sessions. Completed 3-day dietary records at 10 points over 2 year study (assume 5 during year 1) **Control weighing frequency (after BL):** Once at 52 weeks. Brief physician visits at 7 other time points in first year (likely had weight but not stated)

Appendix C Table 2b. Evidence Table of Medication Trials: Intervention Details

Study Reference Quality Rating	Medication Dose/Duration	Behavioral Components
Hill, 1999[190] Fair	**Intervention setting:** Not stated but likely clinical research centers where recruited **Medication:** Orlistat **Dose:** 30, 60, or 120 mg TID **Duration:** 12 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Energy intake to maintain body weight (not give hypoenergetic diet if gaining weight but encouraged to maintain higher weight) **Exercise prescription:** NR **Behavioral intervention description:** Dietary and behavioral counseling provided through the 1 year treatment period to help subjects maintain body weights; 3-day diet record 4 timepoints during 1 year treatment period **Control weighing frequency (after BL):** 10 times 1 year
Hollander, 1998[191] Fair	**Intervention setting:** NR **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Mildly hypocaloric diet (~500 kcal/day deficit) **Exercise prescription:** NR **Behavioral intervention description:** All patients were instructed on the dietary requirements of the study and procedures for completing food intake records **Control weighing frequency (after BL):** 14-25 times over 12 months
Krempf, 2003[193] Fair	**Intervention setting:** 81 hospital centers **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 18 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Individually tailored diet prescription by a dietician beginning with the run-in period including a 20% energy reduction and 30% of energy intake from fat. Reassessed at clinic visits at months 3, 7, 11, 15, and 18. Those who lost weight maintained the diet, those who maintained or gained were decreased by a further 10%, never below 1200 kcal/day **Exercise prescription:** NR **Behavioral intervention description:** Completed 4-day food diaries every 4 months **Control weighing frequency (after BL):** 18 over 18 months
Lindgarde, 2000[194] Swedish Multimorbidity Study Fair	**Intervention setting:** 33 primary care centers **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Mildly hypocaloric diet (-600 kcal/day deficit); minimum diet 1200 kcal; approximately 30% of calories from fat); at 6 months, energy content was reduced another 300 kcal per day **Exercise prescription:** encouraged to increase physical activity by taking a 30 minute walk daily **Behavioral intervention description:** Monthly dietary counseling by a practice nurse as part of a self-help weight control educational package that included leaflets and videotape and asked at each visit how often watch videotape **Control weighing frequency (after BL):** 10 times over 1 year
Miles, 2002[197] Fair	**Intervention setting:** NR **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Reduced-calorie diet (~600 kcal daily deficit) containing 30% of calories as fat, 50% as carbohydrate, and 20% as protein, with a maximum cholesterol content of 300 mg/day. Daily calorie intake was reduced by an additional 200 kcal after 6 months with a minimum intake of 1200 kcal per day. A multivitamin supplement was prescribed to be taken daily at least 2 hours before or after the evening dose of study medication. **Exercise prescription:** Encouraged to increase their level of physical activity **Behavioral intervention description:** Received dietary counseling at baseline and at regular intervals throughout the study **Control weighing frequency (after BL):** Checked 12 times over 12 months

Appendix C Table 2b. Evidence Table of Medication Trials: Intervention Details

Study Reference Quality Rating	Medication Dose/Duration	Behavioral Components
Richelsen, 2007[198] Fair	**Intervention setting:** Not specifically stated but likely clinical research centers where recruited **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 36 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Standard energy-restricted diet (600 kcal daily deficit), dietary and lifestyle counseling, advised to reduce fat to ~30% of total energy **Exercise prescription:** Advice to increase physical activity **Behavioral intervention description:** Dietician provided dietary and lifestyle counseling at monthly visits for 18 months and then every 3 months **Control weighing frequency (after BL):** 24 times over 3 years
Rossner, 2000[199] Fair	**Intervention setting:** centers (assumed to be clinical centers) **Medication:** Orlistat **Dose:** IG1: 60 mg TID IG2: 120 mg TID **Duration:** 2 years **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Nutritionally balanced diet that was designed to cause a 600-kcal daily energy deficit and to supply about 30% of energy as fat **Exercise prescription:** NR **Behavioral intervention description:** Patient received advice from dietician on the dietary requirements of the study and received instructions on accurate completion of food intake diaries. Food diaries assessed by a dietitian and advice given 12 times over year (18 times 2 years). **Control weighing frequency (after BL):** 12 times over 12 months (18 times over 24 months)
Sjostrom, 1998[200] Fair	**Intervention setting:** NR **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Hypocaloric diet with -600 kcal from total estimated energy expenditure (1.3 times BMR) (roughly 30% of energy from fat); minimum 1200 kcal; further reduced 300 kcal at 24 week and down to minimum of 1000 kcal **Exercise prescription:** NR **Behavioral intervention description:** NR **Control weighing frequency (after BL):** 15 times in first year; 8 in year 2
Swinburn, 2005[201] Fair	**Intervention setting:** NR **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Reduce daily dietary fat intake to be between 25-30% of total daily energy intake or about 40 g/day. Otherwise ad libitum diet. **Exercise prescription:** Undertake regular, moderate-intensity physical activity of at least 30 minutes a day on most days **Behavioral intervention description:** Received advice from dietician about identifying the sources of dietary fat and reducing them as much as possible using a variety of strategies including fat reduced cooking methods. Participants completed 5-day diet and physical activity logs immediately after screening and immediately before BL, 12 week, and 52 week visits as part of the advice and goal-setting process. **Control weighing frequency (after BL):** 2 clinic visits over 4 weeks (lead-in) and 13 visits over 52 weeks (treatment)

Appendix C Table 2b. Evidence Table of Medication Trials: Intervention Details

Study Reference Quality Rating	Medication Dose/Duration	Behavioral Components
Torgerson, 2004[202] Torgerson, 2001[291] XENDOS Fair	**Intervention setting:** Medical centers **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 4 years **Prescriber:** NR **Incentives:** NR	**Diet prescription:** 800 kcal/day deficit containing 30% of calories from fat and not more than 300 mg of cholesterol per day. Readjusted every 6 months to account for weight loss **Exercise prescription:** Walk at least 1 extra km/day **Behavioral intervention description:** Dietary counseling every 2 weeks for the first 6 months and monthly thereafter. Kept physical activity diaries **Control weighing frequency (after BL):** 16 times over 4 years (4 times 12 months) *Note: All participants were prescribed the diet and exercise programs*
Metformin Trials		
Fontbonne, 1996[185] BIGPRO Fair	**Intervention setting:** Clinical centers (assumed) **Medication:** Metformin **Dose:** 850 mg BID **Duration:** 12 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Given diet advice to reduce insulin resistance **Exercise prescription:** Given exercise advice to reduce insulin resistance **Behavioral intervention description:** NR except for lifestyle advice to reduce insulin resistance as described above **Control weighing frequency (after BL):** 4 times
Gambineri, 2006[186] Fair	**Intervention setting:** Hospital endocrine clinic **Medication:** Metformin **Dose:** 850 mg BID **Duration:** 12 months (started one month after diet started) **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Hypocaloric diet (-500 kcal from the usual individual energy intake) containing 20% proteins, 30% lipids, and 50% carbohydrates. Final diets ranged between 1200-1400 kcal/day **Exercise prescription:** Invited to maintain their usual physical activity throughout the study, which was checked monthly by the self-administered questionnaire **Behavioral intervention description:** Placed on diet above by same dietician who calculated diet using diet history and 3 day recall; same dietician evaluated compliance with diet monthly according to previously defined method providing quantitative information on daily energy intake and macronutrient composition of the diet consumed during previous month **Control weighing frequency (after BL):** Monthly visits likely included weight but not clear; so probably 12 times
Diabetes Prevention Program Research Group, 1999[142] Haffner, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2006[210] Ratner, 2005[207] Knowler, 2002[206] West, 2008[214] Rubin, 2005[205] Ackermann, 2009[211] Diabetes Prevention Program Good	**Intervention setting:** NR **Medication:** Metformin **Dose:** Started at 850 mg QD and increased to 850 mg BID; dosage adjusted if necessary for GI symptoms **Duration:** NR, average of 2.8 years in DPP before they were unmasked to treatment assignment **Prescriber:** NR, presume research staff **Incentives:** "Rewards deployed according to the judgment of each clinic"	**Diet prescription:** Follow the Food Guide Pyramid and the equivalent of a National Cholesterol Education Program Step 1 diet; **Exercise prescription:** Increase physical activity gradually with a goal of at least 30 minute of an activity such as walking 5 days each week **Behavioral intervention description:** Participants in both groups were provided written information and had an annual 20-30 minute individual session with their case manager addressing the importance of a healthy lifestyle for the prevention of type 2 diabetes; encouraged to lose 5-10% of their initial weight through a combination of diet and exercise; to avoid excessive alcohol intake; to stop smoking if smoker; recommendations reviewed annually **Control weighing frequency (after BL):** Annually

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Orlistat Trials		
Berne, 2005[180] Fair	Mean (SD) at BL, Percent change at 12 mo **BL 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 32.6 (3.1) NR **CG** 32.9 (3.0) NR *Weight, kg* **IG** 95.3 (12.6) -5.0** **CG** 95.7 (12.5) -1.8 *Weight loss ≥5%, n* **IG** -- 51** **CG** -- 12 *Weight loss ≥10%, n* **IG** -- 15* **CG** -- 3 Mean (SD) **Central adiposity:** *Waist circumference, cm* **IG** 108.0 (9.0) 103.0 (8.9)* **CG** 109.0 (9.3) 106.0 (9.1) **Overall adiposity:** NR *** p<0.0001 for change in IG versus CG* ** p<0.005* **IG n analyzed:** 111 **CG n analyzed:** 109	Mean (SD) at BL, Mean change (SD) at 12 mo **BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.5 (1.0) -0.24 (1.00)* **CG** 5.4 (1.1) 0.10 (1.11) *HDL cholesterol, mmol/L* **IG** 1.3 (0.3) -0.01 (0.17)* **CG** 1.2 (0.2) 0.07 (0.23) *LDL cholesterol, mmol/L* **IG** 3.1 (1.0) -0.08 (0.96) **CG** 3.0 (0.8) 0.01 (0.95) *Triglycerides, mmol/L* **IG** 2.6 (1.4) -0.12 (1.06) **CG** 2.8 (2.5) -0.04 (2.41) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 145.0 (18.2) -3.2 **CG** 145.0 (16.1) -3.1 *Diastolic blood pressure, mmHg* **IG** 84.5 (9.7) -2.4 **CG** 84.3 (10.0) -1.9 **Glucose tolerance:** *Hemoglobin A1c, percent* **IG** 7.6 (0.8) -1.1* **CG** 7.6 (0.8) -0.22 *Fasting glucose, mmol/L* **IG** 11.2 (2.6) -1.9* **CG** 10.9 (2.5) -0.26 * p<0.05 for IG versus CG **IG n analyzed:** 111; **CG n analyzed:** 109

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Broom, 2002[181] UK Multimorbidity Study Fair	Mean (SD) at BL, Mean change (SD) at 12 mo **BL 12 mo** **Weight/Relative weight:** *BMI, kg/m^2* **IG** 37.1 (6.4) -- **CG** 37.0 (6.2) -- *Weight, kg* **IG** 100.9 (20.5) -5.8 (8.5)* **CG** 101.8 (19.8) -2.3 (6.4) **Central adiposity:** *Waist circumference, cm* **IG** 107.8 (15.6) -5.99 (--)* **CG** 108.6 (16.4) -2.60 (--) **Overall adiposity:** *Body fat composition, bio-impedence method (BL only)* ** p<0.0001 for difference between IG and CG change at 12 mo* **IG n analyzed:** 259 **CG n analyzed:** 263	Mean (SD) at BL, Mean change (SD) at 12 mo **BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* Total **IG** 5.8 (1.1) -0.12 (--)**** **CG** 5.7 (1.0) 0.16 (--) Patients with Dyslipidemia **IG** 6.10 (--) 0.2 (--) (calc)*** **CG** 5.97 (--) 0.08 (--) (calc) *HDL cholesterol, mmol/L* Total **IG** 1.4 (0.4) -- **CG** 1.4 (0.3) -- Patients with Dyslipidemia **IG** 1.38 (--) 0.03 (--) (calc)* **CG** 1.33 (--) 0.07 (--) (calc) *LDL cholesterol, mmol/L* Total **IG** 3.8 (0.9) -0.30 (--)**** **CG** 3.8 (0.9) -0.02 (--) Patients with Dyslipidemia **IG** 4.20 (--) -0.36 (--) (calc)*** **CG** 4.06 (--) -0.01 (--) (calc) *Triglycerides, mmol/L* **IG** 1.8 (0.8) 0.44 (--) **CG** 1.9 (1.0) 0.17 (--) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 141.1 (15.0) -6.0 (--)** **CG** 139.2 (15.7) -2.3 (--) *Diastolic blood pressure, mmHg* Total **IG** 89.0 (9.7) -5.5 (--)** **CG** 88.1 (10.1) -3.1 (--) Patients with Hypertension **IG** 95.5 (--) -10.2 (--) (calc) **CG** 95.7 (--) -7.2 (--) (calc) **Glucose tolerance:** *OGTT score, mmol/L* Total **IG** 8.0 (2.4) -0.37 (--)* **CG** 8.1 (2.8) 0.09 (--) Patients with Impaired Glucose Tolerance **IG** 11.84 (--) -0.29 (--) (calc) **CG** 12.63 (--) -0.11 (--) (calc) Fasting glucose **IG** -- -0.19 (--)* **CG** -- 0.06 (--)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
(continued) Broom, 2002[181] UK Multimorbidity Study Fair		***** p<0.0001 for difference between IG and CG change at 12 mo* **** p<0.001* *** p<0.01* ** p<0.05* **IG n analyzed:** 259; **CG n analyzed:** 263
Davidson, 1999[182] Fair	Mean (says SD, but believe these are really SEs) at BL, Mean change (SE) at 12 mo **-4 wk 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 36.2 (0.1) -- **CG** 36.5 (0.9) -- *Weight, kg* **IG** 100.7 (0.6) -8.76 (0.37)* **CG** 100.6 (0.9) -5.81 (0.67) % of subjects losing more than 5% of their initial body weight (calc n): IG 65.7† (432) CG 43.6 (97) **Central adiposity:** NR **Overall adiposity:** NR ** p<0.001 for least squares mean difference* †p<0.01 **IG n analyzed:** 657 (assumed N ITT for 12 mo) **CG n analyzed:** 223 (assumed N ITT for 12 mo)	**Lipids:** FIGURE FORM only (IG greater reductions than CG, p<0.05 for LDL, Total Cholesterol) Mean (SE) at BL, 12 mo **-4 wk 12 mo** **Blood pressure:** *Systolic Blood Pressure, mmHg* **IG** 119.4 (0.5) 118.6 (0.6)* **CG** 118.6 (0.9) 119.6 (1.3) *Diastolic Blood Pressure, mmHg* **IG** 76.9 (0.4) 75.9 (0.4)** **CG** 76.1 (0.6) 77.4 (0.9) ** p=0.002 for lowering of SBP by 12 mo in IG versus CG* *** p=0.009 for lowering of DBP by 12 mo in IG versus CG* **Glucose tolerance:** NR Figure only (at 12 mo) IG lower than CG at 12 mo (appears p<0.05, but information in article contradictory)
Derosa, 2003[183] Fair	Mean (SD) (assume SE at followup) **BL 6 mo 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 32.0 (1.3) 30.9 (1.1) 29.0 (1.0) **CG** 31.7 (1.0) 30.4 (0.9) 29.6 (1.0) Mean (SD) at BL, Mean change (SD) at 6 and 12 mo *Weight, kg* **IG** 94.2 (9.8) -5.1 (0.7) -8.6 (1.0) **CG** 95.3 (10.2) -4.2 (0.6) -7.6 (0.7) *Other measures: NR* **Central adiposity:** *Waist circumference, cm* **IG** 100.8 (5.3) -1.9 (0.7) -3.0 (1.0) **CG** 102.3 (6.2) -1.6 (0.5) -2.4 (0.4) **Overall adiposity:** NR **IG n analyzed:** 27 (BL), 25 (6, 12 mo) **CG n analyzed:** 23	Mean (SD) **BL 6 mo 12 mo** **Lipids:** *Total cholesterol, mg/dL* **IG** 260 (20) 242 (24) 221 (23)* **CG** 265 (24) 244 (22) 233 (20) *HDL cholesterol, mg/dL* **IG** 43 (4.0) 43 (3.5) 44 (4.0) **CG** 41 (3.5) 42 (3.0) 42 (3.0) *LDL cholesterol, mg/dL* **IG** 195 (20) 179 (19) 158 (20)* **CG** 194 (22) 183 (20) 173 (19) *Triglycerides, mg/dL* **IG** 132 (32) 111 (18) 97 (19) **CG** 128 (25) 116 (18) 109 (20) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 131 (3) 129 (4) 125 (3) **CG** 132 (5) 130 (4) 128 (3) *Diastolic blood pressure, mmHg* **IG** 85 (4) 84 (4) 81 (2) **CG** 84 (3) 84 (3) 82 (2) **Glucose tolerance:** NR ** p<0.05 for change in IG versus CG* **IG n analyzed:** 25; **CG n analyzed:** 23

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Derosa, 2010[215] Good	Mean (SD) **BL 6 mo 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 33.1 (2.9) 31.6 (1.8) 29.8 (1.2)* **CG** 32.5 (2.3) 31.9 (2.0) 31.6 (1.8) *Weight, kg* **IG** 94.5 (9.6) 90.3 (8.4) 85.0 (5.9)* **CG** 91.7 (8.7) 91.0 (8.3) 89.1 (7.8) *Other measures: NR* **Central adiposity:** *Waist circumference, cm* **IG** 102.0 (6.0) 99.0 (4.0) 95.0 (3.0)* **CG** 101.0 (5.5) 99.5 (4.5) 99.0 (4.0) *Other measures: NR* **Overall adiposity:** NR ** p<0.05 versus CG* **IG n analyzed:** 126 (BL), 119 (6 mo), 113 (12 mo) **CG n analyzed:** 128 (BL), 125 (6 mo), 121 (12 mo)	Mean (SD) **BL 6 mo 12 mo** **Lipids:** *Total cholesterol, mg/dL* **IG** 220 (24) 207 (15) 186 (9)* **CG** 217 (21) 205 (13) 212 (17) *HDL cholesterol, mg/dL* **IG** 45 (7) 46 (8) 46 (8) **CG** 46 (8) 46 (8) 45 (7) *LDL cholesterol, mg/dL* **IG** 153 (15) 144 (8) 126 (6)* **CG** 151 (13) 141 (7) 149 (11) *Triglycerides, mg/dL* **IG** 109 (48) 84 (30) 72 (25) **CG** 99 (41) 92 (37) 88 (32) **Blood pressure:** NR **Glucose tolerance:** *Fasting plasma glucose, mg/dL* **IG** 136 (16) 129 (13) 121 (11) **CG** 133 (15) 127 (13) 120 (10) *Post-prandial plasma glucose, mg/dL* **IG** 174 (24) 163 (17) 149 (13) **CG** 171 (20) 162 (17) 155 (15) *HbA1c, percent* **IG** 8.4 (1.4) 7.7 (0.9) 7.0 (0.5) **CG** 8.2 (1.3) 7.9 (1.1) 7.9 (0.9) ** p<0.05 versus CG* **IG n analyzed:** 126 (BL), 119 (6 mo), 113 (12 mo) **CG n analyzed:** 128 (BL), 125 (6 mo), 121 (12 mo)
Finer, 2000[184] James, 1997[290] Fair	Mean (SD) at BL, LSM change from baseline to 12 mo **BL 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 36.8 (3.6) -- **CG** 36.8 (3.7) -- *Weight, kg* **IG** 97.9 (12.9) -3.29 **CG** 98.4 (15.0) -1.31 *Weight loss ≥5%, percent (calc n):* **IG** -- 35* (38) **CG** -- 21 (23) *Weight loss ≥10%, percent, calc n* **IG** -- 16* (18) **CG** -- 6 (6) *Other measures: Average % loss of initial body weight, IG 2.0 kg (95% CI -3.6, -0.38) difference from CG for change in initial body weight* **Central adiposity:** *Decrease in waist circumference stratified by baseline waist circumference* **Overall adiposity:** NR ** p<0.05 for IG difference in change from CG* **IG n analyzed:** 110; **CG n analyzed:** 108 *Note: Also presents completer analysis*	Mean (SD) at BL, Mean change (SD) at 12 mo **BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.22 (0.96) -0.05 (0.76)* **CG** 5.17 (0.92) 0.30 (0.68) *HDL cholesterol, mmol/L* **IG** 1.11 (0.26) 0.15 (0.23) **CG** 1.08 (0.25) 0.16 (0.21) *LDL cholesterol, mmol/L* **IG** 3.44 (0.82) -0.11 (0.63)* **CG** 3.46 (0.79) 0.21 (0.53) **Blood pressure:** NR **Glucose tolerance:** NR ** p<0.001 for IG difference from CG* **IG n analyzed:** 110 **CG n analyzed:** 108

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Hanefeld, 2002[187] Fair	Mean (SD) at BL, Mean change (NR but SD in table so may be SD) at 12 mo **-4 wk 12 mo** **Weight/Relative weight:** *BMI, kg/m^2* **IG** 34.5 (5.6) -- **CG** 33.7 (5.2) -- *Weight, kg* **IG** 99.4 (17.5) -5.3 (5.1)* **CG** 98.4 (18.5) -3.4 (5.3) *Weight loss ≥5%, percent (calc n)* **IG** -- 51.3** (97) **CG** -- 31.6 (57) **Central adiposity:** *Waist circumference, cm* **IG** 112.4 (12.5) -5.5 (5.3)*** **CG** 112.0 (12.7) -3.0 (5.6) **Overall adiposity:** NR ** p=0.006 for between-group difference* *** p=0.0001 for IG vs CG* **** p<0.01* **IG n analyzed:** 189 (ITT, LOCF) **CG n analyzed:** 180 (ITT, LOCF)	Mean (SD) at BL, Percent change (NR) at 12 mo **-4 wk 12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.8 (1.1) -2.3 (16.3)** **CG** 6.1 (1.4) 1.8 (22.0) *HDL cholesterol, mmol/L* **IG** 1.2 (0.3) 0.6 (20.0) **CG** 1.2 (0.3) 6.4 (24.5)** *LDL cholesterol, mmol/L* **IG** 3.5 (0.9) -2.0 (26.7)* **CG** 3.6 (1.0) 5.1 (34.3) Mean (SD) at BL, Mean change (NR) at 12 mo **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 148.0 (20.4) -4.96 (--) **CG** 147.9 (17.8) -4.98 (--) *Diastolic blood pressure, mmHg* **IG** 87.0 (10.8) -4.78 (--) **CG** 87.2 (10.7) -4.80 (--) **Glucose tolerance:** *Hemoglobin A1c, percent, mean decrease at 12 mo* **IG** 8.6 (1.1) -0.9 (1.3)*** **CG** 8.6 (1.2) -0.4 (1.5) *Fasting glucose, mmol/L* **IG** 10.95 (2.93) -1.6 (2.5)**** **CG** 10.95 (3.17) -0.7 (3.2) ** p<0.05 for between-group difference* *** p<0.01* **** p=0.0003* *****p=0.004* **IG n analyzed:** 189 (ITT, LOCF) **CG n analyzed:** 180 (ITT, LOCF)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Hauptman, 2000[189] Fair	Mean (SE) at -4 weeks, Mean change (SE) at BL, 6, 12 mo **-4 wk BL 6 mo 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG1** 35.8 (0.3) -- -- -- **IG2** 36.0 (0.2) -- -- -- **CG** 36.1 (0.3) -- -- -- *Weight, kg* **IG1** 100.4 (1.00) -2.49 (0.14) -6.92 (0.64)* -7.08 (0.54)* **IG2** 100.5 (0.98) -2.54 (0.15) -8.0 (0.58)* -7.94 (0.57)* **CG** 101.8 (1.00) -2.73 (0.15) -4.70 (0.60) -4.14 (0.56) *Weight loss ≥5%, percent (calc n)* **IG1** -- -- -- 48.8* **IG2** -- -- -- 50.5* (106) **CG** -- -- -- 30.7 (65) *Weight loss ≥10%, percent (calc n)* **IG1** -- -- -- 24.4* **IG2** -- -- --	Mean (SE) **-4 wk BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG1** 5.35 (0.07) 5.02 (0.07) 4.96 (0.08)* **IG2** 5.39 (0.07) 4.99 (0.08) 4.95 (0.08)* **CG** 5.38 (0.07) 5.02 (0.06) 5.32 (0.07) *HDL cholesterol, mmol/L* **IG1** 1.29 (0.02) 1.22 (0.02) 1.27 (0.02)* **IG2** 1.27 (0.02) 1.20 (0.02) 1.26 (0.03) **CG** 1.27 (0.02) 1.17 (0.02) 1.28 (0.02) *LDL cholesterol, mmol/L* **IG1** 3.33 (0.06) 3.11 (0.06) 3.04 (0.07)* **IG2** 3.37 (0.06) 3.16 (0.06) 3.04 (0.08)* **CG** 3.35 (0.06) 3.16 (0.05) 3.41 (0.07) *Triglycerides, mmol/L* **IG1** 1.80 (0.06) 1.65 (0.05) 1.57 (0.07) **IG2** 1.85 (0.06) 1.55 (0.04) 1.61 (0.05) **CG** 1.81 (0.06) 1.67 (0.08) 1.57 (0.07) **Blood pressure:** *Systolic blood pressure, mmHg* **IG1** 124 (1) 121 (1) 123 (1) **IG2** 124 (1) 120 (1) 122 (1) **CG** 123 (1) 121 (1) 124 (1) *Diastolic blood pressure, mmHg* **IG1** 80 (1) 78 (1) 77 (1)* **IG2** 80 (1) 78 (1) 77 (1) **CG** 81 (1) 78 (1) 80 (1) **Glucose tolerance:** *Fasting Serum Glucose, mmol/L* **IG1** 5.62 (0.04) 5.59 (0.03) 5.68 (0.04) **IG2** 5.75 (0.06) 5.66 (0.04) 5.69 (0.04) **CG** 5.66 (0.04) 5.66 (0.04) 5.77 (0.48) ** p<0.05 for change from BL compared with placebo at 12 mo based on least squares means* **IG1 n analyzed:** 213 (ITT) **IG2 n analyzed:** 210 (ITT) **CG n analyzed:** 212 (ITT) Note: 24 month data not abstracted because of high attrition

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Hill, 1999[190] Fair	Mean (SE) at -6 mo, Mean change (SE) from -6 mo to BL and 12 mo **-6 mo BL 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG1** 32.6 (0.2) -- -- **IG2** 32.9 (0.2) -- -- **IG3** 32.8 (0.2) -- -- **CG** 32.8 (0.2) -- -- *Weight, kg* **IG1** 89.3 (0.9) -10.06 (0.31) -5.15 (0.55) **IG2** 92.4 (0.9) -10.00 (0.29) -6.16 (0.49) **IG3** 89.7 (0.9) -9.86 (0.27) -7.24 (0.52)* **CG** 90.8 (0.9) -10.33 (0.31) -5.93 (0.69) *Weight loss >5% maintained, percent (calc n)* **IG1** -- -- -- **IG2** -- -- -- **IG3** -- -- 61.8 (70) **CG** -- -- 49.8 (60) **Central adiposity:** During 1 year treatment period waist circumferences increased slightly in all groups and the resulting mean reductions of 6-8 cm after 1 yr of treatment were not significantly different between groups **Overall adiposity:** NR ** p<0.001 for least-squares mean percentage regain compared with CG (table says also significant for 30 mg tid but text says only 120 mg)* *Note: All reported data are observed rather than derived values, whereas the technique of LOCF was applied only for analyses of statistical significance.* **IG1 n analyzed:** 186 (-6 mo), 119 (BL, 12 mo) **IG2 n analyzed:** 171 (-6 mo), 116 (BL, 12 mo) **IG3 n analyzed:** 179 (-6 mo), 113 (BL, 12 mo) **CG n analyzed:** 184 (-6 mo), 121 (BL, 12 mo)	Mean change (SE) from -6 mo BL and 12 mo **BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG1** -0.39 (0.05) -0.35 (0.08)* **IG2** -0.46 (0.06) -0.50 (0.07)** **IG3** -0.39 (0.05) -0.47 (0.07)** **CG** -0.45 (0.06) -0.28 (0.08) *HDL cholesterol, mmol/L* **IG1** 0.01 (0.04) 0.01 (0.08) **IG2** 0.03 (0.06) -0.04 (0.07)*** **IG3** 0.01 (0.05) -0.03 (0.07) **CG** 0.01 (0.06) 0.01 (0.07) *LDL cholesterol, mmol/L* **IG1** -0.28 (0.04) -0.38 (0.08)** **IG2** -0.34 (0.06) -0.42 (0.07)*** **IG3** -0.24 (0.05) -0.29 (0.07)** **CG** -0.33 (0.06) -0.21 (0.07) *Triacylglycerol, mmol/L* **IG1** -0.23 (0.05) -0.01 (0.08) **IG2** -0.34 (0.06) -0.08 (0.08)† **IG3** -0.29 (0.05) -0.27 (0.06) **CG** -0.29 (0.06) -0.15 (0.07) **Blood pressure:** *Systolic blood pressure, mmHg* **IG1** -- -0.8 (1.1) **IG2** -- -0.4 (1.2) **IG3** -- -3.0 (1.3) **CG** -- -2.6 (1.2) *Diastolic blood pressure* After 12 mo of treatment, reductions in DBP ranged from 0.2-2.0 mmHg and did not differ significantly between groups. **Glucose tolerance:** Fasting glucose decreased slightly (0.02-0.1 mmol/L) in all groups during the 6 mo run-in. After 12 mo of treatment, mean increases of 1-2% above initial values were noted in CG and IG1 compared with slight (~1%) reductions in IG2 and IG3. (Assume not statistically significant, since no mention of statistical significance of results) ** p=0.007 for least-squares mean percentage change compared with CG* *** p=0.001* **** p=0.006* *† p=0.041* **IG1 n analyzed:** 186 (BL), 96 (TC, LDL, 12 mo), 99 (HDL, TG, 12 mo), NR (SBP) **IG2 n analyzed:** 171 (BL), 87 (TC, LDL, 12 mo), 88 (HDL, TG, 12 mo), NR (SBP) **IG3 n analyzed:** 179 (BL), 87 (TC, LDL, 12 mo), 89 (HDL, TG, 12 mo), NR (SBP) **CG n analyzed:** 184 (BL), 102 (TC, LDL, 12 mo), 103 (HDL, TG, 12 mo), NR (SBP)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Hollander, 1998[191] Fair	Mean (SD) at BL, mean change (SE) at 12 mo **BL 57 wk** **Weight/Relative weight:** *BMI, kg/m²* **IG** 34.5 (3.2) -- **CG** 34.0 (3.4) -- *Weight, kg* **IG** 99.6 (14.5) -6.19 (0.51)*** **CG** 99.7 (15.4) -4.31 (0.57) *≥5% weight loss, percent (calc n)* **IG** -- 48.8*** (79) **CG** -- 22.6 (36) *≥10% weight loss, percent (calc n)* **IG** -- 17.9* (29) **CG** -- 8.8 (14) **Central adiposity:** *Waist circumference, cm* **IG** -- -4.8 (0.5) **CG** -- -2.0 (0.5)** **Overall adiposity:** NR *** p<0.001 for IG vs CG ** p<0.01 for IG vs CG * p<0.05 for IG vs CG **IG n analyzed:** 162 **CG n analyzed:** 159	Mean (SD) at BL, mean change (SEM) at 12 mo **BL 52 wk** **Lipids:** *Total cholesterol, mmol/l* **IG** -- -0.08 (0.05)* **CG** -- 0.39 (0.06) **LSM% difference from CG:** -9.14 *HDL cholesterol, mmol/l* **IG** -- 0.06 (0.01) **CG** -- 0.08 (0.01) **LSM% difference from CG:** -1.20 *LDL cholesterol, mmol/l* **IG** -- -0.13 (0.05)* **CG** -- 0.22 (0.06) **LSM% difference from CG:** -12.79 *Triglycerides, mmol/l* **IG** -- -0.01 (0.07)† **CG** -- 0.21 (0.08) **LSM% difference from CG:** -10.62 **Glucose tolerance:** *Hemoglobin A1c, %* **IG** 8.05 (0.98) -0.28 (0.09)* **CG** 8.2 (1.07) 0.18 (0.11) *Fasting glucose, mmol/l* **IG** 8.85 (1.68) -0.02 (0.14)* **CG** 9.09 (1.87) 0.54 (0.15) *Fasting plasma glucose ≥7.77mmol/l at BL* **IG** -- -0.47 (0.19)* **CG** -- 0.36 (0.27) ** p<0.001 for IG vs CG; †p=0.036* **IG n analyzed:** 162 (total); NR (Fasting plasma glucose ≥7.77mmol/l at BL) **CG n analyzed:** 159 (total); NR (Fasting plasma glucose ≥7.77mmol/l at BL)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Krempf, 2003[193] Fair	Mean (SE) at BL, least squares means (SE) at 12 and 18 mo LOCF **BL 12 mo 18 mo** **Weight/Relative weight:** *BMI, kg/m^2* **IG** 36.0 (0.3) -- -2.3 (0.3)** **CG** 36.2 (0.3) -- -1.0 (0.3) *Weight, kg* **IG** 97.0 (0.9) -6.3 (0.5)†† -5.3 (0.5)†† **CG** 97.5 (0.9) -3.3 (0.5) -2.4 (0.5) *≥5% weight loss, percent (calc n)* **IG** -- 65.9*** (170) 58.3*** **CG** -- 46.4 (102) 37.8 *≥10% weight loss, percent* **IG** -- 32.9* (85) 33.6*** **CG** -- 24.5 (54) 16.8 **Central adiposity:** *Waist circumference, cm* **IG** 105.6 (0.8) -- -5.3 (0.7) **CG** 106.5 (0.8) -- -6.5 (0.8)† **Overall adiposity:** Body fat (kg + %) measured by impedancemeter monthly for 18 mo ** p<0.05 for IG vs CG* *** p<0.001 for IG vs CG* **** p<0.0001 for IG vs CG* *† p<0.05 for IG vs CG least squares mean difference* *†† p<0.0001 for IG vs CG least squares mean difference* **IG n analyzed:** 346, 258 (12 mo, 5 + 10% weight loss), 223 (18 mo, 5 + 10% weight loss only) **CG n analyzed:** 350, 220 (12 mo, 5 + 10% weight loss), 196 (18 mo, 5 + 10% weight loss)	Proportion of patients **BL 18 mo** **Lipids:** *Total cholesterol reduced by ≥20%, percent* **IG** -- 10.1 **CG** -- 2.6 *LDL cholesterol reduced by ≥20%, percent* **IG** -- 19.9 **CG** -- 6.6 **IG n analyzed:** NR **CG n analyzed:** NR

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Lindgarde, 2000[194] Swedish Multimorbidity Study Fair	Mean (SD) at -2 wk, Mean change (SD) from -2 wk at BL and 12 mo **-2 wk BL 12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 33.2 (3.0) -- -- **CG** 33.2 (3.1) -- -- *Weight, kg* Total **IG** 96.1 (13.7) -- -5.6 (5.2)* **CG** 95.9 (13.5) -- -4.3 (5.9) *Weight, percent* Patients with type 2 diabetes **IG** -- -- 5.4 (4.6)* **CG** -- -- 3.5 (4.2) *≥5% weight loss, percent (calc n)* Total **IG** -- -- 54.2 (103)** **CG** -- -- 40.9 (76) Patients with type 2 diabetes **IG** -- -- 57.4 (--)* **CG** -- -- 34.1 (--) *≥10% weight loss, percent (calc n)* IG -- -- 19.2 (36) CG -- -- 14.6 (27) **Central adiposity:** *Waist circumference, cm* **IG** 106 (10.8) -- -4.8 (--) **CG** 106 (11.0) -- -4.1 (--) **Overall adiposity:** NR ** p<0.05 for IG v. CG* **IG n analyzed:** 190 (total); 54 (type 2 diabetes); **CG n analyzed:** 186 (total); 44 (type 2 diabetes)	Mean (SD) at -2 wk, Mean change (SD) at BL and 12 mo (except HbA1c) **-2 wk BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 6.15 (1.21) -0.27 (0.64) -0.24 (0.83)* **CG** 6.06 (1.19) -0.35 (0.62) -0.09 (0.82) *LDL cholesterol, mmol/L* **IG** 3.75 (1.38) -0.03 (1.14) -0.25 (1.12)* **CG** 3.66 (1.41) -0.14 (0.88) -0.07 (0.98) *HDL cholesterol, mmol/L* **IG** -- -0.03 (0.19) 0.00 (0.22) **CG** -- -0.06 (0.19) 0.02 (0.20) *Triglycerides, mmol/L* **IG** -- -0.22 (1.11) -0.04 (1.16) **CG** -- -0.19 (0.95) -0.15 (0.93) Improvements in LDL and TC were greater in IG vs CG for patients with type 2 diabetes, though not significant (-4.3% vs. -1.0% and 10.4% vs. -3.9%) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 146 (19) -4.4 (13.5) -4.9 (17.7) **CG** 145 (17) -3.2 (12.3) -4.1 (15.7) *Diastolic blood pressure, mmHg* **IG** 87 (10) -1.6 (6.69) -2.5 (8.9) **CG** 88 (10) -1.6 (8.1) -2.9 (9.2) **Glucose tolerance:** *Hemoglobin A1c, percent* Total **IG** -- 5.7 (1.2) -0.25 (0.78)* **CG** -- 5.5 (0.9) -0.05 (0.51) Patients with type 2 diabetes **IG** -- -- -0.65 (--)* **CG** -- -- -0.14 (--) *Fasting glucose, mmol/L* Total **IG** 6.62 (2.53) -0.09 (1.02) -0.55 (1.65)** **CG** 6.35 (1.96) -0.17 (0.86) -0.09 (1.19) Patients with type 2 diabetes **IG** -- -- -1.63 (--)** **CG** -- -- 0.28 (--) *convert to mg/dL: 0.55=9.9; 0.09=1.6; 1.63=29.4; 0.28=5.0* *** p<0.01 for between-group difference in change from -2 wk* ** p<0.05* **IG n analyzed:** 190 (total); 54 (type 2 diabetes) **CG n analyzed:** 186 (total); 44 (type 2 diabetes)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Miles, 2002[197] Fair	Mean (SE) at BL, Mean change (SE) at 12 mo **BL 12 mo** **Weight/Relative weight:** *BMI, kg/m^2* **IG** -- -- **CG** -- -- *Weight, kg* **IG** 102.1 (1.1) -4.7 (0.3)** **CG** 101.1 (1.0) -1.8 (0.3) *≥5% weight loss, percent (calc n)* **IG** -- 39.0* (98) **CG** -- 15.7 (40) *≥10% weight loss, percent* **IG** -- 14.1* (35) **CG** -- 3.9 (10) **Central adiposity:** NR **Overall adiposity:** NR ** p<0.01 for IG versus CG* *** p<0.0001 for difference in change between IG and CG* **IG n analyzed:** 250 **CG n analyzed:** 254	Mean (SE) **BL 12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.40 (0.06) 5.13 (0.06)* **CG** 5.40 (0.06) 5.46 (0.07) *HDL cholesterol, mmol/L* **IG** 0.98 (0.02) 1.07 (0.02) **CG** 0.98 (0.02) 1.08 (0.02) *LDL cholesterol, mmol/L* **IG** 3.14 (0.06) 2.89 (0.06)* **CG** 3.23 (0.06) 3.18 (0.07) *Triglycerides, mmol/L* **IG** 2.81 (0.11) 2.56 (0.11) **CG** 2.63 (0.09) 2.66 (0.13) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 132.7 (0.9) 130.6 (0.9)* **CG** 132.1 (0.9) 131.8 (0.9) Mean (SE) at BL, Mean change (SE) at 12 mo **Glucose tolerance:** *Fasting glucose, mmol/L* **IG** 11.6 (0.2) -2.0 (0.2)* **CG** 11.1 (0.2) -0.7 (0.2) *Hemoglobin A1c, percent* **IG** 8.87 (0.07) 0.75 (--) **CG** 8.79 (0.07) 0.41 (--) **p<0.05 for difference in change between IG and CG* **IG n analyzed:** 250; **CG n analyzed:** 254

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Richelsen, 2007[198] Fair	Mean (range) **-2 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 37.4 (30.1-45.2) **CG** 37.6 (30.0-45.0) **-2 mo BL 18 mo 36 mo** Mean (SD) at BL, Mean change at 18, 36 mo *Weight, kg* **IG** 110.7 (17.9) -14.5 -11.7 -9.4† **CG** 111.9 (16.0) -14.3 -9.6 -7.2 **12 mo 36 mo** *≥5% weight loss, percent (calc n)* **IG** 85** (130) 67* **CG** 72 (112) 56 *≥10% weight loss, percent* **IG** -- -- -- -- 34 **CG** -- -- -- -- 29 Mean (SD) at -2 mo, Mean change at BL, 18, 36 mo **Central adiposity:** **-2 mo BL 18 mo 36 mo** *Waist circumference, cm* **IG** 119 (12.1) -12 -12 -7.7† **CG** 119 (10.9) -12 -9 -5.4 ** p<0.05 for absolute changes between IG and CG* ***p<0.001 for IG vs CG* *† p<0.05 for absolute changes between IG and CG after 36 mo* **IG n analyzed:** 153 (ITT, LOCF) **CG n analyzed:** 156 (ITT, LOCF)	Mean (SD) at BL, Mean change at 18, 36 mo **-2 mo BL 18 mo 36 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.91 (1.26) -1.2 -0.36 -0.46 **CG** 6.02 (1.08) -1.2 -0.13 -0.46 *HDL cholesterol, mmol/L* **IG** 1.13 (0.26) -0.05 0.06 0.04 **CG** 1.15 (0.26) -0.07 0.11 0.06 *LDL cholesterol, mmol/L* **IG** 3.71 (1.04) -0.75 -0.29 -0.34 **CG** 3.77 (0.94) -0.80 -0.12 -0.38 *Triglycerides, mmol/L* **IG** 2.36 (1.24) -0.89 -0.32 -0.38 **CG** 2.50 (1.41) -0.94 -0.34 -0.43 **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 144 (19.3) -13 -8.2 -7.8 **CG** 144 (17.3) -12 -7.2 -8.2 *Diastolic blood pressure, mmHg* **IG** 90.8 (11.6) -7.2 -5.1 -3.7 **CG** 90.7 (10.4) -7.6 -4.8 -4.7 **Glucose tolerance:** *Hemoglobin A1c, percent* IG 6.32 (0.93) -0.54 -0.43 -0.69 CG 6.28 (0.64) -0.48 -0.34 -0.51 *Fasting glucose, mmol/L* IG 6.44 (1.83) -1.1 -0.67 -0.49 CG 6.27 (1.54) -0.95 -0.45 -0.32 **IG n analyzed:** 153 (ITT, LOCF); **CG n analyzed:** 156 (ITT, LOCF)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Rossner, 2000[199] Fair	Mean (SD) at BL, Mean change (SD) from Week -4 to 12 and 24 months **BL** **12 mo** **24 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG1** 35.2 (3.9) -- -- **IG2** 34.7 (3.7) -- -- **CG** 35.3 (4.1) -- -- *Weight, kg* **IG1** 99.1 (14.3) -8.5 (7.3)** -6.6 (8.3)* **IG2** 96.7 (13.8) -9.4 (6.4)** -7.4 (7.1)** **CG** 97.7 (14.6) -6.4 (6.7) -4.3 (7.4) Percent *≥10% weight loss, percent (calc n)* **IG1** -- 31.2** **IG2** -- 38.3** (93) **CG** -- 18.8 (45) *Significantly more IG2 patients lost more than 5% of their body weight after 1 and 2 years of treatment than CG patients (p<0.001).* Mean (SD) at BL, Mean change (SD) from Week -4 to 12 mo **Central adiposity:** *Waist circumference, cm* **IG1** -- -6.0 **IG2** -- -6.2 **CG** -- -4.7 **Overall adiposity:** NR ** p<0.01 derived from least squares mean differences for IG versus CG* *** p<0.001 derived from least squares mean differences for IG versus CG* *† p<0.005 for IG versus CG* **IG1 n analyzed:** 239† **IG2 n analyzed**: 242† **CG n analyzed:** 237† *† The methods report that an additional 2 participants were not included in the ITT analysis, but they do not report what groups they were from (IG1, IG2, or CG)* *Note: Completer analysis available* *MA: Only include 12-mo outcomes in MA*	Mean (SD) at BL, 12, 24 months **BL** **12 mo** **24 mo** **Lipids:** *Total cholesterol, mmol/L* **IG1** 5.39 (1.10) 5.15 (1.17)** 5.42 (1.06)** **IG2** 5.26 (0.97) 4.91 (0.93)** 5.29 (0.96)** **CG** 5.43 (1.14) 5.38 (1.04) 5.74 (1.04) *HDL cholesterol, mmol/L* **IG1** 1.13 (0.31) 1.26 (0.33) 1.29 (0.36) **IG2** 1.17 (0.30) 1.25 (0.30)* 1.29 (0.32) **CG** 1.17 (0.36) 1.32 (0.35) 1.33 (0.34) *LDL cholesterol, mmol/L* **IG1** 3.49 (0.86) 3.18 (0.82)** 3.42 (0.85)** **IG2** 3.44 (0.86) 3.11 (0.78)** 3.48 (0.87)** **CG** 3.55 (0.98) 3.49 (0.92) 3.83 (0.91) *Triglycerides, mmol/L* **IG1** 1.75 (1.46) 1.77 (1.95) 1.89 (1.83) **IG2** 1.53 (0.97) 1.44 (0.91) 1.43 (0.85) **CG** 1.58 (0.89) 1.50 (0.79) 1.53 (0.81) **Blood pressure:** *Systolic blood pressure, mmHg* **IG1** 128.4 (14.5) 125.7 (15.9) 129.6 (16.7) **IG2** 125.5 (14.9) 122.8 (16.0) 124.9 (16.5) **CG** 127.3 (16.1) 125.4 (18.6) 128.5 (17.5) *Diastolic blood pressure, mmHg* **IG1** 81.5 (10.3) 79.5 (10.0) 81.7 (10.3) **IG2** 79.5 (9.4) 78.6 (10.2)* 79.9 (9.5) **CG** 81.2 (9.8) 79.9 (11.0) 81.2 (9.9) **Glucose tolerance:** *Fasting glucose, mmol/L* **IG1** 5.62 (1.06) 5.57 (0.96)* 5.57 (1.18) **IG2** 5.47 (0.68) 5.48 (0.86)* 5.51 (1.29) **CG** 5.56 (0.95) 5.66 (1.01) 5.54 (0.68) *** p<0.001* ** p<0.05* **IG1 n analyzed:** 239† **IG2 n analyzed:** 242† **CG n analyzed:** 237† *† The methods report that an additional 2 participants were not included in the ITT analysis, but they do not report what groups they were from (IG1, IG2, or CG)*

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Sjostrom, 1998[200] Fair	Mean (range) at BL, Mean change at 12 mo **BL** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 36.0 (28.3-47.2) -- **CG** 36.1 (29.2-43.5) -- *Weight, kg* **IG** 99.1 (61.0-148.6) -10.3*† **CG** 99.8 (64.2-137.2) -6.1 Percent *>5% weight loss, percent (calc) (calc n)* **IG** -- 68.5 (235) **CG** -- 49.2 (167) *>10% weight loss, percent (calc)* **IG** -- 38.8 (133) **CG** -- 17.7 (60) *Statistical significance not reported for 5, 10% weight loss.* Mean (range) at BL, Mean change at 12 mo **Central adiposity:** *Waist circumference, cm* **IG** 105.4 (70-149) -- **CG** 105.9 (71-135) -- **Overall adiposity:** NR * *p<0.001 for LSM weight loss difference from randomization (3.9 kg)* *† Note: change in weight at 12 months is from the start of the 4 week run-in period. The results at baseline are from randomization (4 weeks after the start of the run-in period).* **IG n analyzed:** 343 **CG n analyzed:** 340	LSM (SE) **BL** **12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.39 (0.03) 5.31 (0.04)*** **CG** 5.36 (0.03) 5.59 (0.04) *HDL cholesterol, mmol/L* **IG** 1.15 (0.01) 1.25 (0.01) **CG** 1.16 (0.01) 1.26 (0.01) *LDL cholesterol, mmol/L* **IG** 3.55 (0.03) 3.46 (0.03)*** **CG** 3.55 (0.03) 3.68 (0.03) *Triglycerides, mmol/L* **IG** 1.60 (0.05) 1.53 (0.04) **CG** 1.53 (0.05) 1.59 (0.04) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 129 (0.60) 127 (0.70) **CG** 128 (0.60) 129 (0.71) *Diastolic blood pressure, mmHg* **IG** 82.4 (0.40) 80.3 (0.43)** **CG** 81.9 (0.40) 82.1 (0.43) **Glucose tolerance:** *Fasting blood glucose, mmol/L* **IG** 5.84 (0.03) 5.63 (0.04)* **CG** 5.83 (0.03) 5.77 (0.04) *** *p<0.0001* ** *p=0.0022* * *p=0.0098* **IG n analyzed:** 343 (BL, 12 mo) **CG n analyzed:** 340 (BL, 12 mo)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Swinburn, 2005[201] Fair	Mean (SD) at BL, Mean change (SD) from BL at 12 mo **BL** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 37.6 (5.1) -- **CG** 38.0 (4.9) -- *Weight, kg* **IG** 103.3 (17.8) -4.7 (7.7)* **CG** 106.9 (17.8) -0.9 (4.2) **Central adiposity:** *Waist circumference, cm* **IG** 112.4 (12.8) -5.1 (7.0)* **CG** 114.8 (13.1) -1.9 (4.2) **Overall adiposity:** NR * *p=0.001* **IG n analyzed:** 170 **CG n analyzed:** 169	Mean (SD) at BL, Mean change (SD) from BL at 12 mo **BL** **12 mo** **Lipids:** *Serum total cholesterol, mmol/L* **IG** 5.66 (1.10) -0.08 (0.73)* **CG** 5.53 (0.95) 0.16 (0.68) *Serum HDL cholesterol, mmol/L* **IG** 1.16 (0.28) 0.04 (0.18) **CG** 1.14 (0.33) 0.08 (0.19) *Serum LDL cholesterol, mmol/L* **IG** 3.58 (0.99) -0.12 (0.65)* **CG** 3.47 (0.84) 0.11 (0.62) *Serum Triglycerides, mmol/L* **IG** 1.78 (0.78) 0.01 (0.73) **CG** 1.87 (0.91) -0.06 (0.57) **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 137.3 (15.7) -4.05 (13.0)** **CG** 136.0 (15.2) -0.51 (14.7) *Diastolic blood pressure, mmHg* **IG** 84.0 (9.9) -2.96 (8.01) **CG** 84.5 (9.0) -1.37 (8.59) **Glucose tolerance:** *Glycated hemoglobin, percent* **IG** 6.15 (1.28) -0.04 (0.60)*** **CG** 6.01 (1.18) 0.15 (0.60) *Serum glucose (fasting), mmol/L* **IG** 6.66 (2.62) -0.19 (1.13)*** **CG** 6.29 (1.78) 0.29 (1.42) Median at BL, Mean change (SD) from BL at 12 mo *10-year risk of CVD, percent* **IG** 8.9 -0.01 (0.03) **CG** 10.6 0.00 (0.03) * *p<0.01* ** *p<0.05* *** *p=0.00*1 **IG n analyzed:** 170 **CG n analyzed:** 169 *Note: Blood tests were fasting*

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Torgerson, 2004[202] Torgerson, 2001[291] XENDOS Fair	Mean (SD) at BL, mean change at 1 and 4 years **BL** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 37.3 (4.2) -- **CG** 37.4 (4.5) -- *Weight, kg* **IG** 110.4 (16.3) -10.6* **CG** 110.6 (16.5) -6.2 LSM difference *≥5% weight loss, percent (calc n)* **IG** -- 72.8* (1194) **CG** -- 45.1 (738) *≥10% weight loss, percent* **IG** -- 41.0* (672) **CG** -- 20.8 (340) **Central adiposity:** *Waist circumference, cm* **IG** 115.0 (10.4 -9.6** **CG** 115.4 (10.4) -7.0 **Overall adiposity:** NR ** p<0.001 for IG vs CG* *** p<0.01 for IG vs CG* **IG n analyzed:** 1640 **CG n analyzed:** 1637	Mean (SD) at BL, mean change at 1 and 4 yrs for waist circumference, blood pressure, and glucose tolerance, % mean change at 1 and 4 yrs for others **BL** **12 mo** **Lipids:** *Total cholesterol, mmol/l* **IG** 5.8 (1.0) -8.8* **CG** 5.8 (1.0) -1.3 *HDL cholesterol, mmol/l* **IG** 1.2 (0.3) 3.4* **CG** 1.2 (0.3) 8.5 *LDL cholesterol, mmol/l* **IG** 3.7 (0.9) -11.4* **CG** 3.8 (0.9) -1.6 *Triglycerides, mmol/l* **IG** 1.9 (1.0) -6.2** **CG** 1.9 (1.2) -6.3 **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 130.8 (15.8) -7.3* **CG** 130.4 (15.4) -5.2 *Diastolic blood pressure, mmHg* **IG** 82.0 (10.0) -3.6* **CG** 82.3 (10.0) -2.6 **Glucose tolerance:** *Fasting glucose, mmol/l* **IG** 4.6 (0.6) 0.1* **CG** 4.6 (0.6) 0.2 *Note: 4 year data not presented because of high attrition* **p<0.01 for IG vs CG* ***p<0.05 for IG vs CG* **IG n analyzed:** 1640 (BL), 1487 (1 yr) **CG n analyzed:** 1637 (BL), 1295 (1 yr)
Metformin Trials		
Fontbonne, 1996[185] BIGPRO Fair	Geometric mean (95% tolerance limit) at BL, Mean change (95% CI) at 12 mo **BL** **12 mo** **Weight/Relative weight:** *BMI, kg/m²* **IG** 33.3 (24.6, 45.1) -- **CG** 33.0 (24.0, 45.4) -- *Weight, kg* **IG** -- -2.0 (-3.0, -1.1) **CG** -- -0.8 (-1.6, 0.1) **Central adiposity:** NR **Overall adiposity:** NR **IG n analyzed:** 164 **CG n analyzed:** 160	Arithmetic (SD) mean or geometric mean (95% tolerance limit) at BL, Mean change (95% CI) at 12 mo **BL** **12 mo** **Lipids:** *Total cholesterol, mmol/L* **IG** 5.7 (1.0) 0.05 (-0.08, 0.18) **CG** 5.4 (1.1) 0.21 (0.08, 0.33) *HDL cholesterol, mmol/L* **IG** 1.1 (0.3) 0.05 (-0.02, 0.10) **CG** 1.1 (0.3) 0.10 (0.05, 0.16) *LDL cholesterol, mmol/L* **IG** 3.6 (0.8) -0.02 (-0.15, 0.08) **CG** 3.4 (1.0) 0.10 (0.0, 0.21) *Triglycerides, mmol/L* **IG** 1.6 (0.7, 3.4) 0.10 (-0.01, 0.22) **CG** 1.6 (0.7, 3.5) -0.02 (-0.15, 0.11)

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
(continued) Fontbonne, 1996[185] BIGPRO Fair		**Blood pressure:** *Systolic blood pressure, mmHg* **IG** 134 (16) -0.88 (-3.63, 1.88) **CG** 133 (17) -1.88 (-4.56, 0.79) *Diastolic blood pressure, mmHg* **IG** 81 (10) -0.89 (-2.66, 0.89) **CG** 82 (11) -1.50 (-3.59, 0.66) **Glucose tolerance:** *Fasting glucose, mmol/L* Total **IG** 5.3 (0.8) 0.2 (0.05, 0.4)* **CG** 5.2 (0.6) 0.4 (0.3, 0.6) *Normal glucose tolerance* **IG** 5.2 (0.7)* 0.3 (0.2, 0.4)* **CG** 5.1 (0.6) 0.3 (0.2, 0.5) Abnormal glucose tolerance **IG** 6.0 (0.9)* -0.3 (-0.9, 0.2)* **CG** 5.6 (0.8) 0.8 (0.1, 1.5) ** p<0.05 for two-tailed t-test* **IG n analyzed:** 164 (total); 171 (NGT); 49 (abnormal glucose tolerance) **CG n analyzed:** 160 (total); 175 (NGT); 47 (abnormal glucose tolerance)
Gambineri, 2006[186] Fair	Mean (SD) **BL 7 mo 13 mo†** **Weight/Relative weight:** *BMI, kg/m^2* **IG** 35 (4) 33 (5)* 33 (5)** **CG** 37 (5) 35 (5)* 35 (5)*** *Weight, kg* **IG** 92 (13) 88 (14)* 88 (13)** **CG** 97 (16) 93 (16)* 92 (16)*** **Central adiposity:** *Waist circumference, cm* **IG** 100 (10) 96 (11)*** 95 (10)*** **CG** 102 (10) 98 (11)*** 98 (10)*** **Overall adiposity:** *Total adipose tissue area, Sc adipose tissue area, Visceral adipose tissue area, Sc-to-visceral adipose tissue area ratio* ** p<0.05 for comparison between baseline and followup within group* *** p<0.01 for comparison between baseline and followup within group* **** p<0.001 for comparison between baseline and followup within group* † 12 months of medication/13 months of diet **IG n analyzed:** 20 **CG n analyzed:** 19	Mean (SD) **BL 7 mo 13 mo** **Lipids:** *HDL cholesterol, mg/dL* **IG** 45 (8) 45 (8) 50 (10)** **CG** 47 (10) 47 (11) 53 (11)** *LDL cholesterol, mg/dL* **IG** 113 (34) 104 (34) 99 (37)** **CG** 117 (23) 119 (53) 109 (33) *Triglycerides, mg/dL* **IG** 108 (57) 97 (36) 83 (52) **CG** 114 (68) 101 (65) 113 (58) **Blood pressure:** NR **Glucose tolerance:** *Fasting glucose, mg/dL* **IG** 92 (9) 91 (9) 91 (9) **CG** 89 (11) 89 (10) 88 (9) *** p<0.01 for comparison between baseline and followup within group* **IG n analyzed:** 20 **CG n analyzed:** 19

Appendix C Table 2c. Evidence Table of Medication Trials: Intermediate Outcomes

Study Reference Quality Rating	Anthropomorphic Measures	Other Intermediate Outcomes (Lipids, Glucose Tolerance, Blood Pressure)
Diabetes Prevention Program Research Group, 1999[142] Haffner, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2006[210] Ratner, 2005[207] Knowler, 2002[206] West, 2008[214] Rubin, 2005[205] Ackermann, 2009[211] Diabetes Prevention Program Good	Mean (SD) at BL (median (IQR) for age groups at BL), mean change (SE) at 12 mo, mean change (NR) at 30 mo and 2.8 yrs, mean change (SE) at 36 mo **BL / 12 mo / 30 mo / 2.8 yr** **Weight/Relative weight:** *BMI, kg/m²* **IG** 33.9 (6.6) -0.97 (0.06)* -- -- **CG** 34.2 (6.7) -0.15 (0.06) -- -- *Weight, kg* Total **IG** 94.3 (19.9) -2.72 (0.17)* -1.59 (5.98) -2.1 (--) **CG** 94.3 (20.2) -0.42 (0.17) -- -0.1 (--) **BL / 36 mo††** 25-44 years **IG** 95.0 (28.0) -1.5 (0.3) **CG** 95.5 (29.3) 0.5 (0.3) 45-59 years **IG** 92.2 (26.6) -1.7 (0.2) **CG** 91.5 (27.1) 0.1 (0.2) 60-85 years **IG** 86.4 (19.0) -2.7 (0.3) **CG** 87.8 (21.8) -0.2 (0.3) **Central adiposity:** **BL / 12 mo** *Waist circumference, cm* Total **IG** 104.9 (14.4) -2.23 (0.19)* **CG** 105.2 (14.3) -0.69 (0.19) **BL** 45-59 years **IG** 104.0 (19.7) -1.7 (0.3) **CG** 103.5 (19.6) -0.5 (0.2) 60-85 years **IG** 103.7 (14.1) -2.8 (0.3) **CG** 103.0 (17.8) -0.4 (0.3) **Overall adiposity:** *Body fat measurement (visceral L2-L3, visceral L4-L5, subcutaneous L2-L3, subcutaneous L4-L5) (for subsample, n=758, 68.5%)* ** p<0.001 for mean difference between IG-M vs IG-L vs CG* *†† Assumed* **IG n analyzed:** 1073 (BL, 12 mo, 36 mo); 985 (30 mo); NR (2.8 yr) **CG n analyzed:** 1082 (BL, 12 mo, 36 mo); NR (2.8 yr)	Mean (SD) at BL, % change at 36 mo for total and LDL cholesterol, mean change (SE) at 12, 24, and 36 months all other outcomes **BL / 12 mo / 24 mo / 36 mo††** **Lipids:** *Total cholesterol, mmol/l* **IG** 5.3$ -- -- -0.9* **CG** 5.3$ -- -- -1.2 *HDL cholesterol, mmol/l* **IG** -- -- -- -0.008** **CG** -- -- -- -0.002 *LDL cholesterol, mmol/l* **IG** 3.2$ -- -- -0.3* **CG** 3.2$ -- -- -1.3 *Triglycerides, mmol/l* **IG** -- -- -- -0.08 **CG** -- -- -- -0.13 *Other measures: % with high TG levels or receiving treatment for high triglyceride levels; % with low HDL level* **Blood pressure:** *Systolic blood pressure, mmHg* **IG** 124.0 (14.9) -0.91 (0.4)*** -0.94 (0.4)*** -0.29 (0.5)*** **CG** 123.5 (14.4) -0.90 (0.4) -0.52 (0.4) -0.57 (0.5) *Diastolic blood pressure, mmHg* **IG** 78.2 (9.5) -1.26 (0.2)*** -1.06 (0.2)*** -1.59 (0.3)*** **CG** 78.0 (9.2) -0.89 (0.2) -1.07 (0.2) -1.88 (0.3) *Other measures: %high blood pressure or receiving treatment for high blood pressure* **Glucose tolerance:** *Fasting glucose, mg/dl* **IG** 106.5 (8.3) -4.18 (0.36)† -- -- **CG** 106.7 (8.4) 0.63 (0.36) -- -- *Other measures: HOMA-IR (1135); % with high fasting plasma glucose level; Metabolic syndrome incidence (1139)* *$average of all groups together (assumed)* **p=NS for IG vs CG* ***p=0.002 for IG vs CG* ****p<.001 vs placebo for changes in mean over time for both IG vs CG* *† p<0.001 for mean difference between IG-M vs IG-L vs CG* *†† Assumed* **IG n analyzed:** 1073 (BP at 12 mo: 1017) **CG n analyzed:** 1082 (BP at 12 mo: 1027)

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Orlistat Trials				
Berne, 2005[180] Fair	NR	**BL 12 mo** *Metformin dosage increased, n* **IG** -- 15 **CG** -- 22 *Metformin dosage decreased, n* **IG** -- 7 **CG** -- 1 *Metformin treatment started, n* **IG** -- 2 **CG** -- 0 *Metformin treatment ended, n* **IG** -- 1 **CG** -- 0 *Sulphonylurea dosage increased, n* **IG** -- 1 **CG** -- 9 *Sulphonylurea dosage decreased or ended, n* **IG** -- 11 **CG** -- 4 *Sulphonylurea treatment ended, n* **IG** -- 9 **CG** -- 1 *Sulphonylurea treatment started, n* **IG** -- 0 **CG** -- 2 **IG n analyzed:** 111 **CG n analyzed:** 109	Percent **12 mo** *Subjects with Adverse Events* **IG** 90.1 **CG** 82.6 n *Number of gastrointestinal events* **IG** 103 **CG** 48 *Number of non-gastrointestinal events* **IG** 49 **CG** 72	**Subgroup analyses:** By treatment medication for diabetes **Other:** NR
Broom, 2002[181] UK Multimorbidity Study Fair	NR	NR	Percent **12 mo** *Gastrointestinal events* **IG** 63 **CG** 47 Overall incidence for other adverse events was similar between IG and CG (data not given); 13 IG patients & 17 CG patients experienced serious adverse events, none of which was considered by study investigators to have a probable causal relationship with the study med; 1 death occurred in IG, cause of death was carcino-matosis, which was unrelated to the study med	**Subgroup analyses:** Total, HDL and LDL cholesterol by dyslipidemia; glucose tolerance by IGT; and DBP by hypertension **Other:** NR
Davidson, 1999[182] Fair	NR	NR	Percent **12 mo** *Withdrawn because of adverse events* **IG** 9.1 (calc) **CG** 4.0 (calc) *At least 1 gastrointestinal event* **IG** 79 **CG** 59 Vitamin deficiency: Vitamin D and E levels decreased significantly in IG but mean levels within reference range; 14% IG need vitamin supplementation compared to 6.5% CG over 2 years	**Subgroup analyses:** NR **Other:** Subjects in IG were rerandomized after 12 months. This data is not abstracted due to the high loss of participants after that point

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Derosa, 2003[183] Fair	NR	NR	Percent **12 mo** *Participants dropping out due to adverse events, percent* **IG** 7.4 **CG** 0 No serious adverse events.	**Subgroup analyses:** NR **Other:** NR
Derosa, 2010[215] Good	NR	NR	n (percent) **12 mo** *Withdrew due to adverse events* **IG** 13 (10.3) **CG** 4 (3.1) Majority of reasons for withdrawal (92.3%) were GI related **Other AEs:** Flatulence, constipation, fatty/oily evacuation, increased defecation, fecal urgency, malaise	**Subgroup analyses:** NR **Other:** NR
Finer, 2000[184] James, 1997[290] Fair	NR	NR	**12 mo** *Withdrew because of adverse events, percent* **IG** 8.0 **CG** 6.4 *At least one gastrointestinal event, percent* **IG** 82.1 **CG** 56.4 **Other AEs:** Loose stools, Increased defecation, Abdominal pain, Uncontrolled oily discharge, Fecal urgency, Nausea/vomiting, Discolored feces, Flatulence, Decreased defecation, Upper respiratory tract infection, Pharyngitis, Influenza/influenza syndrome, Headache, Back pain, Gallbladder abnormalities, Renal abnormalities, Mild severity AE*, Moderate severity AE*, Unrelated to test drug AE*, Remotely related to test drug AE*, Possibly related to test drug AE*, Probably related to test drug*, List of AE leading to withdrawl in IG and CG* N (percent) **12 mo** *Patients with adverse events** IG 23 (100) CG 21 (91.3) *Severe Severity** IG 3 (13) CG 6 (26) ** From a subsample of patients only seen at the Aberdeen center (n=23 in IG and n=23 in CG)*	**Subgroup analyses:** NR **Other:** NR

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Hanefeld, 2002[187] Fair	NR	Mean change from BL at 12 mo **-4 week 12 mo** *Anti-DM medication dosage decreased or ended, percent* **IG** -- 9.7 **CG** -- 9.0 *Anti-DM medication dosage increased or started, percent* **IG** -- 14.0 **CG** -- 17.5	**12 mo** *At least one adverse event, percent* **IG** 89 **CG** 88 *At least one gastrointestinal event, percent* **IG** 76 **CG** 46 *Severe gastrointestinal event, n* **IG** 6 **CG** 5 *Withdrew because of GI events related to mode of action of orlistat, percent* **IG** 4 **CG** 2 *Hypoglycemia (at least 1 episode), n* **IG** 2 **CG** 4 All hypoglycemic episodes were mild or moderate and none resulted in hospitalization or any adjustment in antidiabetic medication. No apparent differences in clinical laboratory parameters or vital signs between treatment groups were noted. Levels of fat-soluble vitamins were generally lower in IG than CG, but remained in normal ranges.	**Subgroup analyses:** Patients with type 2 diabetes previously treated with diet alone; effects of IG in patients not on DM medication at baseline **Other:** NR
Hauptman, 2000[189] Fair	NR	N (percent) **24 mo** *Died (acute myocardial infarction)* **IG1** 0 (0) **IG2** 1 (0.5) **CG** 0 (0)	**24 mo** *Withdrew because of adverse event, percent* **IG1** 6.6 **IG2** 11.0 **CG** 7.1 *Withdrew because of GI adverse event, percent* **IG1** 4.7 **IG2** 5.7 **CG** 1.4 *GI events, percent* **IG1** 72** **IG2** 79** **CG** 59 *Requiring supplementation with β-carotene, percent* **IG1** 4.3 **IG2** 6.3 **CG** 2.4 **Other AEs:** Fecal urgency*, oily spotting*, fatty/oily stool*, flatus with discharge*, oOily evacuation*, increased defecation*, fecal incontinence*, 2+ consecutive low vitamin levels for vitamin A, E*, D and β-carotene** ** p<0.005 for IG versus CG* *** p<0.01 for IG versus CG* <1.9% of all patients required and received vitamin A or E supplementation. Almost all patients who needed vitamin supplementation achieved normal levels by the end of the study.	**Subgroup analyses:** NR **Other:** 24 month data not abstracted because of high attrition

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
(continued) Hauptman, 2000[189] Fair			Most GI events were mild-moderate in intensity, limited to 1-2 episodes/patient, and occurred early in treatment. AEs in all groups were transient, mild, or moderate in intensity and resolved without intervention. With the exception of GI events, incidence and type of adverse events were similar in all treatment groups.	
Hill, 1999[190] Fair	NR	NR	% of subjects who reported ≥1 AEs was ~7-8% greater in IG than CG **12 mo** *Reporting gastrointestinal events, percent* **IG1** 82.3 **IG2** 91.8 **IG3** 95.0 **CG** 68.1 *Withdrawals related to gastrointestinal events, percent* **IG1** 5.4 **IG2** 7.0 **IG3** 11.7 **CG** 0.5 **Other AEs:** Flatus with discharge, abdominal pain, fecal urgency, oily spotting. Most subjects experienced only 1-2 episodes and most GI events were mild-moderate in intensity, occurred early during treatment, and resolved spontaneously. Vitamin E and β-carotene were significantly lower in IGs compared to CG at end of study (p<0.001). <4% of subjects met criteria for additional vitamin supplementation and those who did had normal values at end of study.	**Subgroup analyses:** NR **Other:** NR
Hollander, 1998[191] Fair	NR	Percent change *Percent change in average dose of oral sulfonylurea medication* **IG** -23** **CG** -9 *Percent of patients that decreased the amount of oral sulfonylurea medication* **IG** 43.2 **CG** 28.9 Percent *Discontinued sulfonylurea medication* **IG** 11.7 **CG** -- N (percent) *Withdrew from trial prematurely because of elevated plasma glucose levels on 3 or more occasions despite maximal sulfonlyurea medication* **IG** 5 (2.5) **CG** 15 (8.8) *** p=0.0019*	**12 mo** *% with ≥1 GI event* **IG** 79 **CG** 59 Majority of patients in IG experienced 1-2 GI events that occurred early, of mild-moderate intensity, transient, and resolved spontaneously *Withdrew due to GI event , n* **IG** 7 **CG** 2 *Withdrew due to adverse events, n* **IG 12** **CG 23** **Other AEs:** Flatus with discharge, oily spotting, fecal urgency, fatty/oily stool, oily evacuation, fecal incontinence, increased defecation, vitamin D, E or β-carotene supplementation needed (due to 2 or more consecutive low vitamin levels). No evidence for the development of gallstones or renal stones after orlistat treatment. Mean plasma levels of vitamins A, D, E and β -carotene remained within reference range through study. At 12 mo, mean vitamin E and β -carotene levels were lower in IG than CG (p<0.001). No sig change in vitamin E to LDL ratio in either group.	**Subgroup analyses:** HbA1c presented for those with levels of >8% at BL; cholesterol, LDL, and HbA1c changes presented by % of weight loss **Other:** note that unable to locate weight change from randomization; give changes during lead in

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Krempf, 2003[193] Fair	NR	NR	Percent *Withdrew prematurely due to AE* **IG** 6.9 **CG** 3.4 *1+ adverse event* **IG** 86.1, **CG** 72.3, p<0.001 (Difference was because of the % of orlistat patients experiencing GI events, suggesting fat intake was still excessive, although reduced from initial.) N *Withdrew prematurely due to serious adverse events** **IG** 5 **CG** 4 ** 7 of these events were deemed doubtfully related to study by investigators (IG: thrombotic thrombocytopenic purpura, anal abscess, pain hypocondrium, liver disorder; CG: abdominal pain, breast cancer, ulcerative colitis)*	**Subgroup analyses:** Changes in fasting glucose, LDL, HDL, triglycerides, SBP, and DPB presented for those "at risk" per those same measures at BL, however ns at BL for each condition NR **Other:** NR
Lindgarde, 2000[194] Swedish Multimorbidity Study Fair	NR	A higher proportion of IG patients with type 2 diabetes were able to stop or reduce their dosage of anti-diabetic meds compared with CG (23.3% vs. 18.2%)	Percent **12 mo** *Gastrointestinal events* **IG** 80 **CG** 39 Overall incidence for other adverse events was similar between IG and CG. 10 IG patients and 5 CG patients withdrew due to an adverse event. 5 IG patients and 1 CG patient withdrew because of GI events. 19 IG patients and 5 CG patients experienced serious adverse events, none of which were considered by study investigators to have a probable causal relationship with the study medication. 1 death occurred in IG; patient had type 2 diabetes and severe arterio-sclerosis and died as a result of a brain stem infarction.	**Subgroup analyses:** Weight change, fasting glucose, and HbA1c in patients with type 2 diabetes **Other:** NR
Miles, 2002[197] Fair	NR	Mean (SD) **12 mo** *Reduction in metformin dose, mg/day* **IG** -16 (24)* **CG** 49 (24) *Reduction in relative sulfonylurea dose, %†* **IG** -11.5 (3.6)* **CG** -0.9 (2.6) *† Doses standardized to a % of maximum daily dose* ** p<0.05* Twice as many patients in IG vs CG either reduced or discontinued 1 or more diabetes medications (17.1 vs. 8.2%). More CG than IG patients required additional or increased doses of diabetes medication (21.7 vs. 12.2%). These changes in diabetes medication usage were significantly different between groups (p=0.0004)	Percent **12 mo** *Experiencing at least one gastrointestinal event* **IG** 83 **CG** 62 *Mild-Moderate hypoglycemic episodes* **IG** 10 **CG** 4 *Withdrew due to adverse events, n* **IG** 25 **CG** 12 More IG than CG patients discontinued treatment because of an adverse event (10 vs. 5%, p<0.05)	**Subgroup analyses:** NR **Other:** NR

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Richelsen, 2007[198] Fair	NR	n (percent) **BL** **36 mo** *Newly developed Diabetes Mellitus* **IG** -- 8 (5.2)* **CG** -- 17 (10.9) ** p=0.041*	Percent **36 mo** *Withdrawals due to adverse events* **IG** 5 **CG** 5 *Fatty/oily stool* **IG** 23 **CG** 2.5 *Oily spotting* **IG** 17.5 **CG** 0 *Abdominal pain* **IG** 21.5 **CG** 16 *Fecal urgency* **IG** 8.5 **CG** 5 *One or more gastrointestinal event* **IG** 88* **CG** 63 *Serious adverse event* **IG** 18 **CG** 28 ** p<0.01; statistical significance NR for first 5 AEs.*	**Subgroup analyses:** Dietary intake for a subsample (Svendsen) **Other:** Number (IG vs CG) of patients who started with meds with statins (11 vs 11) metformin (13 vs 18) blood pressure (84 vs 90) was same in 2 groups
Rossner, 2000[199] Fair	**QOL** Instrument used: Technology Assessment Group quality-of-life questionnaire Range: NR # of questions: 55 Directionality: NR Description: Measures obesity distress, depression, satisfaction with treatment *NOTE: The study calls this QOL, but it is a QOL scale specific to obesity and might not correspond with other QOL instruments we have*	*QOL* IG1 and IG2 reported significantly greater satisfaction with their weight loss medication versus CG after 1 and 2 years (p<0.001 for IG2, p<0.05 for IG1). IG2 patients also expressed greater satisfaction both with losing weight and their weight loss program (p=0.011 and p=0.002, respectively, after 2 years). Overall satisfaction with treatment, as expressed by the treatment index, was significantly greater among IG1 and IG2 versus CG after 2 years (p<0.001 for IG2, p<0.05 for IG1). IG1 and IG2 patients reported less overweight distress than CG and this became statistically significant after 2 years (p<0.05). There were no significant differences between treatment groups in depression scores after 1 or 2 years	**24 mo** *Withdrew due to severe GI events, percent* **IG1** 6.6 **IG2** 10.3 **CG** 3.4 *Withdrew due to adverse events, percent* **IG1** 9.6 **IG2** 7.9 **CG** 2.5 *Withdrew due to adverse GI events, percent* **IG1** 5 **IG2** 3.7 **CG** 0.8 2 serious adverse events possibly related to orlistat: 1 case of cholelithiasis and diverticulitis. Adverse event profiles were similar in all 3 groups (except GI events) throughout study, generally mild-moderate in intensity and resolved spontaneously. Majority of severe GI events occurred during year 1 (n=38). Majority of vitamin supplement occurred during year 1. Differences in mean plasma values for vitamins D, E and β-carotene between IG1/IG2 and CG were statistically significant (p<0.001). Orlistat had no clinical significant effects on pulse rate or ECG results. **Other AEs:** Fatty/oily stool, fecal urgency, oily spotting, increased defecation, fecal incontinence, flatus with discharge, oily evacuation, vitamin supplement, breast ca	**Subgroup analyses:** Outcomes also reported for completers **Other:** NR

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Sjostrom, 1998[200] Fair	NR	NR	**12 mo** *Adverse event frequency, %* **IG** 94 **CG** 82 *Premature withdrawals due to GI adverse events, %* **IG** 3.5 **CG** 0.6 *Premature withdrawals due to other adverse events, %* **IG** 3.2 **CG** 2.0 Frequency of adverse events slightly higher in IG vs CG in year 1 and similar for all 4 treatment groups in year 2. Patients taking orlistat experienced far fewer GI events in year 2 vs year 1. Serious adverse events reported by 24 CG patients and 25 IG in year 1, only 1 related to treatment. 2 adverse events in year 2 related to treatment. 1 case of GI neoplasm in CG. Events occurring in <5% of patients NR. **Other AEs:** Fecal incontinence, flatus with discharge, fecal urgency, abdominal pain, liquid/soft stool, oily spotting, increased defecation, fatty/oily stool, oily evacuation, headache, 2 consecutive low vitamin A, D, E levels, vitamin supplementation, other reason	**Subgroup analyses:** Bone density measured for a very small subsample (n=30) (Gotfredson, #8364) did not show difference between IG and CG in bone mineral measurement during 1 year **Other:** Authors found low systemic absorption of orlistat after 2 years of treatment with no evidence of accumulation
Swinburn, 2005[201] Fair	**QOL** Instrument used: SF-36 Range: 0-100 for each domain # of questions: NR Directionality: Higher score = better	Mean (SD) at BL, Mean change (SD) at 12 mo *SF-36 Physical functioning* **IG** 75.5 (19.6) 3.23 (1.97) **CG** 75.7 (19.5) 1.32 (18.0) *SF-36 Physical role* **IG** 78.8 (34.6) 1.41 (40.0) **CG** 78.8 (33.4) 3.06 (32.2) *SF-36 Bodily pain* **IG** 72.1 (23.2) 0.70 (22.7) **CG** 75.1 (23.6) -2.33 (22.0) *SF-36 General health* **IG** 69.1 (19.6) 3.28 (14.8) **CG** 70.1 (18.4) 0.13 (14.6) *SF-36 Vitality* **IG** 61.7 (19.8) 5.42 (19.3)* **CG** 62.3 (19.4) -1.51 (19.4) *SF-36 Social functioning* **IG** 83.7 (23.4) 2.88 (24.0) **CG** 86.1 (20.7) -0.77 (25.7) *SF-36 Emotional role* **IG** 84.5 (31.9) 2.58 (36.8) **CG** 90.0 (23.9) -5.48 (31.8) *SF-36 Mental health* **IG** 77.9 (15.6) 3.15 (15.3) **CG** 79.6 (15.7) -0.52 (17.9) ** p=0.006; There were significant changes toward fewer or lower-dose medications in IG for diabetes (p=0.026) and hypertension (p=0.0062), but not for lipids (p=0.42)*	Percent **12 mo** *At least one adverse event* **IG** 94.7 **CG** 93.5 *Serious adverse events* **IG** 9.4 **CG** 7.1 *Gastrointestinal system adverse event* **IG** 82.4* **CG** 60.4 *Withdrew because of GI adverse events* **IG** 2.9 **CG** 1.2 *Withdrew because of adverse events* **IG** 10.0 (calc) **CG** 4.7 (calc) ** p=0.0005* In general, adverse events were mild to moderate in intensity. For all other events reported in more than 10 participants in either group, there were no statistically significant differences between IG and CG.	**Subgroup analyses:** NR **Other:** Change in medications for diabetes mellitus, hypertension, lipids in IG and CG shown in a figure only.

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Torgerson, 2004[202] Torgerson, 2001[291] XENDOS Fair	NR	Cumulative incidence, percent **BL** **4 yr** *Diabetes Mellitus* **IG** 0 6.2** **CG** 0 9.0 *Diabetes Mellitus among those with IGT at baseline* **IG** 0 18.8** **C** 0 28.8 Hazard ratio (95% CI) *Risk of developing diabetes* **IG v. CG** -- 0.63 (0.46, 0.87)** **IGT v. NGT** -- 10.60 (7.30, 5.4)*** **Male v. Female** -- 1.41 (1.02, 1.96)* **>44 v. ≤44 years†** -- 1.44 (1.02, 2.04)* **≥37 vs. < 37 kg/m^2†** -- 1.36 (0.97, 1.91) *† Median* **** p < 0.001* ******* *p < 0.01* ** p < 0.05*	Percent **1 yr** **4 yr** *1+ gastrointestinal event* **IG** 91 36 **CG** 65 23 *1+ SAE, percent* **IG** -- 15 **CG** -- 13 *1+ serious gastrointestinal event* **IG** -- 2 **CG** -- 2 *Withdrew due to AE or laboratory abnormalities* **IG** -- 8 **CG** -- 4 *Death* **IG** -- 0 **CG** -- 0 Mean change from baseline *Vitamin A, µmol/L* **IG** -- -0.22* **CG** -- -0.19 *25-hydroxyvitamin D, nmol/mL* **IG** -- -17.2** **CG** -- -13.0 *Vitamin E, µmol/L* **IG** -- -2.8** **CG** -- 0.4 *Vitamin K1, µg/L* **IG** -- -0.08** **CG** -- -0.07 *1,25-hydroxyvitamin D, pmol/mL* **IG** -- -15.8 **CG** -- -14.0 Proportion that went from normal to having two subsequent, consecutive abnormally low values was similar for Vitamin A (5.5 vs 4.4%) and notably different only for Vitamin E (3.2 vs 0.5%). Proportion for all other vitamin levels were <1% and similar between treatment groups * p<0.05 for IG vs CG ** p<0.001 for IG vs CG	**Subgroup analyses:** Incidence of DM among pts with IGT at BL; HR of developing DM by BL glucose tolerance, sex, age, and BMI; weight loss for completers only, and for all randomized (BL carried forward for dropouts); proportion weight loss ≥5% and ≥10%, and for completers only **Other:** Other intermediate outcomes only reported for 851 and 567 pts in IG and CG respectively at 4 years

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Metformin Trials				
Fontbonne, 1996[185] BIGPRO Fair	NR	During the course of the trial, no patient developed ischemic cardiovascular disease but 5 CG patients were diagnosed with diabetes by local investigators	Reasons for absence at last visit, percent **12 mo** *Side effect of allocated treatment* **IG** 17.5 **CG** 4.3 *Death* **IG** 1.6 **CG** 0 *Diabetes* **IG** 0 **CG** 2.9 *Other health problems* **IG** 7.9 **CG** 5.7 **Other AEs:** Diarrhea*, Nausea/vomiting, Abdominal pain, Constipation, Cramps, Headache/fatigue, Mood shifts, Cutaneous rash, Hunger, Bad taste in mouth *Except for diarrhea and to a much lesser degree, nausea and vomiting, all other reported side effects occurred with similar frequence in both treatment groups	**Subgroup analyses:** Fasting blood glucose by glucose tolerance at baseline **Other:** All participants weighed every 3 months
Gambineri, 2006[186] Fair	NR	N (percent) **BL** **7 mo** **13 mo** *Impaired fasting glucose* **IG** 3 (15) 3 (15) 3 (15) **CG** 2 (11) 1 (5) 2 (11) *Impaired glucose tolerance* **IG** 3 (15) 4 (20) 2 (10) **CG** 2 (11) 1 (5) 0 (0) *Impaired fasting glucose + Impaired glucose tolerance* **IG** 2 (10) 0 (0) 0 (0) **CG** 2 (11) 1 (5) 0 (0) **IG n analyzed:** 20 **CG n analyzed:** 19	Two women who completed the study reported transient abdominal discomfort (abdominal swelling, mild diarrhea, and flatulence) during the first 2 weeks of treatment	**Subgroup analyses:** NR **Other:** NR

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
Diabetes Prevention Program Research Group, 1999[142] Haffner, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2006[210] Ratner, 2005[207] Knowler, 2002[206] West, 2008[214] Rubin, 2005[205] Ackermann, 2009[211] Diabetes Prevention Program Good	**Depression** Instrument used: Beck Depression Inventory or current use of antidepressants (BDI ≥11 threshold used for depression) Range: NR # of questions: NR Directionality: Higher score = worse; used score ≥ 11 as threshold for mild depression **Anxiety** Instrument use: Beck Anxiety Inventory Range: 0-63 # of questions: NR Directionality: Higher score = worse **QOL** Instrument used: Medical Outcomes Study 36-item short form (SF-36); can be used to determine SF-6D, MCS and PCS scores Range: NR # of questions: 36 Directionality: Lower score = worse	**BL 12 mo** *Depression: BDI ≥11 or antidepressant use (%)* **IG-men** 8.1 8.6 **IG-wmn** 19.7 14.7 **CG-men** 9.1 7.5 **CG-wmn** 18.1 17.1 **36 mo** *Diabetes crude cumulative incidence, cases/100 p-y* Total **IG** 7.8 **CG** 11.0 25-44 years **IG** 6.7 **CG** 11.6 45-59 years **IG** 7.6 **CG** 10.8 ≥ 60 years **IG** 9.6 **CG** 10.8 Male **IG** 8.1 **CG** 12.5 Female **IG** 7.6 **CG** 10.3 White **IG** 7.8 **CG** 10.3 Black **IG** 7.1 **CG** 12.4 Hispanic **IG** 8.4 **CG** 11.7 American Indian **IG** 9.7 **CG** 12.9 Asian/Pacific Islander **IG** 7.5 **CG** 12.1 BL BMI 22 to <30 **IG** 8.8 **CG** 9.0 BL BMI 30 to <35 **IG** 7.6 **CG** 8.9 *Diabetes incidence, % lower from CG (95% CI)* **IG** 31 (17, 43)†	**48 mo (3.2 yrs for age groups)** *GI symptoms (diarrhea, flatulence, nausea, vomiting), number of events/100 person-years* Total **IG** 77.8* **CG** 30.7 25-44 years **IG** 82.2 **CG** 32.4 45-59 years **IG** 77.5 **CG** 30.8 60-85 years **IG** 72.2 **CG** 27.8 *Deaths, number/100 person-years* Total **IG** 0.20 **CG** 0.16 25-44 years **IG** 0.11 **CG** 0 45-59 years **IG** 0.13 **CG** 0 60-85 years **IG** 0.48 **CG** 0.86 ** p<0.05 for comparison with CG* **IG n analyzed:** 1073 (22-44 yrs: 318; 45-59 yrs: 541; 60-85 yrs: 214) **CG n analyzed:** 1092 (22-44 yrs: 324; 45-59 yrs: 557; 60-85 yrs: 201) Gastrointestinal complaints were more common in IG (as expected), with rates slightly lower in the middle-age and older groups, although this difference was not statistically significant. The rate of gastrointestinal symptoms was highest in IG. Hospitalization and mortality rates were unrelated to treatment. No deaths were attributed to intervention. Other AEs: Musculoskeletal problems (mostly myalgia, arthritis, arthralgia), Hospital admissions, Rate of hospitalization, Hospital stay	**Subgroup analyses:** Age, gender, race **Other:** 10-year unblinded followup results available (#8173). As has been previously observed with this drug, the IG participants experienced modest weight loss, which was greatest in the oldest age group. Waist circumference was reduced, with the greatest change in the 60-85 year age group. In contrast, there were no significant changes in weight or waist circumference at any age in the CG. After removal of interaction terms, race (p<0.0001) and gender (p=0.0259) main effects were not significant within metformin treatment. Metformin interventions produced significantly larger percent weight loss than CG across the race-gender groups (all p<0.05). The only exception to this pattern was that Hispanic women within the IG did not experience significantly greater percent weight loss than those in CG (p=0.0547). The study had inadequate power to assess the significance of effects within the subgroups, nor were such tests planned. Treatment effects did not differ significantly according either to sex or race or ethnic group. Effect of metformin was less with a lower BMI or a lower fasting glucose concentration than with higher values for those variables.

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Study Reference Quality Rating	Health Outcome Instrument	Health Outcomes	Adverse Effects	Comments
(continued) Diabetes Prevention Program Research Group, 1999[142] Haffner, 2005[212] Orchard, 2005[262] Diabetes Prevention Program Research Group, 2006[210] Ratner, 2005[207] Knowler, 2002[206] West, 2008[214] Rubin, 2005[205] Ackermann, 2009[211] Diabetes Prevention Program Good	**QOL** Instrument used: Quality of Well-Being Scale (QWB-SA) Range: NR # of questions: NR Directionality: Higher score = better	*Nonfatal cardiovascular disease events, %* **IG** 1.7 **CG** 1.5 *Nonfatal cardiovascular disease events, event rate (number of events per 1000 p-y)* **IG** 5.2 **CG** 7.3 *Cardiovascular disease related deaths, n* **IG** 1 **CG** 4 *Antihypertensive pharmacologic therapy prevalence, %* **IG** 32 **CG** 31 ***p<0.001 for IG vs CG* *† Significant by group-sequential log-rank test* *†† Diabetes incidence did not differ by age in CG (11.0, 10.8, 10.3 cases per 100 p-y).Incidence in IG was lowest among youngest participants (6.7 vs 7.7 vs 9.3 cases per 100 p-y), but this trend was not statistically significant (p=0.07).* 12 mo change from BL *Anxiety, Beck Anxiety Inventory* **IG** 3.75 (4.69) -0.15 (4.44) **CG** 3.78 (4.89) -0.25 (4.80) **IG n analyzed:** 1001 (BL), 992 (12 mos) **CG n analyzed:** 1012 (BL), 993 (12 mos) *SF-6D* **IG** 0.797 (0.105) -0.002 (0.108) **CG** 0.788 (0.111) -0.013 (0.106) *SF-36, physical component score* **IG** 50.1 (7.3) 0.22 (7.49) **CG** 50.4 (7.2) -0.04 (7.12) *SF-36, mental component score* **IG** 54.1 (7.7) -0.58 (8.30) **CG** 54.0 (7.4) -1.16 (8.33) **IG n analyzed:** 1067 (BL), 1011 (12 mos) **CG n analyzed:** 1079 (BL), 1018 (12 mos) *Quality of Well-being, QWB-SA* **IG** 0.693 (0.114) 0.017 (0.105) **CG** 0.700 (0.115) 0.013 (0.124) **IG n analyzed:** 707 (BL), 262 (12 mos) **CG n analyzed:** 702 (BL), 252 (12 mos) In a fully adjusted model including both IG and weight change, assignment to either IG was not significantly associated with change in SF-6D at 12 mo vs CG. After adjusting for IG, change in weight asscoiated with significant change at 12 mo for SF-6D (p<0.001), PCS-36 (p<0.001), MCS-36 (p=0.04) for ever 5 kg loss; similar associations at 24 mo		

Appendix C Table 2d. Evidence Table of Medication Trials: Health Outcomes

Abbreviations: AE=adverse event; ANCOVA=analysis of covariance; AUC=area under the curve; BDI=Beck Depression Inventory; bid=two times a day; BL=baseline; BMI=body mass index; BMR=basal metabolic rate; BP=blood pressure; bpm=beats per minute; calc=calculated; carb=carbohydrate; CG=control group; CI=confidence interval; CV=cardiovascular; DBP=diastolic blood pressure; DM=diabetes mellitus; DPP=Diabetes Prevention Program; ECG=electrocardiography; GI=gastrointestinal; GP=general practitioner; HDL=high-density lipoprotein; HOMA=homeostatic model assessment; HR=heart rate; IG=intervention group; IGT=impaired glucose tolerance; IR=insulin resistance; ITT=intention to treat; IQR=interquartile range; LDL=low-density lipoprotein; LOCF=last observation carried forward; LSM=least squares mean; MA=meta-analysis; MI=myocardial infarction; n=number; NA=not applicable; NGT=normal glucose tolerance; NR=not reported; NYHA=New York Heart Association; OGTT=oral glucose tolerance test; PCOS=polycystic ovary syndrome; PCP=primary care practitioner; pt=patient; QOL=quality of life; RCT=randomized controlled trial; SAE=serious adverse event; SBP=systolic blood pressure; Sc=subcutaneous; SD=standard deviation; SE=standard error; SES=socioeconomic status; SF-36=36-Item Short-form Health Survey; TG=triglyceride; tid=three times a day; UK=United Kingdom; US=United States; VLCD=very low calorie diet; WC=waist circumference; WHO=World Health Organization.

Appendix C Table 3a. Evidence Table of Behavioral Harms Trials: Study Characteristics

Study Reference	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Kirk, 2003[128] MET	**Design:** RCT **Location:** Nebraska and Kansas, US **Recruitment Setting:** University of Nebraska-Kearney, University of Kansas and respective communities **Volunteer:** NR	**Inclusion:** Aged 19-30 years; BMI 27-32 kg/m^2 (women) and 27-31 kg/m^2 (men); met or exceeded the 85th percentile for triceps skinfold of the National Health and Nutrition Examination Survey II populations; sedentary and did not exceed 500 calories of physical activity per week **Exclusion:** History of chronic disease; elevated blood pressure (>140/90), lipids (cholesterol>6.7 mmol/L, triglycerides>5.6 mmol/L), or fasting glucose (>7.8 mmol/L); smokers; took medication that would affect physical performance or metabolism; lacked ability to perform laboratory tests or participate in routine moderate intensity exercise	**N Randomized:** Total: 131 IG: 87 CG: 44 **N Analyzed:** Total: 74 IG: 41 CG: 33	**Age (mean):** 23 (calc) **Sex (% female):** 58.1 (calc) **Race/Ethnicity:** *% White:* 82.4 *% African-American:* 8.1 *% Native American:* 1.4 *% Hispanic:* 1.4 *% Asian:* 6.8 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR *Note: Baseline characteristics for completers only (n=74)*
Uusi-Rasi, 2010[135]	**Design:** Cohort **Location:** Finland **Recruitment Setting:** Tampere University Hospital **Volunteer:** NR	**Inclusion:** Aged 25-45 years; BMI > 30 kg/m^2; clinically healthy premenopausal women **Exclusion:** Metabolic bone disease; eating disorders, severe menstrual irregularities; use of estrogen other than hormonal contraceptives; use of medication that could affect the skeleton; recent (<1 year) delivery or lactation, fracture/trauma and related long immobilizaton (> 1 month)	**N Randomized:** Total: 75 IG: 75 CG: NA **N Analyzed:** Total: 62 (82.7%) IG: 62 CG: NA	**Age (mean):** 40.2 **Sex (% female):** 100 **Race/Ethnicity: NR** **SES (income, education):** NR **% Hypertension:** 11.3 (regular use of hypertensive med) **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** Hypothyroidism, other regular medication use *Note: Baseline characteristics for completers only (n=62)*

Appendix C Table 3a. Evidence Table of Behavioral Harms Trials: Study Characteristics

Study Reference	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Warren, 2009[138] SHE	**Design:** RCT **Location:** US **Recruitment Setting:** Community **Volunteer:** Y	**Inclusion:** Aged 25-44 years; BMI 25-35 kg/m^2; stable body weight (<10% change during the past year); premenopausal; sedentary or modestly physically active (<3 weekly sessions of moderate aerobic activity; nonsmoker **Exclusion:** Medical condition or medications that could limit participation in the exercise program or affect study measurements; any positive responses on the Physical Activity Readiness Questionnaire	**N Randomized:** Total: 164 IG: 82 CG: 82 **N Analyzed:** Total: 163 IG: 81 CG: 82	**Age (mean):** 35.7 (calc) **Sex (% female):** 100 **Race/Ethnicity:** *% NonWhite:* 35 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR
Williamson, 2008[137] CALERIE	**Design:** RCT **Location:** US **Recruitment Setting:** Community **Volunteer:** Y	**Inclusion:** Non-smoking, adult men (25-50 years) and women (25-45 years); overweight at screening (25≤BMI<30 kg/m^2); otherwise healthy; not taking medications other than oral contraceptives **Exclusion:** Mental health problems; eating disorders; significant barriers to participation	**N Randomized:** Total: 48 IG1: 12 IG2:12 IG3: 12 CG: 12 **N Analyzed:** Total: 48 IG1: 12 IG2: 12 IG3: 12 CG: 12	**Age (mean):** 38 **Sex (% female):** 56 **Race/Ethnicity:** *% White:* 62.5 *% African American:* 33.3 *% Asian or Latino:* 4.2 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR

Appendix C Table 3b. Evidence Table of Behavioral Harms Trials: Intervention Details and Adverse Effects

Study Reference	Intervention Aim/Theory	Description of Intervention and Control	Adverse Effects	Comments
Kirk, 2003[128] MET	**Aim/theory:** To determine the time course for changes in aerobic capacity, body weight, and composition in overweight adults	**Intervention description:** Walking on treadmill (stationary bike and water aerobics allowed for 20% of total exercise sessions). Exercise progressed from 20 min 3 days/wk at 60% of heart rate reserve to 45 min 5 days/wk at 75% of heart rate reserve at 6 mo and maintained through 16 mo **Control description:** NR **Intervention Duration:** *Individual Sessions* Number: 3 days/wk to 5 days/wk (by 6 mo) Length: 20 min to 45 min (by 6 mo) Time period: 16 mo *Group Sessions*: NR **Who administered intervention:** Providers: Research personnel Training: NR **Intervention Setting:** NR **Incentives:** "Compensated for participation in this project"	"No major adverse events" for either IG or CG	NR
Uusi-Rasi, 2010[135]	**Aim/theory:** To determine the effects of weight reduction on bone turnover, mass and structure among premenopausal obese women	**Intervention description:** Intensive 3-mo weight reduction intervention [low-energy diet (wk 1), very-low-energy diet (wks 2-10, 3 sachets of 585 kJ each and 1 light meal or 5 sachets), low-energy diet and weight maintenance instruction (wks 11-12)]; followed by 9-mo weight maintenance period IG1 (n=20): Large group, 15.5% (mean) weight loss IG2 (n=21): Medium group, 10.5% (mean) weight loss IG3 (n=21): Low group, 5.9% (mean) weight loss **Control description:** NA **Intervention Duration:** *Individual Sessions:* NR *Group Sessions*: Number: 1/week for first 3 mo; 1/month during maintenance period (total 21) Length: NR Time period: 12 mo **Who administered intervention:** Providers: Nutritionist Training: NR **Intervention Setting:** NR **Incentives:** NR	Mean change (assume SD, but not specified) **3 mo** **12 mo** *Total body Bone Mineral Content, g* **IG1(Large)** 8 (155) -30 (--) **IG2(Med)** -50 (161) -48 (--) **IG3(Low)** -17 (131) -5 (--) Bone changes were marginal at 3 mo and 12 mo, no between-group differences Amount of weight loss was not associated with the observed changes in bone traits Only significant change in strength of nonweight-bearing distal radius (mean declines, 3-44%), not statistically significant between groups	5 groups of 15 women each received same intervention; women divided into 3 groups based on tertiles of weight loss at 3 months

Appendix C Table 3b. Evidence Table of Behavioral Harms Trials: Intervention Details and Adverse Effects

Study Reference	Intervention Aim/Theory	Description of Intervention and Control	Adverse Effects	Comments
Warren, 2009[138] SHE	**Aim/theory:** To explore the safety of twice-weekly strength training	**Intervention description:** Strength training twice/week (3 sets of 8-10 repetitions using variable weight machines and free weights). Aerobic warm-up, stretching, and core training. **Control description:** Mailed American Heart Association brochures that recommended 30 minutes of moderate activity most days of the week **Intervention Duration:** *Individual Sessions*: NR *Group Sessions* Number: 2/week Length: NR Time period: 104 weeks **Who administered intervention:** Providers: Fitness trainers (first 16 wks and booster sessions every 12 wks) Training: Certified trainers **Intervention Setting:** Free-living community **Incentives:** NR	24 mo Cumulative incidence of physical activity-related injury per 100 women IG 46.9 CG 13.6 OR (95% CI): 4.0 (1.8, 9.0) Cumulative incidence of strength training injury limiting daily activity for at least 1 week per 100 women IG 33.3 CG 4.9 OR (95% CI): 10.1 (3.0, 34.2) Rate of serious injuries (resulting in loss of work time or major change in daily activities), percent IG 7 CG 7 No life-threatening injuries in either group. IG n analyzed: 81 CG n analyzed: 82	NR
Williamson, 2008[137] CALERIE	**Aim/theory:** To test whether a period of intentional caloric restriction would be associated with increased eating and mood disturbances	**Intervention description:** IG1: 25% calorie restriction of baseline energy requirements IG2: Calorie restriction and 12.5% increased energy expenditure by structured exercise IG3: 890 kcal/day liquid diet until 15% of body weight was lost, followed by a weight maintentance diet **Control description:** Weight maintenance diet **Intervention Duration:** NR **Who administered intervention:** Providers: NR Training: NR **Intervention Setting:** University Research Center **Incentives:** NR	Eating disinhibition reduced in IGs compared to CG (reduction is associated with reduced binge eating) No other group differences on eating disorder scales	NR

Abbreviations: BMI=body mass index; calc=calculated; CG=control group; CI=confidence interval; IG=intervention group; med=medication; MET=Midwest Exercise Trial; NA=not applicable; NR=not reported; RCT=randomized controlled trial; SHE=Strong, Healthy, Empowered; SES=socioeconomic status; US=United States; Y=yes.

Appendix C Table 4a. Evidence Table of Medication Harms Trials: Study Characteristics

Study Reference	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Orlistat Trials				
Acharya, 2006[133] Perrio, 2007[134]	**Design:** Observational Cohort study/Prescription event monitoring **Location:** UK **Recruitment Setting:** Patients identified from dispensed NHS prescription data **Self-Selected:** NR	**Inclusion:** Prescribed orlistat from Dec 1998-Nov 1999; questionnaire returned by GP **Exclusion:** Questionnaires returned with no information or not returned	**N Randomized:** NA **N Analyzed:** Total: 16,021 (45.4% of forms sent)	**Age (median):** 45 **Sex (% female):** 80.1 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** NR **% Dyslipidemia:** NR **Other health problems:** NR
Bakris, 2002[126]	**Design:** RCT **Location:** 41 centers, US **Recruitment Setting:** 41 referral centers **Self-Selected:** NR	**Inclusion:** BMI 28-43 kg/m^2; taking at lease one antihypertensive medication (stable dose for at least 12 weeks prior); had a sitting DBP 96 - 109 mmHg on 2 consecutive visits; easily controlled & stable diabetes allowed **Exclusion:** unstable medical and/or psychiatric illness; recent (within 12 wks) initiation or change in diuretic therapy; previous gastrointestinal surgery for weight reduction, and any active GI disorders such as malabsorption syndrome except more than mild lactose intolerance, diarrhea or constipation; history of bulimia or laxative abuse, substance abuse (including alcohol), and unwillingness or inability to comply with protocol requirements; pregnant or lactating women; the use of nicotine replacement therapy, appetite suppressants, fish-oil supplements, oral retinoids, chronic systemic steriods other than sex hormone replacement & gonadotropin releasing hormone, and acute antidepressant or anxiolytic therapy were prohibited during the study	**N Randomized:** Total: 554 IG: 278 CG: 276 **N Analyzed:** Total: 535 (calc) IG: 267 CG: 265	**Age (mean):** 52.9 (calc) **Sex (% female):** 61.1 (calc) **Race/Ethnicity:** (calc) *% African American:* 11.5 *% Caucasian:* 85.5 *% Hispanic:* 2.4 *% Other:* 0.6 **SES (income, education):** NR **% Hypertension:** 100 **% Diabetes:** 8 **% Dyslipidemia:** 38 (calc) **Other health problems:** NR
Broom, 2002[132]	**Design:** RCT **Location:** UK **Recruitment Setting:** 12 outpatient clinics in the UK specializing in obesity and/or dyslipidaemia **Self-Selected:** NR	**Inclusion:** BMI ≥30 kg/m^2; aged ≥ 18 yrs; total plasma cholesterol ≥ 6.5 mmol/L or LDL-C ≥ 4.2 mmol/L; women of childbearing age who were using adequate contraception **Exclusion:** myocardial infarction or major surgery within previous 3 mo; active GI or pancreatic disease; type 1 diabetes; uncontrolled hypertension; history of carcinoma, GI surgery for weight loss, post-surgical lesions, bulimia or laxative abuse, drug or alcohol abuse; using drugs altering appetite or lipid concentrations, fish oil supplements, retinoids, systemic steroids (other than sex hormone replacements), or anticoagulants	**N Randomized:** Total: 142 IG: 71 CG: 71 **N Analyzed:** Total: 137 (calc) IG: 66 CG: 71	**Age (mean):** 51.5 (calc) **Sex (% female):** 60.6 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 24.8 (calc) **% Dyslipidemia:** 100 **Other health problems:** NR

Appendix C Table 4a. Evidence Table of Medication Harms Trials: Study Characteristics

Study Reference	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Kelley, 2002[127]	**Design:** RCT **Location:** 43 centers, US **Recruitment Setting:** NR **Self-Selected:** NR	**Inclusion:** Age 40-65 yrs; BMI 28-43 kg/m^2; type 2 diabetes; stable weight (<3 kg weight change) for previous 3 mo; treatment with stable daily dose (±10%) of insulin in previous 6 wks; HbA_{1c} of 7.5-12.0% at screening; women required to have negative serum pregnancy test & use an acceptable form of contraception during study period **Exclusion:** Diabetes treatment that included thiazolidinedione or if diabetic meds (except insulin) had changed during previous 12 wks; medical history or presence of renal, hepatic, or endocrine disorder that could affect results of study; previous bariatric surgery; use of approved or experimental weight reduction meds or treatments; presence of malabsorption syndrome, bulimia or laxative abuse, or disorders that could affect study compliance	**N Randomized:** Total: 550 IG: 274 CG: 276 **N Analyzed (ITT):** Total: 535 (calc) IG: 266 CG: 269	**Age (mean):** 57.9 (calc) **Sex (% female):** 56.3 (calc) **Race/Ethnicity:** (calc) *% Caucasian:* 72.0 *% African American:* 16.4 *% Asian:* 1.3 *% Other:* 10.3 **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 100 **% Dyslipidemia:** NR **Other health problems:** NR
Muls, 2001[130]	**Design:** RCT **Location:** 19 centers, Belgium **Recruitment Setting:** NR **Self-Selected:** NR	**Inclusion:** BMI 27-40 kg/m^2; age 18-70 yrs; fasting serum LDL 4.1-6.7 mmol/l and TG <4.5 mmol/l (<400 mg/dl); >75% compliance with therapy and <1 kg weight gain during run in were eligible for randomization **Exclusion:** Patients with serious diseases, diabetes or uncontrolled hypertension; women of childbearing age without adequate contraception; previous bariatric surgery; use of appetite suppressants or lipid lowering meds; evidence of alcohol or substance abuse	**N Randomized:** Total: 294 IG: 147 CG: 147 **N Analyzed:** Total: 290 IG: 147 CG: 143	**Age (mean):** 48.6 (calc) **Sex (% female):** 80.7 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** 100 **Other health problems:** NR *Data for ITT population at BL (n=290)*
Van Gaal, 1998[129]	**Design:** RCT **Location:** 14 centers, Austria, Belgium, Brazil, Finland, Germany, Italy, Sweden, Switzerland, and UK **Recruitment Setting:** NR **Self-Selected:** NR	**Inclusion:** Age ≥18 yrs; BMI 28-43 kg/m^2; to be randomized had to have ≥70% compliance with test medication (placebo) **Exclusion:** weight loss >4 kg in past 3 mo; history/presence of significant medical disorder (diabetes, CVD, uncontrolled hypertension); pancreatic disease; previous GI surgery for weight loss; history of postsurgical adhesions or presence of cancer (except treated basal cell carcinoma); psychiatric or neurological disorder requiring chronic meds or liable to prejudice compliance; alcohol or substance abuse; bulimia or laxative abuse; pregnancy or lactation; postmenopausal women who had amenorrhia for <1 yr; taking meds likely to influence body weight or plasma lipids during past mo; use of anticoagulants, digoxin, antiarrhythmics and lipid-soluble vitamin supplements; gallstones or symptomatic cholelithiasis; lipid-soluable vitamin levels not in clinical reference range or a clinically significant GI disorder	*IG1: 30 mg, IG2: 60mg, IG3: 120 mg, IG4: 240 mg* **N Randomized:** Total: 613 (calc) IG1: 122 IG2: 124 IG3: 122 IG4: 120 CG: 125 **N Analyzed:** (used numbers from table 3) Total: 606 (calc) IG1: 122 IG2: 123 IG3: 120 IG4: 117 CG: 124	**Age (mean):** 42 (calc) **Sex (% female):** 77 (calc) **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems:** NR *Note: Data from ITT before the start of the double-blind treatment (n=605)*

Appendix C Table 4a. Evidence Table of Medication Harms Trials: Study Characteristics

Study Reference	Study Characteristics	Inclusion/Exclusion	CONSORT Numbers Retention	Participant Characteristics
Metformin Trials				
Trolle, 2007[131]	**Design:** RCT **Location:** Denmark **Recruitment Setting:** Patients referred to the outpatient clinic in Holstebro **Self-Selected:** NR	**Inclusion:** Women aged 18-45 years; referred to the outpatient clinic from Sept 2001-Dec 2002 with symptoms indicating Polycystic Ovary Syndrome (PCOS); testosterone value above the upper normal limit and olig- or amnorrhea; taking antihypertensive agents was permitted **Exclusion:** periclimacteric gonadotrophin values; hyperprolactinaemia; diabetes mellitus; impaired thyroid, renal, or hepatic function; hormonal treatment; pregnancy, lactation, or wish for fertility treatment	**N Randomized:** Total: 60 IG: 29 CG: 31 **N Analyzed:** *Per protocol* Total: 38 IG: 19 CG: 19 *ITT Analysis* Total: 56 IG: 27 CG: 29	*ITT* **Age (mean):** 32 **Sex (% female):** 100 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 0 **% Dyslipidemia:** NR **Other health problems:** PCOS
Combination Trials				
Gokcel, 2002[136]	**Design:** RCT **Location:** Adana, Turkey **Recruitment Setting:** Outpatients at the Baskent University Endocrinology and Metabolism Clinic in Turkey **Self-Selected:** NR	**Inclusion:** Females with BMI > 30 kg/m^2 **Exclusion:** existence of endocrine diseases other than type 2 diabetes; uncontrolled hypertension or secondary hypertension; renal or hepatic insufficiency; GI disease; autoimmune disease; isch heart disease; glaucoma; dysrhythmia; lactation/ pregnancy; psychosis & requirement for any drug with central nervous system effects; cathartics, thyroids supplements, or diuretics	**N Randomized:** Total: 150 (calc) IG1: 50 IG2: 50 IG3: 50 **N Analyzed:** NR *IG1: Sibutramine* *IG2: Orlistat* *IG3: Metformin*	**Age (mean):** 42.7 (calc) **Sex (% female):** 100 **Race/Ethnicity:** NR **SES (income, education):** NR **% Hypertension:** NR **% Diabetes:** 10 (calc) **% Dyslipidemia:** NR **Other health problems:** NR

Appendix C Table 4b. Evidence Table of Medication Harms Trials: Intervention Details and Intermediate Outcomes

Study Reference	Medication Dose/Duration	Behavioral Components	Other Intermediate Outcomes (Blood Pressure and Heart Range Changes)
Orlistat Trials			
Acharya, 2006[133] Perrio, 2007[134]	**Intervention setting:** Primary care **Medication:** Orlistat **Dose:** 76.9% were started at 360 mg QD; 22.7% were started on a dose below 360 mg QD; 0.4% were started on a dose of more than 360 mg QD **Duration:** Median duration of treatment was 150 days **Prescriber:** GP **Incentives:** NR	**Diet prescription:** NR **Exercise prescription:** NR **Behavioral intervention description:** NR **Number of visits:** NR	NR
Bakris, 2002[126]	**Intervention setting:** NR **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Nutritionally balanced hypocaloric diet (estimated energy requirements minus 600 kcal/day) with no more than 30% calories from fat; met with a dietician periodically to review dietary instructions and food records **Exercise prescription:** Encouraged to participate in moderate physical activity as deemed appropriate by their physician **Behavioral intervention description:** NR **Number of visits:** After screening visit, patients came for BL visit and 11 follow up visits spread over the 52 week duration of the study (13 visits*) *calc	Mean (SD), Mean change from BL (SD) **BL** **52 wks** *Diastolic Blood Pressure, mmHg* **IG** 98.4 (3.7) -11.4 (8.3) **CG** 98.3 (3.5) -9.2 (8.4) p 0.002 *Systolic Blood Pressure, mmHg* **IG** 154.2 (13.4) -13.3 (15.2) **CG** 150.8 (12.7) -11.0 (15.0) p NS
Broom, 2002[132]	**Intervention setting:** "the clinic" unclear if intervention in outpatient clinics or just recruited from there **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 24 weeks double blind phase, 28 week open-label phase **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Hypocaloric diet containing 30% of calories as fat & a max of 300 mg/day cholesterol. Total energy expenditure was calculated and 600 kcal/day ws subtracted. Achieved by a mild reduction in food intake from each of the 5 major food groups, with dietary advice provided by a dietician **Exercise prescription:** Patients received advice on physical activity **Behavioral intervention description:** NR **Number of visits:** Screening visit, followed by BL assessment, and every four weeks up to week 24. During open-label phase clinic visits were at weeks 30, 36, 44, and 52 (12 visits total*) *calc	Mean (SD) **BL** **24 wks** *Diastolic Blood Pressure, mmHg* **IG** 82.6* (8.3) 80.6 (NR) **CG** 84.0 (9.1) 83.2 (NR) *Systolic Blood Pressure, mmHg* **IG** 136.9 (14.8) 135.8 (NR) **CG** 140.0 (16.4) 138.3 (NR) *Reported as 86.2 in text. 82.6 likely most accurate.

Appendix C Table 4b. Evidence Table of Medication Harms Trials: Intervention Details and Intermediate Outcomes

Study Reference	Medication Dose/Duration	Behavioral Components	Other Intermediate Outcomes (Blood Pressure and Heart Range Changes)
Kelley, 2002[127]	**Intervention setting:** 43 centers in US **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 52 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Nutritionally balanced, energy deficient diet designed to induce wt loss of 0.25-0.5 kg per week. Contained ~30% of calories as fat, 50% as carbs, and 20% as protein, with a max of 300 mg/day of cholesterol. At BL patients received diet instructions from a registered dietician. Additional dietary instruction was provided at predetermined intervals during the study period. Dietary compliance monitored by use of dietary intake records. At wk 24 the prescribed dietary intake was further reduced by 200 kcal/day (min of 1200 kcal/day). Patients were instructed to take a multivitamin at least 2 h before or after evening dose of study drug **Exercise prescription:** Patients were encouraged to participate in moderate physical activity **Behavioral intervention description:** Lifestyle and behavioral modification literature were available to all patients throughout the study; dietary intake records were used to evaluate compliance **Number of visits:** Subjects were seen every 2-4 weeks for study assessment	Mean (SE) **BL** **52 wks** **Change** *Diastolic Blood Pressure, mmHg* **IG** 79.5 (0.5) 77.2 (0.6) -2.3 (0.7) **CG** 80.9 (0.6) 78.0 (0.5) -1.0 (0.5) **p** 0.075 *Systolic Blood Pressure, mmHg* **IG** 135.1 (0.9) 134.0 (1.0) -1.2 (1.0) **CG** 134.9(0.9) 134.0 (1.0) -0.9 (1.0) **p** 0.948 **IG n analyzed:** 266 **CG n analyzed:** 276
Muls, 2001[130]	**Intervention setting:** 19 centers in Belgium **Medication:** Orlistat **Dose:** 120 mg TID **Duration:** 24 weeks double blind phase, 24 week open-label extension **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Patients instructed on a nutritionally balanced low-energy diet containing 30% of energy as fat at start of run-in. Energy content calc from estimated total daily energy expenditure minus 600 kcal/day. Lowest energy intake allowed was 1200 kcal/day. Encouraged to take 3 main meals per day. Dietician assessed dietary compliance weeks 4, 12, and 24. Diet maintained through open-label extension **Exercise prescription:** NR **Behavioral intervention description:** NR **Number of visits:** At the start and end of run-in phase, monthly during double blind phase (6 mo), and at weeks 28, 36, and 48 during open-label extension (11 visits*) *calc	Mean (SD) **BL** **48 wks** *Diastolic Blood Pressure, mmHg* **IG** 83.1 (7.4) -- **CG** 82.2 (8.3) -- *Systolic Blood Pressure, mmHg* **IG** 133.6 (13.3) **--** **CG** 130.6 (12.1) **--**

Appendix C Table 4b. Evidence Table of Medication Harms Trials: Intervention Details and Intermediate Outcomes

Study Reference	Medication Dose/Duration	Behavioral Components	Other Intermediate Outcomes (Blood Pressure and Heart Range Changes)
Van Gaal, 1998[129]	**Intervention setting:** 14 European centers **Medication:** orlistat **Dose:** 30, 60, 120 or 240 mg TID **Duration:** 24 weeks **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Nutritionally balanced, mildly hypocaloric diet designed to result in estimated wt loss of 0.25-0.5 kg/week during run in period. Contained approx 30% calories from fat, 50% as carbohydrates, 20% as protein, and max of 300 mg/day of cholesterol. Number of calories equaled the estimated daily energy expenditure minus 600 kcal per day, with a min of 1200 kcal per day. Diet was adjusted if patient experienced a fall of BMI to 22 kg/m^2 or below on 2 consecutive visits. Received dietary advice from a qualified dietician **Exercise prescription:** NR **Behavioral intervention description:** Required to keep diet diary for 4 days during wks 1 & 2 of lead in period, and during wks 3,5,7,9,13,17, and 21 during treatment period **Number of visits:** Measurements (wt, vital signs, AE's) assessed twice during screening, at day 14 of lead in, and at every clinic visit during treatment period (BL, day 15 & 29, and then every 4 wks) (10 visits*) *calc	No clinically relevant abnormalities related to treatment were observed during treatment period in laboratory values; no changes in relation to hepatocellular damage, vital signs or ECGs; no evidence to support increased cholelithiasis
Metformin Trials			
Trolle, 2007[131]	**Intervention setting:** Dept of Gynaecology & Obstetrics, Hostebro Hospital **Medication:** metformin **Dose:** 850 mg BID **Duration:** 6 months (6 mo on med or placebo, followed by 3 mo washout before being switched to alternate treatment for another 6 mo) **Prescriber:** NR **Incentives:** NR	**Diet prescription:** NR **Exercise prescription:** NR **Behavioral intervention description:** NR **Number of visits:** Participants seen prior to inclusion and every 2nd month during treatment periods (6 visits during 12 mo*) *calc	Change from BL, median (5-95% percentile) *ITT Analysis* **6 mo** *Systolic Blood Pressure, mmHg* p value **IG** -5.4 (-10.8, -0.1) 0.047 **CG** 1 (-3, 5) 0.529 Mean differences between changes: -5.0(-11.2, 1.3), p=0.116

Appendix C Table 4b. Evidence Table of Medication Harms Trials: Intervention Details and Intermediate Outcomes

Study Reference	Medication Dose/Duration	Behavioral Components	Other Intermediate Outcomes (Blood Pressure and Heart Range Changes)
Combination Trials			
Gokcel, 2002[136]	**Intervention setting:** Outpatient clinic **Medication:** Metformin, Orlistat **Dose:** Orlistat: 120 mg TID Metformin: 850 mg BID **Duration:** 6 months **Prescriber:** NR **Incentives:** NR	**Diet prescription:** Recommended to follow weight reducing daily diet of 25 kcal/kg of ideal body weight; 50% calories from carbs, 30% from lipids and 20% from proteins; given a list of foods that were permitted and not permitted, as well as guidelines on recommended portions and possible combinations **Exercise prescription:** NR **Behavioral intervention description:** NR **Number of visits:** Before the start of medication and then monthly up to 6 months of treatment (7 visits*) *calc	*IG2: orlistat IG3: metformin* Mean (SEM) **BL 6 mo p value** *Diastolic Blood Pressure, mmHg* **IG2** 79.77 (1.18) 75.98 (0.84) p < 0.008 **IG3** 83.41 (1.30) 77.61 (0.74) p < 0.0001 *Systolic Blood Pressure, mmHg* **IG2** 127.21 (1.80) 121.74(1.54) p < 0.0001 **IG3** 129.55 (1.98) 123.64 (1.45) p < 0.0001 *Heart rate, beats/minute* **IG2** 80.25 (1.25) 78.77 (0.93) p < 0.03 **IG3** 81.63 (1.37) 79.95 (1.10) p < 0.006 % change from BL *Diastolic Blood Pressure, mmHg* **IG2** 4.75 **IG3** 6.95 *Systolic Blood Pressure, mmHg* **IG2** 4.30 **IG3** 4.56 *Heart rate, beats/minute* **IG2** 2.12 **IG3** 1.84

Appendix C Table 4c. Evidence Table of Medication Harms Trials: Adverse Effects

Study Reference	Adverse Effects	Adverse Effects
Orlistat Trials		
Acharya, 2006[133] Perrio, 2007[134]	*Total adverse events* **IG** -- **CG** -- 368 events in 315 (2.0% of cohort) patients were reported as AEs *Serious adverse events* **IG** -- **CG** -- *Stopped treatment during the first 3 mo of treatment*: 4854 (30.3%) Adverse events most frequently reported as reason for stopping treatment at any time during the study, No (% of 8093*): *Diarrhea* 525 (6.5) *Weight gain* 239 (2.9) *Intolerance* 120 (1.5) *Unspecified side effects* 110 (1.4) *Pain abdomen* 91 (1.1) *Flatulence* 79 (1.0) *Malaise, Lassitude* 70 (0.9) *GI unspecified* 63 (0.8) *Fecal incontinence* 62 (0.8) Reported by GP; could give more than one reason per patient *No. of patients who stopped treatment at any time and for whom the reason(s) for stopping was given	Events most frequently reported as adverse drug effects, No. of events (% of cohort) *Unspecified side effects* 110 (0.7) *Diarrhoea* 75 (0.5) *GI unspecified* 32 (0.2) *Flatulence* 23 (0.1) *Faecal incontinence* 15 (0.09) *Rectal Discharge* 12 (0.07) *Malaise/lassitude* 9 (0.06) *Distension abdominal* 8 (0.05) *Pain abdominal* 8 (0.05) *Nausea, vomiting* 8 (0.05) Selected events assessed as probably related to orlistat treatment (No.) *Skin* Erythema 1 Erthyema nodosum 1 Lichen planus 1 Pruritus 1 Rash 5 Urticaria 2 *Musculoskeletal* Muscle weakness 1 Osteoarthritis 1 Pain joint 1 *Psychiatric* Dreams abnormal 1 Hallucination 1 *Nervous system* Amnesia 1 Demyelination 1 Dizziness 3 Tremor 1 *Eye* Haemorrhage vitreous 1 Hemianopia 1 Retinal vein thrombosis 1 *Ear* Labyrinthitis 1 *Cardiovascular* Deep vein thrombosis 1 Fibrillation atria 1 Hypertension 3 Oedema 1 Swollen ankles 3 Palpitation 1 *Alimentary* Liver funct tests abnormal 2 Pain abdomen 2

Appendix C Table 4c. Evidence Table of Medication Harms Trials: Adverse Effects

Study Reference	Adverse Effects	Adverse Effects
(continued) Acharya, 2006[133] Perrio, 2007[134]		*Metabolic & Endocrine* Hypothyroidism 2 *Female reproductive* Metrorrhagia 1 *Haemopoietic* Haematoma spontaneous 1 *Incidence Densities, incidence/1000 patient months exposure* Diarrhoea 9.29 Abdominal pain 2.51 Intolerance 1.47 Flatulence 1.44 Headache 1.97 Nausea,vomiting 1.57 Rectal discharge 0.91 Depression 2.76 Flatulence 1.44 Headache 1.97 Nausea,vomiting 1.57 Rectal discharge 0.91 Depression 2.76 *Deaths, n(%)* 33 (0.2)* *no instances where GP attributed cause of death to the drug Pregnancy data is available (3 babies born with congenital anomalies), but no associations between exposure and risks are reported by authors
Bakris, 2002[126]	**52 weeks** *Total adverse events* **IG** -- **CG** -- *Participants reporting adverse events (%)* **IG** 89* **CG** 71 *p <0.001 *Possibly associated with study drug* **IG** 0 **CG** 0 *Serious adverse events** **IG** 14 **CG** 15 (calc) *IG: myocardial infarction, chest pain, atrial fibrillation, CG: accelerated hypertension, MI, worsening of atherosclerotic coronary artery disease, chest pain, and ductal carcinoma *in situ.* None were attributed to study medication *Withdrew due to adverse events* **IG** 18* (1 due to serious AE) **CG** 20 (4 due to serious AE) *GI associated: IG: 15; CG: 6	**52 weeks** Most commonly reported: fatty/oily stool, soft stool, liquid stool, oily fecal spotting, flatus with discharge, and fecal urgency (data not reported) *Deaths* **IG** 0 **CG** 0 *Gastrointestinal events (%)** **IG** 72.5 **CG** 43.6 p< 0.001 *occurred early during therapy, frequency tended to decreased with continued treatment *Cardiovascular events* IG -- CG -- *Other body systems (%)* Infectious IG 46.1 CG 37.7 Likely NS as NR Musculoskeletal IG 22.8 CG 15.5 p < 0.05 All other systems IG 61.4 CG 50.6 p < 0.05

Appendix C Table 4c. Evidence Table of Medication Harms Trials: Adverse Effects

Study Reference	Adverse Effects	Adverse Effects
Broom, 2002[132]	**24 weeks** *Total adverse events* **IG** -- **CG** -- *Reported ≥ 1 adverse event, %* **IG** 95.5* **CG** 85.9 *with exception of GI events, not considered to be drug related, most mild or self-limiting *Serious adverse events** **IG** 4 (n=4) **CG** 10 (n=6) *IG: elective cytoscopy and hydrodistension, stroke, sleep disorder, benign fluid-filled breast cyst. CG: radiculitis in right elbow, cellulitis, limb pain, hiatus hernia, gastric ulcer, esophageal reflux, anaemia, pregnancy and cholecystectomy *Serious adverse events reported during open label phase* **IG** 6 **Former CG** 1 *IG: neuropathic toe ulcer, cellulitis, Bell's palsy, dermal bleeding & upper limb injury caused by traffic accident, suicide attempt. CG: abdominal pain *Withdrew due to adverse events* **IG** 11 **CG** 5 7 and 3 respectively for GI events *GI events reported by 54.8% of patients who remained on drug & 75.9% of those who switched to drug during open label phase*	**24 weeks** *Gastrointestinal events, %* IG 86.6 CG 42.3 *Most transient and mild to moderate* Most commonly reported (≥ 5%) (%) IG CG *Liquid stools* 32.8 9.9 *Increased defecation* 23.9 11.3 *Fatty/oily stool* 22.4 4.2 *Soft stool* 22.4 9.9 *Fecal urgency* 16.4 0.0 *Abdominal pain* 13.4 5.6 *Flatulence* 7.5 8.5 *Oily spotting* 6.0 0.0 *Flatus with discharge* 6.0 2.8 *open label phase data available
Kelley, 2002[127]	**52 weeks** *Total adverse events* **IG** -- **CG** -- *Serious adverse events* **IG** -- **CG** -- *Withdrew due to adverse events, n(%)* **IG** 35 (13) **CG** 22 (8) **IG n analyzed:** 274 **CG n analyzed:** 276	**52 weeks** *Deaths* **IG** -- **CG** -- *Vitamin levels* **IG** -- **CG --** *Vitamin supplementation* **IG** -- **CG --** *Gastrointestinal events, (%)* **IG** 80* **CG** 62 *p <0.05 (Most with single episode and mild to moderate intensity) *Cardiovascular events* **IG** -- **CG** -- *Hypoglycemia, (%)* IG 16.9* CG 9.7 p <0.05 4 patients (1 in CG, 3 in IG) required medical intervention for hypoglycemia *Incidence of AEs related to other organ systems was similar in both groups*

Appendix C Table 4c. Evidence Table of Medication Harms Trials: Adverse Effects

Study Reference	Adverse Effects	Adverse Effects
Muls, 2001[130]	**48 weeks** *Total adverse events* **IG** -- **CG** -- *Serious adverse events* **IG** -- **CG** -- *% of group reporting adverse events* **IG** 80 **CG** 67* *p=0.016 Incidence of GI events, *(%)* **IG** 64 **CG** 38 *Withdrew due to adverse events* **IG** 12 **CG** 4	**48 weeks** Most frequently reported adverse events, (%) *Liquid stool* IG 23 CG 8 *Increased defecation* IG 22 CG 5 *Loose stools* IG 16 CG 3 *Decreased defecation* IG 3 CG 12 *Bronchitis* IG 11 CG 6 During open-label extension, AEs were more frequently reported in former CG (81%) than former IG (59%)

Appendix C Table 4c. Evidence Table of Medication Harms Trials: Adverse Effects

Study Reference	Adverse Effects	Adverse Effects
Van Gaal, 1998[129]	*IG1: 30 mg, IG2: 60mg, IG3: 120 mg, IG4: 240 mg* **6 mo** *Total adverse events* **IG1** -- **IG2** -- **IG3** -- **IG4** -- **CG** -- *% of patients with adverse events** **IG1** 79 **IG2** 83 **IG3** 84 **IG4** 87 **CG** 69 *similar in all treatment groups in all body systems, except for gastrointestinal system *Serious adverse events* **IG** 12* **CG** 2 *4 were considered remotely, possibly or probably related to med (fecal incontinence, diverticulitis, and abdominal pain) *Withdrew due to adverse events, n(%)** **IG1** 7 (6) **IG2** 6 (5) **IG3** 2 (2) **IG4** 3 (3) **CG** 3 (2) *11 due to gastrointestinal events (10 in IGs). Main AE withdrawals considered to be related to treatment: CG: abnormal GTT, Urticaria IGs: fecal incontinence, flatulence, liquid stools, abdominal pain, polymyalgia rheumatica, depression, gastritis	*Deaths* **IG1** -- **IG2** -- **IG3** -- **IG4** -- **CG** -- **BL 24 weeks** *Vitamin A, mean (µmol ·1-1)* **IG1** 2.46 2.42 **IG2** 2.50 2.50 **IG3** 2.40 2.50 **IG4** 2.46 2.57 **CG** 2.46 2.49 *Vitamin D, mean (µmol ·1-1)* **IG1** 60.07 56.65 **IG2** 71.19 60.24 **IG3** 61.26 56.10 **IG4** 65.26 54.24* **CG** 68.28 67.01 *Vitamin E, mean (µmol ·1-1)* **IG1** 26.84 27.36* **IG2** 27.42 26.51* **IG3** 26.36 26.66* **IG4** 27.34 25.74* **CG** 27.47 29.70 *Beta-carotene, mean (µmol ·1-1)* **IG1** 0.41 0.32* **IG2** 0.40 0.30* **IG3** 0.43 0.30* **IG4** 0.47 0.28* **CG** 0.42 0.45 *Patients with 2 or more low vitamin levels(%)* **IG1** 4.2 **IG2** 6.7 **IG3** 4.2 **IG4** 12.8 **CG** 3.3 *Received vitamin supplementation, n* **IG1** 2 **IG2** 0 **IG3** 4 **IG4** 8 **CG** 2 **24 weeks** *Patients with at least 1 GI event (%) (mild to moderate, usually when first starting)* **IG1** 60.7 **IG2** 75.6 **IG3** 70.8 **IG4** 82.9 **CG** 46.4

Appendix C Table 4c. Evidence Table of Medication Harms Trials: Adverse Effects

Study Reference	Adverse Effects	Adverse Effects
(continued) Van Gaal, 1998[129]		*Severe Gastrointestinal events, n** **IG1** 9 **IG2** 8 **IG3** 2 **IG4** 10 **CG** 1 **subjectively classified* **p ≤ 0.001 compared to placebo* GI event incidence of 5% or at least twice that of CG *Fatty/oily stool* **IG1** 20.5 **IG2** 31.7 **IG3** 37.5 **IG4** 36.8 **CG** 2.4 *Increased defecation* **IG1** 18.9 **IG2** 18.7 **IG3** 19.2 **IG4** 17.9 **CG** 5.6 *Soft stools* **IG1** 11.5 **IG2** 18.7 **IG3** 13.3 **IG4** 20.5 **CG** 8.1 *Oily spotting* **IG1** 8.2 **IG2** 14.6 **IG3** 12.5 **IG4** 22.2 **CG** 0.0 *Oily evacuation* **IG1** 6.6 **IG2** 5.7 **IG3** 8.3 **IG4** 11.1 **CG** 0.0 *Flatus with discharge* **IG1** 2.5 **IG2** 6.5 **IG3** 7.5 **IG4** 6.0 **CG** 0.0 *Fecal incontinence* **IG1** 1.6 **IG2** 3.3 **IG3** 5.0 **IG4** 7.7 **CG** 0.0

Appendix C Table 4c. Evidence Table of Medication Harms Trials: Adverse Effects

Study Reference	Adverse Effects	Adverse Effects
Metformin Trials		
Trolle, 2007[131]	**6 mo** *Total adverse events* **IG** -- **CG** -- *Participants reporting adverse event, n* **IG** 29* **CG** 2 *mostly gastrointestinal	*Serious adverse events* **IG** 0 **CG** 0 *Withdrew due to adverse events* **IG** 2 **CG** 0
Combination Trials		
Gokcel, 2002[136]	**6 mo** *Withdrew due to adverse events* **IG2** 2 **IG3** 0	**6 mo (n)** *Abdominal Discomfort* **IG2** 22 **IG3** 14

Abbreviations: ACE=angiotensin-converting enzyme; ADA=American Diabetes Association; adj=adjusted; AE=adverse event; BDI=Beck Depression Inventory; BL=baseline; BMI=body mass index; BP=blood pressure; bpm=beats per minute; bts=beats; C=cholesterol; CAD=coronary artery disease; calc=calculated; CG=control group; CGIQ=Caregiver Intelligence Quotient; CHF=congestive heart failure; CIC=Clinical Investigation Center; d=day; DBP=diastolic blood pressure; diff=differ/difference; ECG=electrocardiography; est=estimated; FPG=fasting plasma glucose; FSG=fasting serum glucose; GI=gastrointestinal; GP=general practitioner; HDL=high-density lipoprotein; HR=heart rate; HTN=hypertension; ID=incidence density; IG=intervention group; ITT=intention to treat; LCD=low-calorie diet; LDL=low-density lipoprotein; LOCF=last observation carried forward; LV=left ventricle; LVEF=left ventricle ejection fraction; LVH=left ventricle hypertrophy; LVM=left ventricle mass; LVMI=left ventricle mass/height; maint=maintenance; med=medication; n=number; NA=not applicable; NHS=National Health Service; NR=not reported; NS=not significant; obs=observed; PCOS=polycystic ovary syndrome; PCP=primary care physician; pt=patient; QTc=QT interval; RCT=randomized controlled trial; RMR=resting metabolic rate; Rx=prescription; SBP=systolic blood pressure; SD=standard deviation; SE=standard error; SEM=standard error of the mean; SES=socioeconomic status; TG=triglycerides; UK=United Kingdom; US=United States; WHO=World Health Organization; wt=weight; x=times.

Appendix D Table 1. Studies Excluded From Review for Key Question 1

Reference	Reason for Exclusion
Ashley JM, St Jeor ST, Schrage JP, Perumean-Chaney SE, Gilbertson MC, McCall NL, et al. Weight control in the physician's office. *Arch Intern Med.* 2001;161(13):1599-604.	Does not meet design requirements in inclusion criteria
Bemelmans WJ, Broer J, de Vries JH, Hulshof KF, May JF, Meyboom-De Jong B. Impact of Mediterranean diet education versus posted leaflet on dietary habits and serum cholesterol in a high risk population for cardiovascular disease. *Public Health Nutr.* 2000;3(3):273-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
de Wit LT, Mathus-Vliegen L, Hey C, Rademaker B, Gouma DJ, Obertop H. Open versus laparoscopic adjustable silicone gastric banding: a prospective randomized trial for treatment of morbid obesity. *Ann Surg.* 1999;230(6):800-5.	Not one of the specified interventions
Donnelly JE, Kirk EP, Jacobsen DJ, Hill JO, Sullivan DK, Johnson SL. Effects of 16 mo of verified, supervised aerobic exercise on macronutrient intake in overweight men and women: the Midwest Exercise Trial. *Am J Clin Nutr.* 2003;78(5):950-6.	High or differential attrition
Dujovne CA, Zavoral JH, Rowe E, Mendel CM. Effects of sibutramine on body weight and serum lipids: a double-blind, randomized, placebo-controlled study in 322 overweight and obese patients with dyslipidemia. *Am Heart J.* 2001;142(3):489-97.	Less than 12 months followup
Muir J, Mant D, Jones L, Yudkin P. Effectiveness of health checks conducted by nurses in primary care: results of the OXCHECK study after one year. *BMJ.* 1994;308(6924):308-12.	Not one of the specified interventions
Eiben G, Lissner L. Health Hunters—an intervention to prevent overweight and obesity in young high-risk women. *Int J Obes.* 2006;30(4):691-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Fogelholm M, Kukkonen-Harjula K, Nenonen A, Pasanen M. Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. *Arch Intern Med.* 2000;160(14):2177-84.	Does not meet design requirements in inclusion criteria
Giugliano D, Quatraro A, Consoli G, Minei A, Ceriello A, De RN, et al. Metformin for obese, insulin-treated diabetic patients: improvement in glycaemic control and reduction of metabolic risk factors. *Eur J Clin Pharmacol* 1993;44(2):107-12.	Less than 12 months followup
Gokcel A, Karakose H, Ertorer EM, Tanaci N, Tutuncu NB, Guvener N. Effects of sibutramine in obese female subjects with type 2 diabetes and poor blood glucose control. *Diabetes Care.* 2001;24(11):1957-60.	Not on list of countries with HDI >0.90
Hiratsuka VY, Loo R, Will JC, Oberrecht R, Poindexter P. Cardiovascular disease risk factor screening among Alaska Native women: the Traditions of the Heart Project. *Int J Circumpolar Health.* 2007;66(Suppl 1):39-44.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Imperial Cancer Research Fund OXCHECK Study Group. Effectiveness of health checks conducted by nurses in primary care: final results of the OXCHECK study. *BMJ.* 1995;310(6987):1099-104.	Not one of the specified interventions
Jakicic JM, Winters C, Lang W, Wing RR. Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *JAMA.* 1999;282(16):1554-60.	Does not meet design requirements in inclusion criteria
Jeffery RW, French SA. Preventing weight gain in adults: design, methods and one year results from the Pound of Prevention study. *Int J Obes Relat Metab Disord.* 1997;21(6):457-64.	Study of overweight/obesity prevention
Leermakers EA, Perri MG, Shigaki CL, Fuller PR. Effects of exercise-focused versus weight-focused maintenance programs on the management of obesity. *Addict Behav.* 1999;24(2):219-27.	Does not meet design requirements in inclusion criteria
Rothacker DQ, Staniszewski BA, Ellis PK. Liquid meal replacement vs traditional food: a potential model for women who cannot maintain eating habit change. *J Am Diet Assoc.* 2001;101(3):345-7.	Does not meet design requirements in inclusion criteria
Sbrocco T, Nedegaard RC, Stone JM, Lewis EL. Behavioral choice treatment promotes continuing weight loss: preliminary results of a cognitive-behavioral decision-based treatment for obesity. *J Consult Clin Psychol.* 1999;67(2):260-6.	Does not meet design requirements in inclusion criteria
Schriefer SP, Landis SE, Turbow DJ, Patch SC. Effect of a computerized body mass index prompt on diagnosis and treatment of adult obesity. *Fam Med.* 2009;41(7):502-7.	No weight outcomes
Van Gaal LF, Broom JI, Enzi G, Toplak H. Efficacy and tolerability of orlistat in the treatment of obesity: a 6-month dose-ranging study. *Eur J Clin Pharmacol.*	Less than 12 months followup

Appendix D Table 1. Studies Excluded From Review for Key Question 1

Reference	Reason for Exclusion
1998;54(2):125-32.	
Wadden TA, Berkowitz RI, Sarwer DB, Prus-Wisniewski R, Steinberg C. Benefits of lifestyle modification in the pharmacologic treatment of obesity: a randomized trial. *Arch Intern Med.* 2001;161(2):218-27.	Does not meet design requirements in inclusion criteria
Weiner R, Bockhorn H, Rosenthal R, Wagner D. A prospective randomized trial of different laparoscopic gastric banding techniques for morbid obesity. *Surg Endosc.* 2001;15(1):63-8.	Not one of the specified interventions
Wing RR, Anglin K. Effectiveness of a behavioral weight control program for blacks and whites with NIDDM. *Diabetes Care.* 1996;19(5):409-13.	Does not meet design requirements in inclusion criteria

Appendix D Table 2. Studies Excluded From Review for Key Question 2

Reference	Reason for Exclusion
Aadahl M, von Huth Smith L, Pisinger C, et al. Five-year change in physical activity is associated with changes in cardiovascular disease risk factors. *Prev Med.* 2009;48(4):326-31.	Does not meet design requirements in inclusion criteria
Acharya NV, Wilton LV, Shakir SA. Safety profile of orlistat: results of a prescription-event monitoring study. *Int J Obes.* 2006;30:1645-52.	Does not meet design requirements in inclusion criteria
Agurs-Collins TD, Kumanyika SK, Ten Have TR, Adams-Campbell LL. A randomized controlled trial of weight reduction and exercise for diabetes management in older African-American subjects. *Diabetes Care.* 1997;20:1503-11.	Less than 12 months followup
Akinson RL. Conjugated linoleic acid for altering body composition and treating obesity. In: Yurawecz MP, Mossoba MM, Kramer JK, et al, eds. *Advances in Conjugated Linoleic Acid Research.* Vol 1. Champaign, IL: AOCS Press; 1999:348-53.	Does not meet design requirements in inclusion criteria
Alhassan S, Kim S, Bersamin A, et al. Dietary adherence and weight loss success among overweight women: results from the A TO Z weight loss study. *Int J Obes.* 2008;32:985-91.	Comparative effectiveness
Allen P, Thompson JL, Herman CJ, et al. Impact of periodic follow-up testing among urban American Indian women with impaired fasting glucose. *Prev Chronic Dis.* 2008;5(3):A76.	Not one of the specified interventions
Andersen RE, Wadden TA, Bartlett SJ, et al. Effects of lifestyle activity vs structured aerobic exercise in obese women: a randomized trial. *JAMA.* 1999;281:335-40.	Comparative effectiveness
Anderson JW, Grant L, Gotthelf L, Stifler LT. Weight loss and long-term follow-up of severely obese individuals treated with an intense behavioral program. *Int J Obes.* 2007;31:488-93.	Does not meet design requirements in inclusion criteria
Anderssen SA, Carroll S, Urdal P, Holme I. Combined diet and exercise intervention reverses the metabolic syndrome in middle-aged males: results from the Oslo Diet and Exercise Study. *Scand J Med Sci Sports.* 2007;17:687-95.	No weight or harms outcomes
Anderssen SA, Holme I, Urdal P, Hjermann I. Associations between central obesity and indexes of hemostatic, carbohydrate and lipid metabolism: results of a 1-year intervention from the Oslo Diet and Exercise Study. *Scand J Med Sci Sports.* 1998;8:109-15.	Does not include specified weight outcomes
Andersson K, Karlstrom B, Freden S, et al. A two-year clinical lifestyle intervention program for weight loss in obesity. *Food Nutr Res.* 2008;52.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Andrade AM, Coutinho SR, Silva MN, et al. The effect of physical activity on weight loss is mediated by eating self-regulation. *Patient Educ Couns*. 2010;79(3):320-6.	No weight or harms outcomes
Annunziato RA, Timko CA, Crerand CE, et al. A randomized trial examining differential meal replacement adherence in a weight loss maintenance program after one-year follow-up. *Eat Behav.* 2009;10:176-83.	Comparative effectiveness
Apfelbaum M, Vague P, Ziegler O, et al. Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. *Am J Med.* 1999;106:179-84.	Sibutramine intervention
Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA.* 2003;289:2083-93.	Not one of the specified interventions
Appel LJ, Espeland MA, Easter L, et al. Effects of reduced sodium intake on hypertension control in older individuals: results from the Trial of Nonpharmacologic Interventions in the Elderly (TONE). *Arch Intern Med.* 2001;161:685-93.	No weight or harms outcomes
Arterburn D, DeLaet D, Schauer D. Obesity in adults. *Clin Evid (Online).* 2008.	Does not meet design requirements in inclusion criteria
Ash S, Reeves M, Bauer J, et al. A randomised control trial comparing lifestyle groups, individual counselling and written information in the management of weight and health outcomes over 12 months. *Int J Obes.* 2006;30:1557-64.	Comparative effectiveness
Ashley JM, St Jeor ST, Schrage JP, et al. Weight control in the physician's office. *Arch Intern Med.* 2001;161:1599-604.	Comparative effectiveness
Ashutosh K, Methrotra K, Fragale-Jackson J. Effects of sustained weight loss and exercise on aerobic fitness in obese women. *J Sports Med Phys Fitness.* 1997;37:252-7.	Comparative effectiveness

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Reference	Reason for Exclusion
Avenell A, Brown TJ, McGee MA, et al. What are the long-term benefits of weight reducing diets in adults? A systematic review of randomized controlled trials. *J Hum Nutr Diet.* 2004;17:317-35.	Does not meet design requirements in inclusion criteria
Babamoto KS, Sey KA, Camilleri AJ, et al. Improving diabetes care and health measures among Hispanics using community health workers: results from a randomized controlled trial. *Health Educ Behav.* 2009;36:113-26.	Less than 12 months followup
Bach DS, Rissanen AM, Mendel CM, et al. Absence of cardiac valve dysfunction in obese patients treated with sibutramine. *Obes Res.* 1999;7:363-9.	Sibutramine intervention
Bacon L, Keim NL, Van Loan MD, et al. Evaluating a "non-diet" wellness intervention for improvement of metabolic fitness, psychological well-being and eating and activity behaviors. *Int J Obes Relat Metab Disord.* 2002;26:854-65.	Comparative effectiveness
Bakris G, Calhoun D, Egan B, et al. Orlistat improves blood pressure control in obese subjects with treated but inadequately controlled hypertension. *J Hypertens.* 2002;20:2257-67.	High or differential attrition
Balducci S, Zanuso S, Nicolucci A, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutr Metab Cardiovasc Dis.* 2010;20:608-17.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Barr SI, McCarron DA, Heaney RP, et al. Effects of increased consumption of fluid milk on energy and nutrient intake, body weight, and cardiovascular risk factors in healthy older adults. *J Am Diet Assoc.* 2000;100:810-7.	Not one of the specified interventions
Bauer C, Fischer A, Keller U. Effect of sibutramine and of cognitive-behavioural weight loss therapy in obesity and subclinical binge eating disorder. *Diabetes Obes Metab.* 2006;8:289-95.	Less than 12 months followup
Beck-da-Silva L, Higginson L, Fraser M, et al. Effect of orlistat in obese patients with heart failure: a pilot study. *Congest Heart Fail.* 2005;11:118-23.	Less than 12 months followup
Bemelmans WJ, Broer J, de Vries JH, et al. Impact of Mediterranean diet education versus posted leaflet on dietary habits and serum cholesterol in a high risk population for cardiovascular disease. *Public Health Nutr.* 2000;3:273-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Bergstrom I, Lombardo C, Brinck J. Physical training decreases waist circumference in postmenopausal borderline overweight women. *Acta Obstet Gynecol Scand.* 2009;88:308-13.	Focus on patients in subgroups other than specified conditions
Bhargava A, Guthrie JF. Unhealthy eating habits, physical exercise and macronutrient intakes are predictors of anthropometric indicators in the Women's Health Trial Feasibility Study In Minority Populations. *Br J Nutr.* 2002;88:719-28.	Not one of the specified interventions
Blumenthal JA, Sherwood A, Gullette EC, et al. Exercise and weight loss reduce blood pressure in men and women with mild hypertension: effects on cardiovascular, metabolic, and hemodynamic functioning. *Arch Intern Med.* 2000;160:1947-58.	Less than 12 months followup
Bo S, Ciccone G, Baldi C, et al. Effectiveness of a lifestyle intervention on metabolic syndrome: a randomized controlled trial. *J Gen Intern Med.* 2007;22:1695-703.	Not one of the specified interventions
Bo S, Ciccone G, Guidi S, et al. Diet or exercise: what is more effective in preventing or reducing metabolic alterations? *Eur J Endocrinol.* 2008;159:685-91.	Not one of the specified interventions
Borg P, Kukkonen-Harjula K, Fogelholm M, Pasanen M. Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: a randomized trial. *Int J Obes Relat Metab Disord.* 2002;26:676-83.	Comparative effectiveness
Botomino A, Bruppacher R, Krahenbuhl S, Hersberger KE. Change of body weight and lifestyle of persons at risk for diabetes after screening and counselling in pharmacies. *Pharm World Sci.* 2008;30:222-6.	Does not meet design requirements in inclusion criteria
Bowen D, Clifford CK, Coates R, et al. The Women's Health Trial Feasibility Study in Minority Populations: design and baseline descriptions. *Ann Epidemiol.* 1996;6:507-19.	Not one of the specified interventions
Bowen J, Noakes M, Clifton PM. A high dairy protein, high-calcium diet minimizes bone turnover in overweight adults during weight loss. *J Nutr.* 2004;134:568-73.	Less than 12 months followup
Bowerman S, Bellman M, Saltsman P, et al. Implementation of a primary care physician network obesity management program. *Obes Res.* 2001;9(Suppl 4):S321-5.	Less than 12 months followup

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Reference	Reason for Exclusion
Bravata DM, Smith-Spangler C, Sundaram V, et al. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA.* 2007;298:2296-304.	Does not meet design requirements in inclusion criteria
Brinkworth GD, Noakes M, Keogh JB, et al. Long-term effects of a high-protein, low-carbohydrate diet on weight control and cardiovascular risk markers in obese hyperinsulinemic subjects. *Int J Obes Relat Metab Disord.* 2004;28:661-70.	Comparative effectiveness
Brinkworth GD, Noakes M, Parker B, et al. Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: one-year follow-up of a randomised trial. *Diabetologia.* 2004;47:1677-86.	Comparative effectiveness
Broom I, Hughes E, Dodson P, Reckless J. The role of orlistat in the treatment of obese patients with mild to moderate hypercholesterolaemia: consequences for coronary risk. *Br J Cardiol.* 2002;9:460-8.	Less than 12 months followup
Brownell KD. The LEARN Program for Weight Management. New Haven, CT: American Health Publishing Company; 2000.	Comparative effectiveness
Bryan J, Tiggemann M. The effect of weight-loss dieting on cognitive performance and psychological well-being in overweight women. *Appetite.* 2001;36:147-56.	Less than 12 months followup
Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA.* 2004;292:1724-37.	Does not meet design requirements in inclusion criteria
Burke V, Beilin LJ, Cutt HE, et al. A lifestyle program for treated hypertensives improved health-related behaviors and cardiovascular risk factors, a randomized controlled trial. *J Clin Epidemiol.* 2007;60:133-41.	No weight or harms outcomes
Burke V, Mansour J, Beilin LJ, Mori TA. Long-term follow-up of participants in a health promotion program for treated hypertensives (ADAPT). *Nutr Metab Cardiovasc Dis.* 2008;18:198-206.	No weight or harms outcomes
Burke V, Mori TA, Giangiulio N, et al. An innovative program for changing health behaviours. *Asia Pac J Clin Nutr.* 2002;11(Suppl 3):S586-97.	High or differential attrition
Caan B, Neuhouser M, Aragaki A, et al. Calcium plus vitamin D supplementation and the risk of postmenopausal weight gain. *Arch Intern Med.* 2007;167:893-902.	Not one of the specified interventions
Calle-Pascual AL, Rodriguez C, Camacho F, et al. Behaviour modification in obese subjects with type 2 diabetes mellitus. *Diabetes Res Clin Pract.* 1992;15:157-62.	Does not meet design requirements in inclusion criteria
Campbell PT, Campbell KL, Wener MH, et al. A yearlong exercise intervention decreases CRP among obese postmenopausal women. *Med Sci Sports Exerc.* 2009;41:1533-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Carr DB, Utzschneider KM, Boyko EJ, et al. A reduced-fat diet and aerobic exercise in Japanese Americans with impaired glucose tolerance decreases intra-abdominal fat and improves insulin sensitivity but not beta-cell function. *Diabetes.* 2005;54:340-7.	Comparative effectiveness
Carr LJ, Bartee RT, Dorozynski CM, et al. Eight-month follow-up of physical activity and central adiposity: results from an Internet-delivered randomized control trial intervention. *J Phys Act Health.* 2009;6:444-55.	Comparative effectiveness
Castaneda C, Layne JE, Munoz-Orians L, et al. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes Care.* 2002;25:2335-41.	Less than 12 months followup
Chang MW, Nitzke S, Brown R. Design and outcomes of a Mothers In Motion behavioral intervention pilot study. *J Nutr Educ Behav.* 2010;42(Suppl 3):S11-21.	Less than 12 months followup
Charles MA, Morange P, Eschwege E, et al. Effect of weight change and metformin on fibrinolysis and the von Willebrand factor in obese nondiabetic subjects: the BIGPRO1 study. *Diabetes Care.* 1998;21:1967-72.	No weight or harms outcomes
Cheyette C. Weight No More: a randomised controlled trial for people with type 2 diabetes on insulin therapy. *Pract Diabetes Int.* 2007;24:450-6.	High or differential attrition
Chiasson JL, Lau DC, Leiter LA, et al. Fluoxetine has potential in obese NIDDM—multicenter Canadian trial. *Diabetes*. 1989;38(Suppl 2):A154.	Not one of the specified interventions
Clark M, Hampson SE, Avery L, Simpson R. Effects of a tailored lifestyle self-management intervention in patients with type 2 diabetes. *Br J Health Psychol.* 2004;9:365-79.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Clarke KK, Freeland-Graves J, Klohe-Lehman DM, et al. Promotion of physical activity in low-income mothers using pedometers. *J Am Diet Assoc.* 2007;107:962-7.	Less than 12 months followup

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Reference	Reason for Exclusion
Clifford PA, Tan SY, Gorsuch RL. Efficacy of a self-directed behavioral health change program: weight, body composition, cardiovascular fitness, blood pressure, health risk, and psychosocial mediating variables. *J Behav Med.* 1991;14:303-23.	Comparative effectiveness
Cocco G, Pandolfi S, Rousson V. Sufficient weight reduction decreases cardiovascular complications in diabetic patients with the metabolic syndrome: a randomized study of orlistat as an adjunct to lifestyle changes (diet and exercise). *Heart Drug.* 2005;5:68-74.	Less than 12 months followup
Coker RH, Williams RH, Yeo SE, et al. The impact of exercise training compared to caloric restriction on hepatic and peripheral insulin resistance in obesity. *J Clin Endocrinol Metabol.* 2009;94:4258-66.	Less than 12 months followup
Corpeleijn E, Feskens EJ, Jansen EH, et al. Improvements in glucose tolerance and insulin sensitivity after lifestyle intervention are related to changes in serum fatty acid profile and desaturase activities: the SLIM study. *Diabetologia.* 2006;49:2392-401.	Not one of the specified interventions
Counterweight Project Team. Evaluation of the Counterweight Programme for obesity management in primary care: a starting point for continuous improvement. *Br J Gen Pract.* 2008;58:548-54.	Does not meet design requirements in inclusion criteria
Counterweight Project Team. Influence of body mass index on prescribing costs and potential cost savings of a weight management programme in primary care. *J Health Serv Res Policy.* 2008;13:158-66.	Does not meet design requirements in inclusion criteria
Cousins JH, Rubovits DS, Dunn JK, et al. Family versus individually oriented intervention for weight loss in Mexican American women. *Public Health Rep.* 1992;107:549-55.	Comparative effectiveness
Cuellar GE, Ruiz AM, Monsalve MC, Berber A. Six-month treatment of obesity with sibutramine 15 mg; a double-blind, placebo-controlled monocenter clinical trial in a Hispanic population. *Obes Res.* 2000;8:71-82.	Not on list of countries with HDI > 0.90
Culturally appropriate lifestyle interventions promote weight loss in rural dwelling people with type 2 diabetes. *Evid Based Healthc Pub Health.* 2005;9:231-2.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dale KS, Mann JI, McAuley KA, et al. Sustainability of lifestyle changes following an intensive lifestyle intervention in insulin resistant adults: follow-up at 2-years. *Asia Pac J Clin Nutri.* 2009;18:114-20.	Comparative effectiveness
Dale KS, McAuley KA, Taylor RW, et al. Determining optimal approaches for weight maintenance: a randomized controlled trial. *Can Med Assoc J.* 2009;180:E39-46.	Comparative effectiveness
Davies MJ, Heller S, Skinner TC, et al. Effectiveness of the Diabetes Education and Self Management for Ongoing and Newly Diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. *BMJ.* 2008;336:491-5.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Davis BR, Blaufox MD, Oberman A, et al. Reduction in long-term antihypertensive medication requirements: effects of weight reduction by dietary intervention in overweight persons with mild hypertension. *Arch Intern Med.* 1993;153:1773-82.	No weight or harms outcomes
de Wit LT, Mathus-Vliegen L, Hey C, et al. Open versus laparoscopic adjustable silicone gastric banding: a prospective randomized trial for treatment of morbid obesity. *Ann Surg.* 1999;230:800-5.	Not one of the specified interventions
Delahanty LM, Nathan DM. Implications of the Diabetes Prevention Program and Look AHEAD clinical trials for lifestyle interventions. *J Am Diet Assoc.* 2008;108(Suppl 1):S66-72.	Comparative effectiveness
Delecluse C, Colman V, Roelants M, et al. Exercise programs for older men: mode and intensity to induce the highest possible health-related benefits. *Prev Med.* 2004;39:823-33.	Less than 12 months followup
Dennis KE, Tomoyasu N, McCrone SH, et al. Self-efficacy targeted treatments for weight loss in postmenopausal women. *Sch Inq Nurs Pract.* 2001;15:259-76.	Comparative effectiveness
Derosa G, Cicero AF, Murdolo G, et al. Efficacy and safety comparative evaluation of orlistat and sibutramine treatment in hypertensive obese patients. *Diabetes Obes Metab.* 2005;7:47-55.	Comparative effectiveness
Devine A, Prince RL, Bell R. Nutritional effect of calcium supplementation by skim milk powder or calcium tablets on total nutrient intake in postmenopausal women. *Am J Clin Nutr.* 1996;64:731-7.	Comparative effectiveness

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Reference	Reason for Exclusion
Di Francesco V, Sacco T, Zamboni M, et al. Weight loss and quality of life improvement in obese subjects treated with sibutramine: a double-blind randomized multicenter study. *Ann Nutr Metab.* 2007;51:75-81.	Sibutramine intervention
Di Loreto C, Fanelli C, Lucidi P, et al. Validation of a counseling strategy to promote the adoption and the maintenance of physical activity by type 2 diabetic subjects. *Diabetes Care.* 2003;26:404-8.	Comparative effectiveness
Ditschuneit HH, Flechtner-Mors M, Johnson TD, Adler G. Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *Am J Clin Nutr.* 1999;69:198-204.	Comparative effectiveness
Donnelly JE, Hill JO, Jacobsen DJ, et al. Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med.* 2003;163:1343-50.	High or differential attrition
Donnelly JE, Jacobsen DJ, Heelan KS, et al. The effects of 18 months of intermittent vs. continuous exercise on aerobic capacity, body weight and composition, and metabolic fitness in previously sedentary, moderately obese females. *Int J Obes Relat Metab Disord.* 2000;24:566-72.	Comparative effectiveness
Donnelly JE, Kirk EP, Jacobsen DJ, et al. Effects of 16 mo of verified, supervised aerobic exercise on macronutrient intake in overweight men and women: the Midwest Exercise Trial. *Am J Clin Nutr.* 2003;78:950-6.	High or differential attrition
Donnelly JE, Smith BK, Dunn L, et al. Comparison of a phone vs clinic approach to achieve 10% weight loss. *Int J Obes (London).* 2007;31:1270-6.	Less than 12 months followup
Due A, Larsen TM, Mu H, et al. Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease, and diabetes: a 6-mo randomized, controlled trial. *Am J Clin Nutr.* 2008;88:1232-41.	Less than 12 months followup
Dujovne CA, Zavoral JH, Rowe E, Mendel CM. Effects of sibutramine on body weight and serum lipids: a double-blind, randomized, placebo-controlled study in 322 overweight and obese patients with dyslipidemia. *Am Heart J.* 2001;142:489-97.	Sibutramine intervention
Dunn AL, Marcus BH, Kampert JB, et al. Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. *JAMA.* 1999;281:327-34.	Comparative effectiveness
Dunstan DW, Daly RM, Owen N, et al. Home-based resistance training is not sufficient to maintain improved glycemic control following supervised training in older individuals with type 2 diabetes. *Diabetes Care.* 2005;28:3-9.	Comparative effectiveness
Dutton GR, Davis MP, Welsch MA, Brantley PJ. Promoting physical activity for low-income minority women in primary care. *Am J Health Behav.* 2007;31:622-31.	No weight or harms outcomes
Dymek MP, Le Grange D, Neven K, Alverdy J. Quality of life after gastric bypass surgery: a cross-sectional study. *Obes Res.* 2002;10:1135-42.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dymek MP, Le Grange D, Neven K, Alverdy J. Quality of life and psychosocial adjustment in patients after Roux-en-Y gastric bypass: a brief report. *Obes Surg.* 2001;11:32-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dyson PA, Hammersley MS, Morris RJ, et al. The Fasting Hyperglycaemia Study, II: randomized controlled trial of reinforced healthy-living advice in subjects with increased but not diabetic fasting plasma glucose. *Metabolism.* 1997;46:50-5.	Not one of the specified interventions
Dzator JA, Hendrie D, Burke V, et al. A randomized trial of interactive group sessions achieved greater improvements in nutrition and physical activity at a tiny increase in cost. *J Clin Epidemiol.* 2004;57:610-19.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Early JL, Apovian CM, Aronne LJ, et al. Sibutramine plus meal replacement therapy for body weight loss and maintenance in obese patients. *Obesity (Silver Spring).* 2007;15:1464-72.	Sibutramine intervention
Eddy DM, Schlessinger L, Kahn R. Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. *Ann Intern Med.* 2005;143:251-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Eiben G, Lissner L. Health Hunters—an intervention to prevent overweight and obesity in young high-risk women. *Int J Obes.* 2006;30:691-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss

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Reference	Reason for Exclusion
Elhayany A, Lustman A, Abel R, et al. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. *Diabetes Obes Metab.* 2010;12:204-9.	Comparative effectiveness
Elmer PJ, Obarzanek E, Vollmer WM, et al. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. *Ann Intern Med.* 2006;144:485-95.	Comparative effectiveness
Ely AC, Banitt A, Befort C, et al. Kansas primary care weighs in: a pilot randomized trial of a chronic care model program for obesity in 3 rural Kansas primary care practices. *J Rural Health.* 2008;24:125-32.	Less than 12 months followup
Eriksson KM, Westborg CJ, Eliasson MC. A randomized trial of lifestyle intervention in primary healthcare for the modification of cardiovascular risk factors. *Scand J Pub Health.* 2006;34:453-61.	Not one of the specified interventions
Esposito K, Giugliano F, Di Palo C, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. *JAMA.* 2004;291:2978-84.	Comparative effectiveness
Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA.* 2004;292:1440-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Esposito K, Pontillo A, Di Palo C, et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. *JAMA.* 2003;289:1799-804.	Comparative effectiveness
Fabricatore AN, Wadden TA, Moore RH, et al. Predictors of attrition and weight loss success: results from a randomized controlled trial. *Behav Res Ther.* 2009;47:685-91.	Comparative effectiveness
Fanghanel G, Cortinas L, Sanchez-Reyes L, Berber A. A clinical trial of the use of sibutramine for the treatment of patients suffering essential obesity. *Int J Obes Relat Metab Disord.* 2000;24:144-50.	Less than 12 months followup
Fanghanel G, Cortinas L, Sanchez-Reyes L, et al. Safety and efficacy of sibutramine in overweight Hispanic patients with hypertension. *Adv Ther.* 2003;20:101-13.	Less than 12 months followup
Faria AN, Ribeiro Filho FF, Kohlmann NE, et al. Effects of sibutramine on abdominal fat mass, insulin resistance and blood pressure in obese hypertensive patients. *Diabetes Obes Metab.* 2005;7:246-53.	Less than 12 months followup
Faria AN, Ribeiro Filho FF, Lerario DD, et al. Effects of sibutramine on the treatment of obesity in patients with arterial hypertension. *Arq Bras Cardiol.* 2002;78:172-80.	Less than 12 months followup
Faulconbridge LF, Wadden TA, Berkowitz RI, et al. Changes in symptoms of depression with weight loss: results of a randomized trial. *Obesity (Silver Spring).* 2009;17:1009-16.	No placebo in medication trial
Ferre R, Plana N, Merino J, et al. Effects of therapeutic lifestyle changes on peripheral artery tonometry in patients with abdominal obesity. *Nutr Metab Cardiovasc Dis.* 2010 Aug 11. [Epub ahead of print]	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Figueroa A, Going SB, Milliken LA, et al. Effects of exercise training and hormone replacement therapy on lean and fat mass in postmenopausal women. *J Gerontol A Biol Sci Med Sci.* 2003;58:266-70.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Finer N, Bloom SR, Frost GS, et al. Sibutramine is effective for weight loss and diabetic control in obesity with type 2 diabetes: a randomised, double-blind, placebo-controlled study. *Diabetes Obes Metab.* 2000;2:105-12.	Sibutramine intervention
Finkelstein EA, Linnan LA, Tate DF, Leese PJ. A longitudinal study on the relationship between weight loss, medical expenditures, and absenteeism among overweight employees in the WAY to Health study. *J Occup Environ Med.* 2009;51:1367-73.	Conducted primarily in a non-relevant setting
Finley CE, Barlow CE, Greenway FL, et al. Retention rates and weight loss in a commercial weight loss program. *Int J Obes (Lond).* 2007;31:292-8.	Does not meet design requirements in inclusion criteria
Fitzgibbon ML, Stolley MR, Schiffer L, et al. Obesity Reduction Black Intervention Trial (ORBIT): 18-month results. *Obesity (Silver Spring).* 2010;18:2317-25.	No weight or harms outcomes
Flechtner-Mors M, Ditschuneit HH, Johnson TD, et al. Metabolic and weight loss effects of long-term dietary intervention in obese patients: four-year results. *Obes Res.* 2000;8:399-402.	Comparative effectiveness

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Reference	Reason for Exclusion
Fleming RM. The effect of high-, moderate-, and low-fat diets on weight loss and cardiovascular disease risk factors. *Prev Cardiol.* 2002;5:110-8.	Comparative effectiveness
Flood A, Mitchell N, Jaeb M, et al. Energy density and weight change in a long-term weight-loss trial. *Int J Behav Nutr Phys Act.* 2009;6:57.	Study of overweight/obesity prevention
Focht BC, Rejeski WJ, Ambrosius WT, et al. Exercise, self-efficacy, and mobility performance in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum.* 2005;53:659-65.	Comparative effectiveness
Fogelholm M, Kukkonen-Harjula K, Nenonen A, Pasanen M. Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. *Arch Intern Med.* 2000;160:2177-84.	Comparative effectiveness
Fogelholm M, Kukkonen-Harjula K, Oja P. Eating control and physical activity as determinants of short-term weight maintenance after a very-low-calorie diet among obese women. *Int J Obes Relat Metab Disord.* 1999;23:203-10.	Comparative effectiveness
Fontana L, Villareal DT, Weiss EP, et al. Calorie restriction or exercise: effects on coronary heart disease risk factors: a randomized, controlled trial. *Am J Physiol Endocrinol Metab.* 2007;293:E197-202.	Comparative effectiveness
Fontbonne A, Diouf I, Baccara-Dinet M, et al. Effects of 1-year treatment with metformin on metabolic and cardiovascular risk factors in non-diabetic upper-body obese subjects with mild glucose anomalies: a post-hoc analysis of the BIGPRO1 trial. *Diabetes Metab.* 2009;35:385-91.	No weight or harms outcomes
Fossati M, Amati F, Painot D, et al. Cognitive-behavioral therapy with simultaneous nutritional and physical activity education in obese patients with binge eating disorder. *Eat Weight Disord.* 2004;9:134-8.	Focus on patients in subgroups other than specified conditions
Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med.* 2009;169:1619-26.	Comparative effectiveness
Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med.* 2003;348:2082-90.	Comparative effectiveness
Foster-Schubert KE, McTiernan A, Frayo RS, et al. Human plasma ghrelin levels increase during a one-year exercise program. *J Clin Endocrinol Metab.* 2005;90:820-5.	No weight or harms outcomes
Fujimoto WY, Jablonski KA, Bray GA, et al. Body size and shape changes and the risk of diabetes in the Diabetes Prevention Program. *Diabetes.* 2007;56:1680-5.	No weight or harms outcomes
Gambineri A, Pelusi C, Genghini S, et al. Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome. *Clin Endocrinol.* 2004;60:241-9.	No weight or harms outcomes
Gaullier JM, Halse J, Hoye K, et al. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. *Am J Clin Nutr.* 2004;79:1118-25.	Not one of the specified interventions
Gaullier JM, Halse J, Hoye K, et al. Supplementation with conjugated linoleic acid for 24 months is well tolerated by and reduces body fat mass in healthy, overweight humans. *J Nutr.* 2005;135:778-84.	Not one of the specified interventions
Ghroubi S, Elleuch H, Chikh T, et al. Physical training combined with dietary measures in the treatment of adult obesity: a comparison of two protocols. *Ann Phys Rehab Med.* 2009;52:394-413.	Not on list of countries with HDI > 0.90
Giugliano D, Quatraro A, Consoli G, et al. Metformin for obese, insulin-treated diabetic patients: improvement in glycaemic control and reduction of metabolic risk factors. *Eur J Clin Pharmacol.* 1993;44:107-12.	Less than 12 months followup
Glasgow RE, La Chance PA, Toobert DJ, et al. Long-term effects and costs of brief behavioural dietary intervention for patients with diabetes delivered from the medical office. *Patient Educ Couns.* 1997;32:175-84.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Glasgow RE, Nelson CC, Kearney KA, et al. Reach, engagement, and retention in an Internet-based weight loss program in a multi-site randomized controlled trial. *J Med Internet Res.* 2007;9:e11.	No weight or harms outcomes
Godoy-Matos A, Carraro L, Vieira A, et al. Treatment of obese adolescents with sibutramine: a randomized, double-blind, controlled study. *J Clin Endocrinol Metab.* 2005;90:1460-5.	Focus on children or adolescents
Gokcel A, Gumurdulu Y, Karakose H, et al. Evaluation of the safety and efficacy of sibutramine, orlistat and metformin in the treatment of obesity. *Diabetes Obes Metab.* 2002;4:49-55.	Comparative effectiveness

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Reference	Reason for Exclusion
Gokcel A, Karakose H, Ertorer EM, et al. Effects of sibutramine in obese female subjects with type 2 diabetes and poor blood glucose control. *Diabetes Care.* 2001;24:1957-60.	Not on list of countries with HDI >0.90
Gold BC, Burke S, Pintauro S, et al. Weight loss on the web: a pilot study comparing a structured behavioral intervention to a commercial program. *Obesity (Silver Spring).* 2007;15:155-64.	Comparative effectiveness
Gotfredsen A, Westergren HH, Andersen T. Influence of orlistat on bone turnover and body composition. *Int J Obes Relat Metab Disord.* 2001;25:1154-60.	No weight or harms outcomes
Greaves CJ, Middlebrooke A, O'Loughlin L, et al. Motivational interviewing for modifying diabetes risk: a randomised controlled trial. *Br J Gen Pract.* 2008;58:535-40.	Less than 12 months followup
Grimm RH Jr, Grandits GA, Cutler JA, et al. Relationships of quality-of-life measures to long-term lifestyle and drug treatment in the Treatment of Mild Hypertension Study. *Arch Intern Med.* 1997;157:638-48.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Guisado JA, Vaz FJ, Alarcon J, et al. Psychopathological status and interpersonal functioning following weight loss in morbidly obese patients undergoing bariatric surgery. *Obes Surg.* 2002;12:835-40.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Gunther CW, Legowski PA, Lyle RM, et al. Dairy products do not lead to alterations in body weight or fat mass in young women in a 1-y intervention. *Am J Clin Nutr*. 2005;81:751-6.	Study of overweight/obesity prevention
Gurka MJ, Wolf AM, Conaway MR, et al. Lifestyle intervention in obese patients with type 2 diabetes: impact of the patient's educational background. *Obesity (Silver Spring).* 2006;14:1085-92.	Comparative effectiveness
Gustafson A, Khavjou O, Stearns SC, et al. Cost-effectiveness of a behavioral weight loss intervention for low-income women: the Weight-Wise Program. *Prev Med.* 2009;49:390-5.	Less than 12 months followup
Guy-Grand B, Drouin P, Eschwege E, et al. Effects of orlistat on obesity-related diseases—a six-month randomized trial. *Diabetes Obes Metab.* 2004;6:375-83.	Less than 12 months followup
Hainer V, Kunesova M, Bellisle F, et al. Psychobehavioral and nutritional predictors of weight loss in obese women treated with sibutramine. *Int J Obes (Lond).* 2005;29:208-16.	Less than 12 months followup
Hakala K, Maasilta P, Sovijarvi AR. Upright body position and weight loss improve respiratory mechanics and daytime oxygenation in obese patients with obstructive sleep apnoea. *Clin Physiol.* 2000;20:50-5.	Does not meet design requirements in inclusion criteria
Hall WD, Feng Z, George VA, et al. Low-fat diet: effect on anthropometrics, blood pressure, glucose, and insulin in older women. *Ethn Dis.* 2003;13:337-43.	Less than 12 months followup
Hansen D, Astrup A, Toubro S, et al. Predictors of weight loss and maintenance during 2 years of treatment by sibutramine in obesity: results from the European multi-centre STORM trial. *Int J Obes Rel Metab Dis.* 2001;25:496-501.	High or differential attrition
Hansen DL, Toubro S, Stock MJ, et al. The effect of sibutramine on energy expenditure and appetite during chronic treatment without dietary restriction. *Int J Obes Relat Metab Disord.* 1999;23:1016-24.	Sibutramine intervention
Harvey BJ, Gold BC, Lauber R, Starinski A. The impact of calcium and dairy product consumption on weight loss. *Obes Res.* 2005;13:1720-6.	Comparative effectiveness
Harvey-Berino J, Pintauro S, Buzzell P, et al. Does using the Internet facilitate the maintenance of weight loss? *Int J Obes Relat Metab Disord.* 2002;26:1254-60.	Comparative effectiveness
Harvey-Berino J, Pintauro S, Buzzell P, Gold EC. Effect of internet support on the long-term maintenance of weight loss. *Obes Res.* 2004;12:320-9.	Comparative effectiveness
Harvey-Berino J, Pintauro SJ, Gold EC. The feasibility of using Internet support for the maintenance of weight loss. *Behav Modif.* 2002;26:103-16.	Less than 12 months followup
Haskell WL, Alderman EL, Fair JM, et al. Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease: the Stanford Coronary Risk Intervention Project (SCRIP). *Circulation.* 1994;89:975-90.	Not one of the specified interventions
Haub MD, Simons TR, Cook CM, et al. Calcium-fortified beverage supplementation on body composition in postmenopausal women. *Nutr J.* 2005;4:21.	Not one of the specified interventions
Hauner H, Meier M, Wendland G, et al. Weight reduction by sibutramine in obese subjects in primary care medicine: the SAT Study. *Exp Clin Endocrinol Diabetes.* 2004;112:201-7.	Sibutramine intervention

Appendix D Table 2. Studies Excluded From Review for Key Question 2

Reference	Reason for Exclusion
Hawley G, Horwath C, Gray A, et al. Sustainability of health and lifestyle improvements following a non-dieting randomised trial in overweight women. *Prev Med.* 2008;47:593-9.	Comparative effectiveness
Hays NP, Starling RD, Sullivan DH, et al. Effects of an ad libitum, high carbohydrate diet and aerobic exercise training on insulin action and muscle metabolism in older men and women. *J Gerontol A Biol Sci Med Sci.* 2006;61:299-304.	Comparative effectiveness
Hazenberg BP. Randomized, double-blind, placebo-controlled, multicenter study of sibutramine in obese hypertensive patients. *Cardiology.* 2000;94:152-8.	Sibutramine intervention
Hensrud DD. Dietary treatment and long-term weight loss and maintenance in type 2 diabetes. *Obes Res.* 2001;9(Suppl 4):S348-53.	Does not meet design requirements in inclusion criteria
Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med.* 2005;142:323-32.	No weight or harms outcomes
Hermann LS, Kalen J, Katzman P, et al. Long-term glycaemic improvement after addition of metformin to insulin in insulin-treated obese type 2 diabetes patients. *Diabetes Obes Metab.* 2001;3:428-34.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Heshka S, Anderson JW, Atkinson RL, et al. Weight loss with self-help compared with a structured commercial program: a randomized trial. *JAMA.* 2003;289:1792-8.	Comparative effectiveness
Heymsfield SB, Segal KR, Hauptman J, et al. Effects of weight loss with orlistat on glucose tolerance and progression to type 2 diabetes in obese adults. *Arch Intern Med.* 2000;160:1321-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hivert MF, Langlois MF, Berard P, et al. Prevention of weight gain in young adults through a seminar-based intervention program. *Int J Obes (London).* 2007;31:1262-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hoeger KM, Kochman L, Wixom N, et al. A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertil Steril.* 2004;82:421-9.	High or differential attrition
Hooper L. Primary prevention of CVD: diet and weight loss. *Clin Evid.* 2007.	Does not meet design requirements in inclusion criteria
Hope AA, Kumanyika SK, Shults J, Holmes WC. Changes in health-related quality of life among African-Americans in a lifestyle weight loss program. *Qual Life Res.* 2010;19:1025-33.	Does not meet design requirements in inclusion criteria
Howard BV, Manson JE, Stefanick ML, et al. Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. *JAMA.* 2006;295:39-49.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hsieh CJ, Wang PW, Liu RT, et al. Orlistat for obesity: benefits beyond weight loss. *Diabetes Res Clin Pract.* 2005;67:78-83.	Not on list of countries with HDI > 0.90
Hunter GR, Brock DW, Byrne NM, et al. Exercise training prevents regain of visceral fat for 1 year following weight loss. *Obesity.* 2010;18:690-5.	Comparative effectiveness
Jacobs DR, Sluik D, Rokling-Andersen MH, et al. Association of 1-y changes in diet pattern with cardiovascular disease risk factors and adipokines: results from the 1-y randomized Oslo Diet and Exercise Study. *Am J Clin Nutr.* 2009;89:509-17.	No weight or harms outcomes
Jakicic JM, Jaramillo SA, Balasubramanyam A, et al. Effect of a lifestyle intervention on change in cardiorespiratory fitness in adults with type 2 diabetes: results from the Look AHEAD Study. *Int J Obes.* 2009;33:305-16.	Comparative effectiveness
Jakicic JM, Marcus BH, Gallagher KI, et al. Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *JAMA.* 2003;290:1323-30.	Comparative effectiveness
Jakicic JM, Otto AD, Lang W, et al. The effect of physical activity on 18-month weight change in overweight adults. *Obesity (Silver Spring).* 2011;19:100-9.	Comparative effectiveness
Jakicic JM, Winters C, Lang W, Wing RR. Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *JAMA.* 1999;282:1554-60.	Comparative effectiveness
Jalkanen L. The effect of a weight reduction program on cardiovascular risk factors among overweight hypertensives in primary health care. *Scand J Soc Med.* 1991;19:66-71.	Other quality issues
James WP, Astrup A, Finer N, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. *Lancet.* 2000;356:2119-25.	Sibutramine intervention

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Reference	Reason for Exclusion
Janssen I, Fortier A, Hudson R, Ross R. Effects of an energy-restrictive diet with or without exercise on abdominal fat, intermuscular fat, and metabolic risk factors in obese women. *Diabetes Care.* 2002;25:431-8.	Comparative effectiveness
Jarjou LM, Prentice A, Sawo Y, et al. Randomized, placebo-controlled, calcium supplementation study in pregnant Gambian women: effects on breast-milk calcium concentrations and infant birth weight, growth, and bone mineral accretion in the first year of life. *Am J Clin Nutr.* 2006;83:657-66.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Jarrett RJ, Keen H, Murrells T. Changes in blood pressure and body weight over ten years in men selected for glucose intolerance. *J Epidemiol Community Health.* 1987;41:145-51.	Comparative effectiveness
Jeffery RW, French SA. Preventing weight gain in adults: design, methods and one year results from the Pound of Prevention study. *Int J Obes Relat Metab Disord.* 1997;21:457-64.	Study of overweight/obesity prevention
Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr.* 2003;78:684-9.	Comparative effectiveness
Jehn ML, Patt MR, Appel LJ, Miller ER III. One year follow-up of overweight and obese hypertensive adults following intensive lifestyle therapy. *J Hum Nutr Diet.* 2006;19:349-54.	Comparative effectiveness
Jensen LB, Kollerup G, Quaade F, Sorensen OH. Bone minerals changes in obese women during a moderate weight loss with and without calcium supplementation. *J Bone Miner Res.* 2001;16:141-7.	Less than 12 months followup
Jirik-Babb P, Geliebter A. Comparison of psychological characteristics of binging and nonbinging obese, adult, female outpatients. *Eat Weight Disord.* 2003;8:173-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Johansson K, Neovius M, Lagerros YT, et al. Effect of a very low energy diet on moderate and severe obstructive sleep apnoea in obese men: a randomised controlled trial. *BMJ.* 2009;339:b4609.	Less than 12 months followup
Jordan J, Scholze J, Matiba B, et al. Influence of sibutramine on blood pressure: evidence from placebo-controlled trials. *Int J Obes.* 2005;29:509-16.	Does not meet design requirements in inclusion criteria
Kajaste S, Brander PE, Telakivi T, et al. A cognitive-behavioral weight reduction program in the treatment of obstructive sleep apnea syndrome with or without initial nasal CPAP: a randomized study. *Sleep Med.* 2004;5:125-31.	Not one of the specified interventions
Kalter-Leibovici O, Younis-Zeidan N, Atamna A, et al. Lifestyle intervention in obese Arab women: a randomized controlled trial. *Arch Intern Med.* 2010;170:970-6.	Comparative effectiveness
Kamioka H, Nakamura Y, Okada S, et al. Effectiveness of comprehensive health education combining lifestyle education and hot spa bathing for male white-collar employees: a randomized controlled trial with 1-year follow-up. *J Epidemiol.* 2009;19:219-30.	Conducted primarily in a non-relevant setting
Kansanen M, Vanninen E, Tuunainen A, et al. The effect of a very low-calorie diet-induced weight loss on the severity of obstructive sleep apnoea and autonomic nervous function in obese patients with obstructive sleep apnoea syndrome. *Clin Physiol.* 1998;18:377-85.	Does not meet design requirements in inclusion criteria
Karhunen L, Franssila-Kallunki A, Rissanen P, et al. Effect of orlistat treatment on body composition and resting energy expenditure during a two-year weight-reduction programme in obese Finns. *Int J Obes Relat Metab Disord.* 2000;24:1567-72.	No weight or harms outcomes
Katzer L, Bradshaw AJ, Horwath CC, et al. Evaluation of a "nondieting" stress reduction program for overweight women: a randomized trial. *Am J Health Promot.* 2008;22:264-74.	Comparative effectiveness
Kaukua JK, Pekkarinen TA, Rissanen AM. Health-related quality of life in a randomised placebo-controlled trial of sibutramine in obese patients with type II diabetes. *Int J Obes Relat Metab Disord.* 2004;28:600-5.	Sibutramine intervention
Kawano M, Shono N, Yoshimura T, et al. Improved cardio-respiratory fitness correlates with changes in the number and size of small dense LDL: randomized controlled trial with exercise training and dietary instruction. *Intern Med.* 2009;48:25-32.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Keating GM, Jarvis B. Orlistat: in the prevention and treatment of type 2 diabetes mellitus. *Drugs.* 2120;61:2107-19.	Does not meet design requirements in inclusion criteria

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Reference	Reason for Exclusion
Kelley DE, Bray GA, Pi-Sunyer FX, et al. Clinical efficacy of orlistat therapy in overweight and obese patients with insulin-treated type 2 diabetes: a 1-year randomized controlled trial. *Diabetes Care.* 2002;25:1033-41.	High or differential attrition
Keogh JB, Luscombe-Marsh ND, Noakes M, et al. Long-term weight maintenance and cardiovascular risk factors are not different following weight loss on carbohydrate-restricted diets high in either monounsaturated fat or protein in obese hyperinsulinaemic men and women. *Br J Nutr.* 2007;97:405-10.	Comparative effectiveness
Keranen AM, Savolainen MJ, Reponen AH, et al. The effect of eating behavior on weight loss and maintenance during a lifestyle intervention. *Prev Med.* 2009;49:32-8.	Comparative effectiveness
Kerr J, Patrick K, Norman G, et al. Randomized control trial of a behavioral intervention for overweight women: impact on depressive symptoms. *Depress Anxiety.* 2008;25:555-8.	No weight or harms outcomes
Ketola E, Makela M, Klockars M. Individualised multifactorial lifestyle intervention trial for high-risk cardiovascular patients in primary care. *Br J Gen Pract.* 2001;51:291-4.	Not one of the specified interventions
Kim SH, Lee YM, Jee SH, Nam CM. Effect of sibutramine on weight loss and blood pressure: a meta-analysis of controlled trials. *Obes Res.* 2003;11:1116-23.	Does not meet design requirements in inclusion criteria
Kim SI, Kim HS. Effectiveness of mobile and Internet intervention in patients with obese type 2 diabetes. *Int J Med Inf.* 2008;77:399-404.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kim Y, Pike J, Adams H, et al. Telephone intervention promoting weight-related health behaviors. *Prev Med.* 2010;50:112-7.	Comparative effectiveness
Kirk EP, Jacobsen DJ, Gibson C, et al. Time course for changes in aerobic capacity and body composition in overweight men and women in response to long-term exercise: the Midwest Exercise Trial (MET). *Int J Obes Relat Metab Disord.* 2003;27:912-9.	High or differential attrition
Kirk SF, Harvey EL, McConnon A, et al. A randomised trial of an Internet weight control resource: the UK Weight Control Trial. *BMC Health Serv Res.* 2003;3:19.	No weight or harms outcomes
Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet.* 2009;274:1677-86.	No weight or harms outcomes
Kolotkin RL, Norquist JM, Crosby RD, et al. One-year health-related quality of life outcomes in weight loss trial participants: comparison of three measures. *Health Qual Life Outcomes.* 2009;7:53.	Not one of the specified interventions
Kostis JB, Wilson AC, Hooper WC, et al. Association of angiotensin-converting enzyme DD genotype with blood pressure sensitivity to weight loss. *Am Heart J.* 2002;144:625-9.	No weight or harms outcomes
Kostis JB, Wilson AC, Shindler DM, et al. Persistence of normotension after discontinuation of lifestyle intervention in the trial of TONE. *Am J Hypertens.* 2002;15:732-4.	No weight or harms outcomes
Krakoff J, Clark JM, Crandall JP, et al. Effects of metformin and weight loss on serum alanine aminotransferase activity in the Diabetes Prevention Program. *Obesity (Silver Spring).* 2010;18:1762-7.	No weight or harms outcomes
Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med.* 2002;347:1483-92.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kukkonen-Harjula KT, Borg PT, Nenonen AM, Fogelholm MG. Effects of a weight maintenance program with or without exercise on the metabolic syndrome: a randomized trial in obese men. *Prev Med.* 2005;41:784-90.	Comparative effectiveness
Kuller LH, Kinzel LS, Pettee KK, et al. Lifestyle intervention and coronary heart disease risk factor changes over 18 months in postmenopausal women: the Women On the Move Through Activity and Nutrition (WOMAN study) clinical trial. *J Womens Health (Larchmt).* 2006;15:962-74.	Comparative effectiveness
Kuller LH, Kriska AM, Kinzel LS, et al. The clinical trial of Women On the Move Through Activity and Nutrition (WOMAN) study. *Contemp Clin Trials.* 2006;28:370-81.	Comparative effectiveness
Kumanyika SK, Cook NR, Cutler JA, et al. Sodium reduction for hypertension prevention in overweight adults: further results from the Trials of Hypertension Prevention phase II. *J Hum Hypertens.* 2005;19:33-45.	Not focused on behavioral or pharmacological interventions designed to promote weight loss

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Reference	Reason for Exclusion
Kumanyika SK, Shults J, Fassbender J, et al. Outpatient weight management in African-Americans: the Healthy Eating and Lifestyle Program (HELP) study. *Prev Med.* 2005;41:488-502.	Comparative effectiveness
Kumanyika SK, Wadden TA, Shults J, et al. Trial of family and friend support for weight loss in African American adults. *Arch Intern Med.* 2009;169:1795-804.	Comparative effectiveness
Laaksonen DE, Laitinen T, Schonberg J, et al. Weight loss and weight maintenance, ambulatory blood pressure and cardiac autonomic tone in obese persons with the metabolic syndrome. *J Hypertens.* 2003;21:371-8.	No weight or harms outcomes
Laaksonen DE, Lindstrom J, Lakka TA, et al. Physical activity in the prevention of type 2 diabetes: the Finnish Diabetes Prevention Study. *Diabetes.* 2005;54:158-65.	No weight or harms outcomes
Lally P, Chipperfield A, Wardle J. Healthy habits: efficacy of simple advice on weight control based on a habit-formation model. *Int J Obes (Lond).* 2008;32:700-7.	Less than 12 months followup
Larsen TM, Dalskov S, van Baak M, et al. The Diet, Obesity and Genes (Diogenes) dietary study in eight European countries—a comprehensive design for long-term intervention. *Obes Rev.* 2009;76-91.	Comparative effectiveness
Lasser VI, Raczynski JM, Stevens VJ, et al. Trials of Hypertension Prevention, phase II: structure and content of the weight loss and dietary sodium reduction interventions. *Ann Epidemiol.* 1995;5:156-64.	No weight or harms outcomes
Laws R; Counterweight Project Team. A new evidence-based model for weight management in primary care: the Counterweight Programme. *J Hum Nutr Diet.* 2004;17:191-208.	Does not meet design requirements in inclusion criteria
Layman DK, Evans EM, Erickson D, et al. A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *J Nutr.* 2009;139:514-21.	Comparative effectiveness
Leermakers EA, Perri MG, Shigaki CL, Fuller PR. Effects of exercise-focused versus weight-focused maintenance programs on the management of obesity. *Addict Behav.* 1999;24:219-27.	Comparative effectiveness
Lehtovirta M, Forsen B, Gullstrom M, et al. Metabolic effects of metformin in patients with impaired glucose tolerance. *Diabet Med.* 2001;18:578-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Leibbrand R, Fichter MM. Maintenance of weight loss after obesity treatment: is continuous support necessary? *Behav Res Ther.* 2002;40:1275-89.	Focus on patients in subgroups other than specified conditions
Leinum CJ, Dopp JM, Morgan BJ. Sleep-disordered breathing and obesity: pathophysiology, complications, and treatment. *Nutr Clin Pract.* 2009;24:675-87.	Does not meet design requirements in inclusion criteria
Lejeune MP, Kovacs EM, Westerterp-Plantenga MS. Additional protein intake limits weight regain after weight loss in humans. *Br J Nutr.* 2005;93:281-9.	Less than 12 months followup
Liao D, Asberry PJ, Shofer JB, et al. Improvement of BMI, body composition, and body fat distribution with lifestyle modification in Japanese Americans with impaired glucose tolerance. *Diabetes Care.* 2002;25:1504-10.	Comparative effectiveness
Lien LF, Brown AJ, Ard JD, et al. Effects of PREMIER lifestyle modifications on participants with and without the metabolic syndrome. *Hypertension.* 2007;50:609-16.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Ligibel JA, Giobbie-Hurder A, Olenczuk D, et al. Impact of a mixed strength and endurance exercise intervention on levels of adiponectin, high molecular weight adiponectin and leptin in breast cancer survivors. *Cancer Causes Control.* 2009;20:1523-8.	Less than 12 months followup
Linde JA, Jeffery RW, Finch EA, et al. Are unrealistic weight loss goals associated with outcomes for overweight women? *Obes Res.* 2004;12:569-76.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Lindegarde F. Orlistat with diet was effective and safe for weight loss and coronary risk reduction in obesity. *Evid Based Med.* 2001;6:54.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Lindholm A, Bixo M, Bjorn I, et al. Effect of sibutramine on weight reduction in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Fertil Steril.* 2008;89:1221-8.	Less than 12 months followup
Lindholm LH, Ekbom T, Dash C, et al. The impact of health care advice given in primary care on cardiovascular risk. *BMJ.* 1995;310:1105-9.	Comparative effectiveness
Lindstrom J, Eriksson JG, Valle TT, et al. Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish Diabetes Prevention Study: results from a randomized clinical trial. *J Am Soc Nephrol.* 2003;14:S108-13.	No weight or harms outcomes

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Reference	Reason for Exclusion
Lindström J, Ilanne PP, Peltonen M et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet.* 2006;368:1673-1679.	No weight or harms outcomes
Lindstrom J, Peltonen M, Eriksson JG et al. High-fibre, low-fat diet predicts long-term weight loss and decreased type 2 diabetes risk: the Finnish Diabetes Prevention Study. *Diabetologia.* 2006;49:912-920.	No weight or harms outcomes
Littman AJ, Vitiello MV, Foster-Schubert K et al. Sleep, ghrelin, leptin and changes in body weight during a 1-year moderate-intensity physical activity intervention. *Int J Obes.* 2007;31:466-475.	No weight or harms outcomes
Logue E, Sutton K, Jarjoura D, Smucker W, Baughman K, Capers C. Transtheoretical model-chronic disease care for obesity in primary care: a randomized trial. *Obes Res.* 2005;13:917-927.	Comparative effectiveness
Logue EE, Jarjoura DG, Sutton KS, Smucker WD, Baughman KR, Capers CF. Longitudinal relationship between elapsed time in the action stages of change and weight loss. *Obes Res.* 2004;12:1499-1508.	Does not meet design requirements in inclusion criteria
Lojander J, Mustajoki P, Ronka S, Mecklin P, Maasilta P. A nurse-managed weight reduction programme for obstructive sleep apnoea syndrome. *J Intern Med.* 1998;244:251-255.	Does not meet design requirements in inclusion criteria
Lombard CB, Deeks AA, Ball K, Jolley D, Teede HJ. Weight, physical activity and dietary behavior change in young mothers: short term results of the HeLP-her cluster randomized controlled trial. *Nutrition Journal.* 2009;8:17.	Less than 12 months followup
Look AHEAD Research Group, Bray G, Gregg E et al. Baseline characteristics of the randomised cohort from the Look AHEAD (Action for Health in Diabetes) study. *Diabetes & Vascular Disease Research.* 2006;3:202-215.	Comparative effectiveness
Look AHEAD Research Group, Wadden TA, West DS et al. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity.* 2006;14:737-752.	Comparative effectiveness
Lucas CP, Boldrin MN, Reaven GM. Effect of orlistat added to diet (30% of calories from fat) on plasma lipids, glucose, and insulin in obese patients with hypercholesterolemia. *Am J Cardiol.* 2003;91:961-964.	Comparative effectiveness
Lucas KH, Kaplan-Machlis B. Orlistat--a novel weight loss therapy. *Ann Pharmacother.* 2001;35:314-328.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Major GC, Alarie F, Dore J, Phouttama S, Tremblay A. Supplementation with calcium + vitamin D enhances the beneficial effect of weight loss on plasma lipid and lipoprotein concentrations. *Am J Clin Nutr.* 2007;85:54	Not one of the specified interventions
Malone DC, Raebel MA, Porter JA et al. Cost-effectiveness of sibutramine in the LOSE Weight Study: evaluating the role of pharmacologic weight-loss therapy within a weight management program. *Journal of Managed Care Pharmacy.* 2005;11:458-468.	Comparative effectiveness
Malone M, Alger-Mayer S. Binge status and quality of life after gastric bypass surgery: a one-year study. *Obes Res.* 2004;12:473-481.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Manini TM, Newman AB, Fielding R, et al. Effects of exercise on mobility in obese and nonobese older adults. *Obesity (Silver Spring).* 2010;18:1168-75.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Manning RM, Jung RT, Leese GP, Newton RW. The comparison of four weight reduction strategies aimed at overweight patients with diabetes mellitus: four-year follow-up. *Diabet Med.* 1998;15:497-502.	Comparative effectiveness
Marinilli PA, Gorin AA, Raynor HA, Tate DF, Fava JL, Wing RR. Successful weight-loss maintenance in relation to method of weight loss. *Obesity.* 2008;16:2456-2461.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Marshall NS, Grunstein RR. Losing weight in moderate to severe obstructive sleep apnoea. *BMJ.* 2009;339:b4363.	Conducted primarily in a non-relevant setting
Maruthur NM, Wang NY, Appel LJ. Lifestyle interventions reduce coronary heart disease risk: results from the PREMIER Trial. *Circulation.* 2009;119:2026	Not one of the specified interventions
Mata J, Silva MN, Vieira PN et al. Motivational "spill-over" during weight control: increased self-determination and exercise intrinsic motivation predict eating self-regulation. *Health Psychol.* 2009;28:709-716.	No weight or harms outcomes

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Reference	Reason for Exclusion
Mathus-Vliegen EM; Balance Study Group. Long-term maintenance of weight loss with sibutramine in a GP setting following a specialist guided very-low-calorie diet: a double-blind, placebo-controlled, parallel group study. *Eur J Clin Nutr.* 2005;59(Suppl 1):S31-8.	Sibutramine intervention
Matvienko OA, Hoehns JD. A lifestyle intervention study in patients with diabetes or impaired glucose tolerance: translation of a research intervention into practice. *J Am Board Fam Med.* 2009;22:535-43.	Does not meet design requirements in inclusion criteria
McConnon A, Kirk SF, Cockroft JE, et al. The Internet for weight control in an obese sample: results of a randomised controlled trial. *BMC Health Serv Res.* 2007;7:206.	High or differential attrition
McConnon A, Kirk SF, Ransley JK. Process evaluation of an Internet-based resource for weight control: use and views of an obese sample. *J Nutr Educ Beha.* 2009;41:261-7.	No weight or harms outcomes
McLaughlin T, Carter S, Lamendola C, et al. Clinical efficacy of two hypocaloric diets that vary in overweight patients with type 2 diabetes: comparison of moderate fat versus carbohydrate reductions. *Diabetes Care.* 2007;30:1877-9.	Comparative effectiveness
McMahon FG, Fujioka K, Singh BN, et al. Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. *Arch Intern Med.* 2000;160:2185-91.	Sibutramine intervention
McMahon FG, Weinstein SP, Rowe E, et al. Sibutramine is safe and effective for weight loss in obese patients whose hypertension is well controlled with angiotensin-converting enzyme inhibitors. *J Hum Hypertens.* 2002;16:5-11.	Sibutramine intervention
McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low fat, low-energy diet for weight loss in overweight adults. *Int J Obes Relat Metab Disord.* 2001;25:1503-11.	Comparative effectiveness
McNulty SJ, Ur E, Williams G. A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. *Diabetes Care.* 2003;26:125-31.	Sibutramine intervention
McTiernan A, Sorensen B, Irwin ML et al. Exercise effect on weight and body fat in men and women. *Obesity.* 2007;15:1496-512.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Meenan RT, Vogt TM, Williams AE, et al. Economic evaluation of a worksite obesity prevention and intervention trial among hotel workers in Hawaii. *J Occup Environ Med.* 2010;52(Suppl 1):S8-13.	Conducted primarily in a non-relevant setting
Mengham LH, Morris BF, Palmer CR, White AJ. Is intensive dietetic intervention effective for overweight patients with diabetes mellitus? A randomised controlled trial in a general practice. *Pract Diab Int.* 1999;16:8.	Comparative effectiveness
Menon T, Quaddus S, Cohen L. Revision of failed vertical banded gastroplasty to non-resectional Scopinaro biliopancreatic diversion: early experience. *Obes Surg.* 2006;16:1420-4.	Comparative effectiveness
Messerli-Burgy N, Znoj H, Laederach K. Eating behavior, emotional regulation, and coping strategies in obese patients following a comprehensive weight reduction program. *Verhaltenstherapie.* 2007;17:56.	Does not meet design requirements in inclusion criteria
Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum.* 2004;50:1501-10.	Comparative effectiveness
Micic D, Ivkovic-Lazar T, Dragojevic R, et al. Orlistat, a gastrointestinal lipase inhibitor, in therapy of obesity with concomitant hyperlipidemia. *Med Pregl.* 1999;52:323-33.	Less than 12 months followup
Molenaar EA, van Ameijden EJ, Vergouwe Y, et al. Effect of nutritional counselling and nutritional plus exercise counselling in overweight adults: a randomized trial in multidisciplinary primary care practice. *Fam Pract.* 2010;27:143-50.	High or differential attrition
Molitch ME, Fujimoto W, Hamman RF, et al. The Diabetes Prevention Program and its global implications. *J Am Soc Nephrol.* 2003;14(Suppl 2):S103-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Morgan PJ, Lubans DR, Collins CE, et al. 12-Month outcomes and process evaluation of the SHED-IT RCT: an Internet-based weight loss program targeting men. *Obesity (Silver Spring).* 2011;19:142-51.	Conducted primarily in a non-relevant setting

Appendix D Table 2. Studies Excluded From Review for Key Question 2

Reference	Reason for Exclusion
Muls E, Kolanowski J, Scheen A, Van Gaal L. The effects of orlistat on weight and on serum lipids in obese patients with hypercholesterolemia: a randomized, double-blind, placebo-controlled, multicentre study. *Int J Obes Relat Metab Disord.* 2001;25:1713-21.	Less than 12 months followup
Multiple Risk Factor Intervention Trial Research Group. Multiple Risk Factor Intervention Trial: risk factor changes and mortality results. *JAMA.* 1982;248:1465-77	Not one of the specified interventions
Munsch S, Biedert E, Keller U. Evaluation of a lifestyle change programme for the treatment of obesity in general practice. *Swiss Med Wkly.* 2003;133:148-54.	High or differential attrition
Murawski ME. Problem solving and the management of obesity in women from underserved rural settings. *Dissert Abstr Int B Sci Eng*. 2008;69:690.	Comparative effectiveness
Nahmias J, Kirschner M, Karetzky MS. Weight loss and OSA and pulmonary function in obesity. *N J Med.* 1993;90:48-53.	Does not meet design requirements in inclusion criteria
Nakata Y, Ohkawara K, Lee DJ, et al. Effects of additional resistance training during diet-induced weight loss on bone mineral density in overweight premenopausal women. *J Bone Min Metab.* 2008;26:172-7.	Less than 12 months followup
Nanchahal K, Townsend J, Letley L, et al. Weight-management interventions in primary care: a pilot randomised controlled trial. *Br J Gen Pract.* 2009;59:e157-66.	Less than 12 months followup
Nauta H, Hospers H, Jansen A. One-year follow-up effects of two obesity treatments on psychological well-being and weight. *Br J Health Psychol.* 2001;6:271-84.	Comparative effectiveness
Neaton JD, Grimm RH Jr, Cutler JA. Recruitment of participants for the Multiple Risk Factor Intervention Trial (MRFIT). *Control Clin Trials.* 1987;8(Suppl 4):S41-53.	Not one of the specified interventions
Nelson MS, Robbins AS, Thornton JA. An intervention to reduce excess body weight in adults with or at risk for type 2 diabetes. *Mil Med.* 2006;171:409-14.	Less than 12 months followup
Nicklas BJ, Ambrosius W, Messier SP, et al. Diet-induced weight loss, exercise, and chronic inflammation in older, obese adults: a randomized controlled clinical trial. *Am J Clin Nutr*. 2004;79:544-51.	Comparative effectiveness
Nowson CA, Worsley A, Margerison C, et al. Blood pressure change with weight loss is affected by diet type in men. *Am J Clin Nutr*. 2005;81:983-9.	Comparative effectiveness
Ockene IS, Hebert JR, Ockene JK, et al. Effect of physician-delivered nutrition counseling training and an office-support program on saturated fat intake, weight, and serum lipid measurements in a hyperlipidemic population: Worcester Area Trial for Counseling in Hyperlipidemia (WATCH). *Arch Intern Med.* 1999;159:725-31.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Olson TP, Dengel DR, Leon AS, Schmitz KH. Changes in inflammatory biomarkers following one-year of moderate resistance training in overweight women. *Int J Obes (Lond).* 2007;31:996-1003.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Olson TP, Dengel DR, Leon AS, Schmitz KH. Moderate resistance training and vascular health in overweight women. *Med Sci Sports Exerc.* 2006;38:1558-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Osei-Assibey G, Kyrou I, Adi Y, et al. Dietary and lifestyle interventions for weight management in adults from minority ethnic/non-white groups: a systematic review. *Obes Rev.* 2010;11:769-76.	Does not meet design requirements in inclusion criteria
Ostbye T, Krause KM, Lovelady CA, et al. Active Mothers Postpartum: a randomized controlled weight-loss intervention trial. *Am J Prev Med.* 2009;37:173-80.	Less than 12 months followup
O'Toole ML, Sawicki MA, Artal R. Structured diet and physical activity prevent postpartum weight retention. *J Womens Health*. 2003;12:991-8.	Comparative effectiveness
Page RC, Harnden KE, Cook JT, Turner RC. Can life-styles of subjects with impaired glucose tolerance be changed? A feasibility study. *Diabet Med.* 1992;9:562-6.	Not one of the specified interventions
Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. *Diabetes Care.* 1997;20:537-44.	Not on list of countries with HDI > 0.90
Papalazarou A, Yannakoulia M, Kavouras SA, et al. Lifestyle intervention favorably affects weight loss and maintenance following obesity surgery. *Obesity (Silver Spring).* 2010;18:1348-53.	Comparative effectiveness
Park SK, Park JH, Kwon YC, et al. The effect of combined aerobic and resistance exercise training on abdominal fat in obese middle-aged women. *J Physiol Anthropol Appl Human Sci.* 2003;22:129-35.	Does not meet design requirements in inclusion criteria

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Reference	Reason for Exclusion
Pasquali R, Colella P, Cirignotta F, et al. Treatment of obese patients with obstructive sleep apnea syndrome (OSAS): effect of weight loss and interference of otorhinolaryngoiatric pathology. *Int J Obes.* 1990;14:207-17.	Does not meet design requirements in inclusion criteria
Paul-Ebhohimhen V, Avenell A. A systematic review of the effectiveness of group versus individual treatments for adult obesity. *Obesity Facts.* 2009;2:17-24.	Does not meet design requirements in inclusion criteria
Perreault L, Kahn SE, Christophi CA, et al. Regression from pre-diabetes to normal glucose regulation in the diabetes prevention program. *Diabetes Care.* 2009;32:1583-8.	No weight or harms outcomes
Perreault L, Ma Y, Dagogo-Jack S, et al. Sex differences in diabetes risk and the effect of intensive lifestyle modification in the Diabetes Prevention Program. *Diabetes Care.* 2008;31:1416-21.	No weight or harms outcomes
Perri MG, Limacher MC, Durning PE, et al. Extended-care programs for weight management in rural communities: the Treatment of Obesity in Underserved Rural Settings (TOURS) randomized trial. *Arch Intern Med*. 2008;168:2347-54.	Comparative effectiveness
Perrio MJ, Wilton LV, Shakir SA. The safety profiles of orlistat and sibutramine: results of prescription-event monitoring studies in England. *Obesity.* 2007;15:2712-22.	Does not meet design requirements in inclusion criteria
Petrofsky J, Batt J, Berk L, et al. The effect of an aerobic dance and diet program on cardiovascular fitness, body composition, and weight loss in women. *J Appl Res.* 2008;8:179-88.	Less than 12 months followup
Phelan S, Wadden TA, Berkowitz RI, et al. Impact of weight loss on the metabolic syndrome. *Int J Obes.* 2007;31:1442-8.	Does not meet design requirements in inclusion criteria
Philippou E, Neary NM, Chaudhri O, et al. The effect of dietary glycemic index on weight maintenance in overweight subjects: a pilot study. *Obesity*. 2009;17:396-401.	Comparative effectiveness
Pinkston MM, Poston WS, Reeves RS, et al. Does metabolic syndrome mitigate weight loss in overweight Mexican American women treated for 1-year with orlistat and lifestyle modification? *Eat Weight Disord.* 2006;11:e35-41.	No placebo in medication trial
Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the Look AHEAD trial. *Diabetes Care*. 2007;30:1374-83.	Comparative effectiveness
Porter JA, Raebel MA, Conner DA, et al. The Long-term Outcomes of Sibutramine Effectiveness on Weight (LOSE Weight) study: evaluating the role of drug therapy within a weight management program in a group-model health maintenance organization. *Am J Manag Care.* 2004;10:369-76.	No placebo in medication trial
Poston WS 2nd, Haddock CK, Olvera NE, et al. Evaluation of a culturally appropriate intervention to increase physical activity. *Am J Health Behav.* 2001;25:396-406.	Not one of the specified interventions
Poston WS 2nd, Haddock CK, Pinkston MM, et al. Evaluation of a primary care-oriented brief counselling intervention for obesity with and without orlistat. *J Intern Med.* 2006;260:388-98.	Does not meet design requirements in inclusion criteria
Poston WS, Reeves RS, Haddock CK, et al. Weight loss in obese Mexican Americans treated for 1-year with orlistat and lifestyle modification. *Int J Obes Relat Metab Disord.* 2003;27:1486-93.	No placebo in medication trial
Potteiger JA, Jacobsen DJ, Donnelly JE, Hill JO. Glucose and insulin responses following 16 months of exercise training in overweight adults: the Midwest Exercise Trial. *Metabolism.* 2003;52:1175-81.	High or differential attrition
Potteiger JA, Kirk EP, Jacobsen DJ, Donnelly JE. Changes in resting metabolic rate and substrate oxidation after 16 months of exercise training in overweight adults. *Int J Sport Nutr Exerc Metab.* 2008;18:79-95.	High or differential attrition
Pritchard JE, Nowson CA, Wark JD. A worksite program for overweight middle-aged men achieves lesser weight loss with exercise than with dietary change. *J Am Diet Assoc.* 1997;97:37-42.	Conducted primarily in a non-relevant setting
Promrat K, Kleiner DE, Niemeier HM, et al. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. *Hepatology.* 2010;51:121-9.	Focus on patients in subgroups other than specified conditions
Proper KI, Hildebrandt VH, Van der Beek AJ, et a.. Effect of individual counseling on physical activity fitness and health: a randomized controlled trial in a workplace setting. *Am J Prev Med.* 2003;24:218-26.	Not focused on behavioral or pharmacological interventions designed to promote weight loss

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Reference	Reason for Exclusion
Provencher V, Begin C, Tremblay A, et al. Health-at-every-size and eating behaviors: 1-year follow-up results of a size acceptance intervention. *J Am Diet Assoc.* 2009;109:1854-61.	Not one of the specified interventions
Racette SB, Deusinger SS, Inman CL, et al. Worksite Opportunities for Wellness (WOW): effects on cardiovascular disease risk factors after 1 year. *Prev Med.* 2009;49:108-14.	Conducted primarily in a non-relevant setting
Racette SB, Weiss EP, Obert KA, et al. Modest lifestyle intervention and glucose tolerance in obese African Americans. *Obes Res*. 2001;9:348-55.	Comparative effectiveness
Racette SB, Weiss EP, Villareal DT, et al. One year of caloric restriction in humans: feasibility and effects on body composition and abdominal adipose tissue. *J Gerontol A Biol Sci Med Sci*. 2006;61:943-50.	Comparative effectiveness
Ramachandran A, Snehalatha C, Mary S, et al. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia*. 2006;49:289-97.	Not on list of countries with HDI > 0.90
Ramirez EM, Rosen JC. A comparison of weight control and weight control plus body image therapy for obese men and women. *J Consult Clin Psychol*. 2001;69:440-6.	Comparative effectiveness
Randomised trial of jejunoileal bypass versus medical treatment in morbid obesity. *Lancet.* 1979;2:1255-8.	Not one of the specified interventions
Rapoport L, Clark M, Wardle J. Evaluation of a modified cognitive-behavioural programme for weight management. *Int J Obes Relat Metab Disord*. 2000;24:1726-37.	Comparative effectiveness
Ratner RE; Diabetes Prevention Program. An update on the Diabetes Prevention Program. *Endocr Pract.* 2006;12(Suppl 1):20-4.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Razquin C, Martinez JA, Martinez-Gonzalez MA, et al. A 3 years follow-up of a Mediterranean diet rich in virgin olive oil is associated with high plasma antioxidant capacity and reduced body weight gain. *Eur J Clin Nutr.* 2009;63:1387-93.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Reaven G, Segal K, Hauptman J, et al. Effect of orlistat-assisted weight loss in decreasing coronary heart disease risk in patients with syndrome X. *Am J Cardiol.* 2001;87:827-31.	Other quality issues
Redmon JB, Bertoni AG, Connelly S, et al. Effect of the Look AHEAD study intervention on medication use and related cost to treat cardiovascular disease risk factors in individuals with type 2 diabetes. *Diabetes Care*. 2010;33:1153-8.	Comparative effectiveness
Reid IR, Horne A, Mason B, et al. Effects of calcium supplementation on body weight and blood pressure in normal older women: a randomized controlled trial. *J Clin Endocrinol Metab.* 2005;90:3824-9.	Not one of the specified interventions
Rejeski WJ, Focht BC, Messier SP, et al. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol*. 2002;21:419-26.	Comparative effectiveness
Renzaho AM, Mellor D, Boulton K, Swinburn B. Effectiveness of prevention programmes for obesity and chronic diseases among immigrants to developed countries—a systematic review. *Pub Health Nutr.* 2010;13:438-50.	Does not meet design requirements in inclusion criteria
Ricci TA, Chowdhury HA, Heymsfield SB, et al. Calcium supplementation suppresses bone turnover during weight reduction in postmenopausal women. *J Bone Miner Res.* 1998;13:1045-50.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Rimmer JH, Rauworth A, Wang E, et al. A randomized controlled trial to increase physical activity and reduce obesity in a predominantly African American group of women with mobility disabilities and severe obesity. *Prev Med.* 2009;48:473-9.	Less than 12 months followup
Rissanen P, Vahtera E, Krusius T, et al. Weight change and blood coagulability and fibrinolysis in healthy obese women. *Int J Obes Relat Metab Disord.* 2001;25:212-8.	No weight or harms outcomes
Rock CL, Flatt SW, Sherwood NE, et al. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *JAMA*. 2010;304:1803-10.	Comparative effectiveness
Rock CL, Pakiz B, Flatt SW, Quintana EL. Randomized trial of a multifaceted commercial weight loss program. *Obesity*. 2007;15:939-49.	Comparative effectiveness

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Reference	Reason for Exclusion
Rosenfalck AM, Hendel H, Rasmussen MH, et al. Minor long-term changes in weight have beneficial effects on insulin sensitivity and beta-cell function in obese subjects. *Diabetes Obes Metab.* 2002;4:19-28.	No weight or harms outcomes
Ross R, Blair SN, Godwin M, et al. Prevention and Reduction of Obesity Through Active Living (PROACTIVE): rationale, design and methods. *Br J Sports Med.* 2009;43:57-63.	No weight or harms outcomes
Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obes Res.* 2004;12:789-98.	Comparative effectiveness
Rothacker DQ, Staniszewski BA, Ellis PK. Liquid meal replacement vs traditional food: a potential model for women who cannot maintain eating habit change. *J Am Diet Assoc.* 2001;101:345-7.	Comparative effectiveness
Rothert K, Strecher VJ, Doyle LA, et al. Web-based weight management programs in an integrated health care setting: a randomized, controlled trial. *Obesity.* 2006;14:266-72.	Less than 12 months followup
Ryan DH, Johnson WD, Myers VH, et al. Nonsurgical weight loss for extreme obesity in primary care settings: results of the Louisiana Obese Subjects Study. *Arch Intern Med.* 2010;170:146-54.	No placebo in medication trial
Sabbioni ME, Dickson MH, Eychmuller S, et al. Intermediate results of health related quality of life after vertical banded gastroplasty. *Int J Obes Relat Metab Disord.* 2002;26:277-80.	Not one of the specified interventions
Saccone A, Israel A. Effects of experimenter versus significant other-controlled reinforcement and choice of target behavior on weight loss. *Behav Ther*. 1978;9:271-8.	Precedes search period
Salas SJ, Fernández BJ, Ros E, et al. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. *Arch Intern Med.* 2008;168:2449-58.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Samaras K, Ashwell S, Mackintosh AM, et al. Will older sedentary people with non-insulin-dependent diabetes mellitus start exercising? A health promotion model. *Diabetes Res Clin Pract.* 1997;37:121-8.	Not one of the specified interventions
Sampol G, Munoz X, Sagales MT, et al. Long-term efficacy of dietary weight loss in sleep apnoea/hypopnoea syndrome. *Eur Respir J.* 1998;12:1156-9.	Does not meet design requirements in inclusion criteria
Samsa GP, Kolotkin RL, Williams GR, et al. Effect of moderate weight loss on health-related quality of life: an analysis of combined data from 4 randomized trials of sibutramine vs placebo. *Am J Manag Care.* 2001;7:875-83.	Does not meet design requirements in inclusion criteria
Sanchez-Reyes L, Fanghanel G, Yamamoto J, et al. Use of sibutramine in overweight adult Hispanic patients with type 2 diabetes mellitus: a 12-month, randomized, double-blind, placebo-controlled clinical trial. *Clin Ther.* 2004;26:1427-35.	Not on list of countries with HDI > 0.90
Sarac S, Sarac F. Cardiac valve evaluation and adipokine levels in obese women treated with sibutramine. *Anadolu Kardiyoloji Dergisi.* 2010;10:226-32.	Does not meet design requirements in inclusion criteria
Sarwer DB, von Sydow GA, Vetter ML, Wadden TA. Behavior therapy for obesity: where are we now? *Curr Opin Endocrinol Diabetes Obes.* 2009;16:347-52.	Does not meet design requirements in inclusion criteria
Sbrocco T, Nedegaard RC, Stone JM, Lewis EL. Behavioral choice treatment promotes continuing weight loss: preliminary results of a cognitive-behavioral decision-based treatment for obesity. *J Consult Clin Psychol.* 1999;67:260-6.	Comparative effectiveness
Schmitz KH, Hannan PJ, Stovitz SD, et al. Strength training and adiposity in premenopausal women: Strong, Healthy, and Empowered study. *Am J Clin Nutr.* 2007;86:566-72.	No weight or harms outcomes
Schuler G, Hambrecht R, Schlierf G, et al. Regular physical exercise and low-fat diet: effects on progression of coronary artery disease. *Circulation.* 1992;86:1-11.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Schuster RJ, Tasosa J, Terwoord NA. Translational research—implementation of NHLBI Obesity Guidelines in a primary care community setting: the Physician Obesity Awareness Project. *J Nutr Health Aging.* 2008;12:S764-9.	Comparative effectiveness
Serrano-Rios M, Melchionda N, Moreno-Carretero E. Role of sibutramine in the treatment of obese type 2 diabetic patients receiving sulphonylurea therapy. *Diabet Med.* 2002;19:119-24.	Sibutramine intervention
Shapses SA, Heshka S, Heymsfield SB. Effect of calcium supplementation on weight and fat loss in women. *J Clin Endocrinol Metab.* 2004;89:632-7.	Not one of the specified interventions

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Reference	Reason for Exclusion
Shea MK, Houston DK, Nicklas BJ, et al. The effect of randomization to weight loss on total mortality in older overweight and obese adults: the ADAPT Study. *J Gerontol A Biol Sci Med Sci.* 2010;65:519-25.	Comparative effectiveness
Sherwood NE, Jeffery RW, Pronk NP, et al. Mail and phone interventions for weight loss in a managed-care setting: Weigh-To-Be 2-year outcomes. *Int J Obes.* 2006;30:1565-73.	High or differential attrition
Short KR, Vittone JL, Bigelow ML, et al. Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. *Diabetes.* 2003;52:1888-96.	Less than 12 months followup
Siegel JM, Prelip ML, Erausquin JT, Kim SA. A worksite obesity intervention: results from a group-randomized trial. *Am J Public Health.* 2010;100:327-33.	Conducted primarily in a non-relevant setting
Silva MN, Markland D, Carraca EV, et al. Exercise autonomous motivation predicts three-year weight loss in women. *Med Sci Sports Exerc.* 2011;43:728-37.	Study of overweight/obesity prevention
Simmons D, Rush E, Crook N; Te Wai o Rona Diabetes Prevention Strategy Team. Development and piloting of a community health worker-based intervention for the prevention of diabetes among New Zealand Maori in Te Wai o Rona: Diabetes Prevention Strategy. *Public Health Nutr.* 2008;11:1318-25.	Focus on patients in subgroups other than specified conditions
Sircar AR, Kumar A, Lal M. Clinical evaluation of sibutramine in obese type 2 diabetic patients refractory to dietary management. *J Assoc Physicians India.* 2001;49:885-8.	Less than 12 months followup
Sjostrom L. Analysis of the XENDOS study (Xenical in the Prevention of Diabetes in Obese Subjects). *Endocr Pract.* 2006;12(Suppl 1):31-3.	No weight or harms outcomes
Skender ML, Goodrick GK, Del Junco DJ, et al. Comparison of 2-year weight loss trends in behavioral treatments of obesity: diet, exercise, and combination interventions. *J Am Diet Assoc.* 1996;96:342-6.	Comparative effectiveness
Skinner TC, Carey ME, Cradock S, et al. Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND): process modelling of pilot study. *Patient Educ Couns.* 2006;64:369-77.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE—a randomized controlled study. *Arch Intern Med.* 2004;164:31-9.	Less than 12 months followup
Smith IG, Goulder MA. Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. *J Fam Pract.* 2001;50:505-12.	Sibutramine intervention
Smith PL, Gold AR, Meyers DA, et al. Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med.* 1985;103:850-5.	Less than 12 months followup
Southard BH, Southard DR, Nuckolls J. Clinical trial of an Internet-based case management system for secondary prevention of heart disease. *J Cardiopulm Rehabil.* 2003;23:341-8.	Less than 12 months followup
Sramek JJ, Leibowitz MT, Weinstein SP, et al. Efficacy and safety of sibutramine for weight loss in obese patients with hypertension well controlled by beta-adrenergic blocking agents: a placebo-controlled, double-blind, randomised trial. *J Hum Hypertens.* 2002;16:13-9.	Less than 12 months followup
Stahre L, Hallstrom T. A short-term cognitive group treatment program gives substantial weight reduction up to 18 months from the end of treatment: a randomized controlled trial. *Eat Weight Disord.* 2005;10:51-8.	High or differential attrition
Stefanick ML, Mackey S, Sheehan M, et al. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. *N Engl J Med.* 1998;339:12-20.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Stenius-Aarniala B, Poussa T, Kvarnstrom J, et al. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ.* 2000;320:827-32.	Comparative effectiveness
Stensel DJ, Brooke-Wavell K, Hardman AE, et al. The influence of a 1-year programme of brisk walking on endurance fitness and body composition in previously sedentary men aged 42-59 years. *Eur J Appl Physiol Occup Physiol.* 1994;68:531-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Stern L, Iqbal N, Seshadri P, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med.* 2004;140:778-85.	Comparative effectiveness
Stuart RB. A three-dimensional program for the treatment of obesity. *Behav Res Ther.* 1971;9:177-86.	Precedes search period

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Reference	Reason for Exclusion
Sun Q, Townsend MK, Okereke OI, et al. Adiposity and weight change in mid-life in relation to healthy survival after age 70 in women: prospective cohort study. *BMJ.* 2009;339:b3796.	Does not meet design requirements in inclusion criteria
Suratt PM, McTier RF, Findley LJ, et al. Effect of very-low-calorie diets with weight loss on obstructive sleep apnea. *Am J Clin Nutr.* 1992;56:S182-4.	Does not meet design requirements in inclusion criteria
Svendsen M, Helgeland M, Tonstad S. The long-term influence of orlistat on dietary intake in obese subjects with components of metabolic syndrome. *J Hum Nutr Diet.* 2009;22:55-63.	No weight or harms outcomes
Svetkey LP, Pollak KI, Yancy WS Jr, et al. Hypertension Improvement Project: randomized trial of quality improvement for physicians and lifestyle modification for patients. *Hypertension.* 2009;54:1226-33.	Not one of the specified interventions
Swinburn BA, Metcalf PA, Ley SJ. Long-term (5-year) effects of a reduced-fat diet intervention in individuals with glucose intolerance. *Diabetes Care.* 2001;24:619-24.	Conducted primarily in a non-relevant setting
Swinburn BA, Woollard GA, Chang EC, Wilson MR. Effects of reduced-fat diets consumed ad libitum on intake of nutrients, particularly antioxidant vitamins. *J Am Diet Assoc.* 1999;99:1400-5.	Conducted primarily in a non-relevant setting
Tanco S, Linden W, Earle T. Well-being and morbid obesity in women: a controlled therapy evaluation. *Int J Eat Disord.* 1998;23:325-39.	Less than 12 months followup
Tanumihardjo SA, Valentine AR, Zhang Z, et al. Strategies to increase vegetable or reduce energy and fat intake induce weight loss in adults. *Exp Biol Med.* 2009;234:542-52.	Comparative effectiveness
Tate DF, Jackvony EH, Wing RR. A randomized trial comparing human e-mail counseling, computer-automated tailored counseling, and no counseling in an Internet weight loss program. *Arch Intern Med.* 2006;166:1620-5.	Less than 12 months followup
Tate DF, Jackvony EH, Wing RR. Effects of Internet behavioral counseling on weight loss in adults at risk for type 2 diabetes: a randomized trial. *JAMA.* 2003;289:1833-6.	Comparative effectiveness
Tate DF, Jeffery RW, Sherwood NE, Wing RR. Long-term weight losses associated with prescription of higher physical activity goals: are higher levels of physical activity protective against weight regain? *Am J Clin Nutr.* 2007;85:954-9.	Comparative effectiveness
Tate DF, Wing RR, Winett RA. Using Internet technology to deliver a behavioral weight loss program. *JAMA.* 2001;285:1172-7.	Less than 12 months followup
Teixeira PJ, Going SB, Houtkooper LB, et al. Resistance training in postmenopausal women with and without hormone therapy. *Med Sci Sports Exerc.* 2003;35:555-62.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
ODES Investigators. The Oslo Diet and Exercise Study (ODES): design and objectives. *Control Clin Trials.* 1993;14:229-43.	No weight or harms outcomes
Thomas TR, Warner SO, Dellsperger KC, et al. Exercise and the metabolic syndrome with weight regain. *J Appl Physiol.* 2010;109:3-10.	Comparative effectiveness
Thompson WG, Rostad HN, Janzow DJ, et al. Effect of energy-reduced diets high in dairy products and fiber on weight loss in obese adults. *Obes Res.* 2005;13:1344-53.	Comparative effectiveness
Tiikkainen M, Bergholm R, Rissanen A, et al. Effects of equal weight loss with orlistat and placebo on body fat and serum fatty acid composition and insulin resistance in obese women. *Am J Clin Nutr.* 2004;79:22-30.	Less than 12 months followup
Tinker LF, Bonds DE, Margolis KL, et al. Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: the Women's Health Initiative randomized controlled dietary modification trial. *Arch Intern Med.* 2008;168:1500-11.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Toft U, Kristoffersen L, Ladelund S, et al. The effect of adding group-based counselling to individual lifestyle counselling on changes in dietary intake: the Inter99 study—a randomized controlled trial. *Int J Behav Nutr Phys Act.* 2008;5:59.	No weight or harms outcomes
Toobert DJ, Glasgow RE, Radcliffe JL. Physiologic and related behavioral outcomes from the Women's Lifestyle Heart Trial. *Ann Behav Med.* 2000;22:1-9.	Focus on patients in subgroups other than specified conditions
What is TOPS (Take Off Pounds Sensibly). Milwaukee, WI: TOPS Club, Inc; 2011. http://www.tops.org/TOPSInformation/AboutTOPS.aspx	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Trento M, Passera P, Tomalino M, et al. Group visits improve metabolic control in type 2 diabetes: a 2-year follow-up. *Diabetes Care.* 2001;24:995-1000.	Comparative effectiveness

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Reference	Reason for Exclusion
Trolle B, Flyvbjerg A, Kesmodel U, Lauszus FF. Efficacy of metformin in obese and non-obese women with polycystic ovary syndrome: a randomized, double-blinded, placebo-controlled cross-over trial. *Hum Reprod.* 2007;22:2967-73.	Less than 12 months followup
Tsai AG, Wadden TA, Rogers MA, et al. A primary care intervention for weight loss: results of a randomized controlled pilot study. *Obesity (Silver Spring).* 2010;18:1614-8.	Comparative effectiveness
Tsai AG, Wadden TA. Treatment of obesity in primary care practice in the United States: a systematic review. *J Gen Intern Med.* 2009;24:1073-9.	Does not meet design requirements in inclusion criteria
Tseng MC, Lee MB, Chen SY, et al. Response of Taiwanese obese binge eaters to a hospital-based weight reduction program. *J Psychosom Res.* 2004;57:279-85.	Focus on patients in subgroups other than specified conditions
Tuomilehto H, Peltonen M, Partinen M, et al. Sleep duration, lifestyle intervention, and incidence of type 2 diabetes in impaired glucose tolerance: the Finnish Diabetes Prevention Study. *Diabetes Care.* 2009;32:1965-71.	No weight or harms outcomes
Tuomilehto HP, Seppa JM, Partinen MM, et al. Lifestyle intervention with weight reduction: first-line treatment in mild obstructive sleep apnea. *Am J Resp Crit Care Med.* 2009;179:320-7.	Less than 12 months followup
Turnin MC, Bourgeois O, Cathelineau G, et al. Multicenter randomized evaluation of a nutritional education software in obese patients. *Diabetes Metab.* 2001;27:139-47.	Comparative effectiveness
Tuthill A, Quinn A, McColgan D, et al. A prospective randomized controlled trial of lifestyle intervention on quality of life and cardiovascular risk score in patients with obesity and type 2 diabetes. *Diabetes Obes Metab.* 2007;9:917-9	Less than 12 months followup
Uusi-Rasi K, Rauhio A, Kannus P, et al. Three-month weight reduction does not compromise bone strength in obese premenopausal women. *Bone.* 2010;46:1286-93.	Does not meet design requirements in inclusion criteria
Van Aggel-Leijssen DP, Saris WH, Hul GB, van Baak MA. Long-term effects of low-intensity exercise training on fat metabolism in weight-reduced obese men. *Metabolism.* 2002;51:1003-10.	Comparative effectiveness
Van Aggel-Leijssen DP, Saris WH, Hul GB, van Baak MA. Short-term effects of weight loss with or without low-intensity exercise training on fat metabolism in obese men. *Am J Clin Nutr.* 2001;73:523-31.	Comparative effectiveness
Van Aggel-Leijssen DP, Saris WH, Wagenmakers AJ, et al. The effect of low-intensity exercise training on fat metabolism of obese women. *Obes Res.* 2001;9:86-96.	Comparative effectiveness
Van Aggel-Leijssen DP, Saris WH, Wagenmakers AJ, et al. Effect of exercise training at different intensities on fat metabolism of obese men. *J Appl Physiol.* 2002;92:1300-9.	Comparative effectiveness
Van Gaal LF, Broom JI, Enzi G, Toplak H. Efficacy and tolerability of orlistat in the treatment of obesity: a 6-month dose-ranging study. *Eur J Clin Pharmacol.* 1998;54:125-32.	Less than 12 months followup
van Sluijs EM, van Poppel MN, Twisk JW, et al. Effect of a tailored physical activity intervention delivered in general practice settings: results of a randomized controlled trial. *Am J Public Health.* 2005;95:1825-31.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
van Wier MF, Ariens GA, Dekkers JC, et al. ALIFE@Work: a randomised controlled trial of a distance counselling lifestyle programme for weight control among an overweight working population. *BMC Public Health.* 2006;6:140.	Less than 12 months followup
van Wier MF, Ariens GA, Dekkers JC, et al. Phone and e-mail counselling are effective for weight management in an overweight working population: a randomized controlled trial. *BMC Public Health.* 2009;9:6.	Less than 12 months followup
VanWormer JJ, Martinez AM, Benson GA, et al. Telephone counseling and home telemonitoring: the Weigh By Day Trial. *Am J Health Behav.* 2009;33:445-54.	Comparative effectiveness
Velthuis MJ, Schuit AJ, Peeters PH, Monninkhof EM. Exercise program affects body composition but not weight in postmenopausal women. *Menopause.* 2009;16:777-84.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Venditti EM, Bray GA, Carrion-Petersen ML, et al. First versus repeat treatment with a lifestyle intervention program: attendance and weight loss outcomes. *Int J Obes.* 2008;32:1537-44.	No weight or harms outcomes
Veverka DV, Anderson J, Auld GW, et al. Use of the stages of change model in improving nutrition and exercise habits in enlisted Air Force men. *Mil Med.* 2003;168:373-9.	Less than 12 months followup

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Reference	Reason for Exclusion
Vidgren HM, Agren JJ, Valve RS, et al. The effect of orlistat on the fatty acid composition of serum lipid fractions in obese subjects. *Clin Pharmacol Ther.* 1999;66:315-22.	No weight or harms outcomes
Villareal DT, Banks MR, Patterson BW, et al. Weight loss therapy improves pancreatic endocrine function in obese older adults. *Obesity.* 2008;16:1349-54.	No weight or harms outcomes
Villareal DT, Fontana L, Weiss EP, et al. Bone mineral density response to caloric restriction-induced weight loss or exercise-induced weight loss: a randomized controlled trial. *Arch Intern Med.* 2006;166:2502-10.	Comparative effectiveness
Vissers D, Verrijken A, Mertens I, et al. Effect of long-term whole body vibration training on visceral adipose tissue: a preliminary report. *Obesity Facts.* 2010;3:93-100.	Other quality issues
Volpe SL, Kobusingye H, Bailur S, Stanek E. Effect of diet and exercise on body composition, energy intake and leptin levels in overweight women and men. *J Am Coll Nutr.* 2008;27:195-208.	Comparative effectiveness
von Huth SL, Ladelund S, Borch-Johnsen K, Jorgensen T. A randomized multifactorial intervention study for prevention of ischaemic heart disease (Inter99): the long-term effect on physical activity. *Scand J Public Health.* 2008;36:380-8.	No weight or harms outcomes
Wadden TA, Berkowitz RI, Sarwer DB, et al. Benefits of lifestyle modification in the pharmacologic treatment of obesity: a randomized trial. *Arch Intern Med.* 2001;161:218-27.	Comparative effectiveness
Wadden TA, Berkowitz RI, Womble LG, et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity. *N Engl J Med.* 2005;353:2111-20.	No placebo in medication trial
Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity.* 2009;17:713-22.	Comparative effectiveness
Wardle J, Rogers P, Judd P, et al. Randomized trial of the effects of cholesterol-lowering dietary treatment on psychological function. *Am J Med.* 2000;108:547-53.	Less than 12 months followup
Waring ME, Roberts MB, Parker DR, Eaton CB. Documentation and management of overweight and obesity in primary care. *J Am Board Fam Med.* 2009;22:544-52.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Warren M, Schmitz KH. Safety of strength training in premenopausal women: musculoskeletal injuries from a two-year randomized trial. *Am J Health Promot.* 2009;23:309-14.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Warziski MT, Sereika SM, Styn MA, et al. Changes in self-efficacy and dietary adherence: the impact on weight loss in the PREFER study. *J Behav Med.* 2008;31:81-92.	Comparative effectiveness
Wassertheil-Smoller S, Oberman A, Blaufox MD, et al. The Trial of Antihypertensive Interventions and Management (TAIM) study: final results with regard to blood pressure, cardiovascular risk, and quality of life. *Am J Hypertens.* 1992;5:37-44.	No weight or harms outcomes
Wee CC, Davis RB, Phillips RS. Stage of readiness to control weight and adopt weight control behaviors in primary care. *J Gen Intern Med.* 2005;20:410-5.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Weiner R, Bockhorn H, Rosenthal R, Wagner D. A prospective randomized trial of different laparoscopic gastric banding techniques for morbid obesity. *Surg Endosc.* 2001;15:63-8.	Not one of the specified interventions
Weiss EP, Racette SB, Villareal DT, et al. Improvements in glucose tolerance and insulin action induced by increasing energy expenditure or decreasing energy intake: a randomized controlled trial. *Am J Clin Nutr.* 2006;84:1033-42.	Comparative effectiveness
West DS, DiLillo V, Bursac Z, et al. Motivational interviewing improves weight loss in women with type 2 diabetes. *Diabetes Care.* 2007;30:1081-7.	Comparative effectiveness
Whittemore R, Melkus G, Wagner J, et al. Translating the Diabetes Prevention Program to primary care: a pilot study. *Nurs Res.* 2009;58:2-12.	Less than 12 months followup
Williamson DA, Martin CK, Anton SD, et al. Is caloric restriction associated with development of eating-disorder symptoms? Results from the CALERIE trial. *Health Psychol.* 2008;27(Suppl 1)S32:-42.	Comparative effectiveness
Williamson DA, Rejeski J, Lang W, et al. Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. *Arch Intern Med.* 2009;169:163-71.	Comparative effectiveness
Williamson DF. Re: randomized trial of weight loss and total mortality. *J Gerontol A Biol Sci Med Sci.* 2010;65:904.	Does not meet design requirements in inclusion criteria

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Reference	Reason for Exclusion
Wing RR, Anglin K. Effectiveness of a behavioral weight control program for blacks and whites with NIDDM. *Diabetes Care.* 1996;19:409-13.	Comparative effectiveness
Wing RR, Creasman JM, West DS, et al. Improving urinary incontinence in overweight and obese women through modest weight loss. *Obstetrics Gynecol.* 2010;116:284-92.	Comparative effectiveness
Wing RR, Epstein LH, Paternostro-Bayles M, et al. Exercise in a behavioural weight control programme for obese patients with type 2 (non-insulin-dependent) diabetes. *Diabetologia.* 1988;31:902-9.	Comparative effectiveness
Wing RR, Tate DF, Gorin AA, et al. STOP regain: are there negative effects of daily weighing? *J Consult Clin Psychol.* 2007;75:652-6.	No weight or harms outcomes
Wing RR, Tate DF, Gorin AA, et al. A self-regulation program for maintenance of weight loss. *N Engl J Med.* 2006;355:1563-71.	Comparative effectiveness
Wing RR, West DS, Grady D, et al. Effect of weight loss on urinary incontinence in overweight and obese women: results at 12 and 18 months. *J Urol.* 2010;184:1005-10.	Comparative effectiveness
Wing RR. Behavioral approaches to the treatment of obesity. In: Bray G, Bouchard C, James WP, eds. *Handbook of Obesity*. New York: Marcel Dekker; 1998:855-73.	Does not meet design requirements in inclusion criteria
Wing RR. Behavioral weight control. In: Wadden TA, Stunkard AJ, eds. *Handbook of Obesity Treatment*. New York: Guilford Press; 2002:301-16.	Does not meet design requirements in inclusion criteria
Wirth A, Krause J. Long-term weight loss with sibutramine: a randomized controlled trial. *JAMA.* 2001;286:1331-9.	Sibutramine intervention
Wister A, Loewen N, Kennedy-Symonds H, et al. One-year follow-up of a therapeutic lifestyle intervention targeting cardiovascular disease risk. *Can Med Assoc J.* 2007;177:859-65.	Not one of the specified interventions
Wolf AM, Conaway MR, Crowther JQ, et al. Translating lifestyle intervention to practice in obese patients with type 2 diabetes: Improving Control with Activity and Nutrition (ICAN) study. *Diabetes Care.* 2004;27:1570-6.	Comparative effectiveness
Wolf AM, Siadaty MS, Crowther JQ, et al. Impact of lifestyle intervention on lost productivity and disability: Improving Control with Activity and Nutrition. *J Occup Environ Med.* 2009;51:139-45.	Comparative effectiveness
Womble LG, Wadden TA, McGuckin BG, et al. A randomized controlled trial of a commercial internet weight loss program. *Obes Res.* 2004;12:1011-8.	Comparative effectiveness
Wong SY, Lau EM, Lau WW, Lynn HS. Is dietary counselling effective in increasing dietary calcium, protein and energy intake in patients with osteoporotic fractures? A randomized controlled clinical trial. *J Hum Nutr Diet.* 2004;17:359-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Woo J, Sea MM, Tong P, et al. Effectiveness of a lifestyle modification programme in weight maintenance in obese subjects after cessation of treatment with orlistat. *J Eval Clin Pract.* 2007;13:853-9.	Less than 12 months followup
Wosje KS, Kalkwarf HJ. Lactation, weaning, and calcium supplementation: effects on body composition in postpartum women. *Am J Clin Nutr.* 2004;80:423-9.	Not one of the specified interventions
Wright AD, Cull CA, MacLeod KM, et al. Hypoglycemia in type 2 diabetic patients randomized to and maintained on monotherapy with diet, sulfonylurea, metformin, or insulin for 6 years from diagnosis: UKPDS73. *J Diabetes Complications.* 2006;20:395-401.	Comparative effectiveness
Wylie-Rosett J, Swencionis C, Ginsberg M, et al. Computerized weight loss intervention optimizes staff time: the clinical and cost results of a controlled clinical trial conducted in a managed care setting. *J Am Diet Assoc.* 2001;101:1155-62.	Comparative effectiveness
Yancey AK, McCarthy WJ, Harrison GG, et al. Challenges in improving fitness: results of a community-based, randomized, controlled lifestyle change intervention. *J Womens Health.* 2006;15:412-29.	Not one of the specified interventions
Yassine HN, Marchetti CM, Krishnan RK, et al. Effects of exercise and caloric restriction on insulin resistance and cardiometabolic risk factors in older obese adults—a randomized clinical trial. *J Gerontol A Biol Sci Med Sci.* 2009;64:90-5.	Comparative effectiveness
Yates T, Davies M, Gorely T, et al. Effectiveness of a pragmatic education program designed to promote walking activity in individuals with impaired glucose tolerance: a randomized controlled trial. *Diabetes Care.* 2009;32:1404-10.	Not one of the specified interventions
Yeh MC, Rodriguez E, Nawaz H, et al. Technical skills for weight loss: 2-y follow-up results of a randomized trial. *Int J Obes Relat Metab Disord.* 2003;27:1500-6.	Comparative effectiveness

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Reference	Reason for Exclusion
Zannad F, Gille B, Grentzinger A, et al. Effects of sibutramine on ventricular dimensions and heart valves in obese patients during weight reduction. *Am Heart J.* 2002;144:508-15.	Sibutramine intervention
Zavoral JH. Treatment with orlistat reduces cardiovascular risk in obese patients. *J Hypertens.* 1998;16:2013-7.	Other quality issues
Zemel MB, Richards J, Mathis S, et al. Dairy augmentation of total and central fat loss in obese subjects. *Int J Obes.* 2005;29:391-7.	Not one of the specified interventions
Zemel MB, Richards J, Milstead A, Campbell P. Effects of calcium and dairy on body composition and weight loss in African-American adults. *Obes Res.* 2005;13:1218-25.	Less than 12 months followup
Zemel MB, Thompson W, Milstead A, et al. Calcium and dairy acceleration of weight and fat loss during energy restriction in obese adults. *Obes Res.* 2004;12:582-90.	Comparative effectiveness
The Hypertension Prevention Trial: three-year effects of dietary changes on blood pressure. *Arch Intern Med.* 1990;150:153-62.	No weight outcomes
Anderssen S, Holme I, Urdal P, Hjermann I. Diet and exercise intervention have favourable effects on blood pressure in mild hypertensives: the Oslo Diet and Exercise Study (ODES). *Blood Press.* 1995;4:343-9.	No weight outcomes
Berne C; Orlistat Study Team. A randomized study of orlistat in combination with a weight management programme in obese patients with type 2 diabetes treated with metformin. *Diabet Med.* 2005;22:612-8.	No weight outcomes
Burke V, Beilin LJ, Cutt HE, et al. Effects of a lifestyle programme on ambulatory blood pressure and drug dosage in treated hypertensive patients: a randomized controlled trial. *J Hypertens.* 2005;23:1241-9.	No weight outcomes
Christian JG, Bessesen DH, Byers TE, et al. Clinic-based support to help overweight patients with type 2 diabetes increase physical activity and lose weight. *Arch Intern Med.* 2008;168:141-6.	No weight outcomes
Cohen MD, D'Amico FJ, Merenstein JH. Weight reduction in obese hypertensive patients. *Fam Med.* 1991;23:25-8.	No weight outcomes
Cussler EC, Teixeira PJ, Going SB, et al. Maintenance of weight loss in overweight middle-aged women through the Internet. *Obesity.* 2008;16:1052-60.	No weight outcomes
Davidson MH, Hauptman J, DiGirolamo M, et al. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat: a randomized controlled trial. *JAMA.* 1999;281:235-42.	No weight outcomes
Davis BR, Oberman A, Blaufox MD, et al. Effect of antihypertensive therapy on weight loss. *Hypertension.* 1992;19:393-9.	No weight outcomes
Davis BR, Blaufox MD, Hawkins CM, et al. Trial of Antihypertensive Interventions and Management: design, methods, and selected baseline results. *Control Clin Trials.* 1989;10:11-30.	No weight outcomes
Derosa G, Maffioli P, Salvadeo SA, et al. Comparison of orlistat treatment and placebo in obese type 2 diabetic patients. *Exp Opin Pharmacother.* 2010;11:1971-82.	No weight outcomes
Derosa G, Mugellini A, Ciccarelli L, Fogari R. Randomized, double-blind, placebo-controlled comparison of the action of orlistat, fluvastatin, or both on anthropometric measurements, blood pressure, and lipid profile in obese patients with hypercholesterolemia prescribed a standardized diet. *Clin Ther.* 2003;25:1107-22.	No weight outcomes
Finer N, James WP, Kopelman PG, et al. One-year treatment of obesity: a randomized, double-blind, placebo-controlled, multicentre study of orlistat, a gastrointestinal lipase inhibitor. *Int J Obes Relat Metab Disord.* 2000;24:306-13.	No weight outcomes
Frank LL, Sorensen BE, Yasui Y, et al. Effects of exercise on metabolic risk variables in overweight postmenopausal women: a randomized clinical trial. *Obes Res.* 2005;13:615-25.	No weight outcomes
Gambineri A, Patton L, Vaccina A, et al. Treatment with flutamide, metformin, and their combination added to a hypocaloric diet in overweight-obese women with polycystic ovary syndrome: a randomized, 12-month, placebo-controlled study. *J Clin Endocrinol Metab.* 2006;91:3970-80.	No weight outcomes
Haapala I, Barengo NC, Biggs S, et al. Weight loss by mobile phone: a 1-year effectiveness study. *Public Health Nutr.* 2009;12:2382-91.	No weight outcomes

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Reference	Reason for Exclusion
Hanefeld M, Sachse G. The effects of orlistat on body weight and glycaemic control in overweight patients with type 2 diabetes: a randomized, placebo-controlled trial. *Diabetes Obes Metab.* 2002;4:415-23.	No weight outcomes
Hansson L, Zanchetti A. The Hypertension Optimal Treatment (HOT) study—patient characteristics: randomization, risk profiles, and early blood pressure results. *Blood Press.* 1994;3:322-7.	No weight outcomes
Hill JO, Hauptman J, Anderson JW, et al. Orlistat, a lipase inhibitor, for weight maintenance after conventional dieting: a 1-y study. *Am J Clin Nutr.* 1999;69:1108-16.	No weight outcomes
Hollander PA, Elbein SC, Hirsch IB, et al. Role of orlistat in the treatment of obese patients with type 2 diabetes: a 1-year randomized double-blind study. *Diabetes Care.* 1998;21:1288-94.	No weight outcomes
Hollis JF, Satterfield S, Smith F, et al. Recruitment for phase II of the Trials of Hypertension Prevention: effective strategies and predictors of randomization. *Ann Epidemiol.* 1995;5:140-8.	No weight outcomes
Irwin ML, Yasui Y, Ulrich CM, et al. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. *JAMA.* 2003;289:323-30.	No weight outcomes
James WP, Avenell A, Broom J, Whitehead J. A one-year trial to assess the value of orlistat in the management of obesity. *Int J Obes Relat Metab Disord.* 1997;21(Suppl 3):S24-30.	No weight outcomes
Jeffery RW, Wing RR. Long-term effects of interventions for weight loss using food provision and monetary incentives. *J Consult Clin Psychol.* 1995;63:793-6.	No weight outcomes
Jeffery RW, Wing RR, Thorson C, et al. Strengthening behavioral interventions for weight loss: a randomized trial of food provision and monetary incentives. *J Consult Clin Psychol.* 1993;61:1038-45.	No weight outcomes
Jones DW, Miller ME, Wofford MR, et al. The effect of weight loss intervention on antihypertensive medication requirements in the Hypertension Optimal Treatment (HOT) study. *Am J Hypertens.* 1999;12:1175-80.	No weight outcomes
Kastarinen MJ, Puska PM, Korhonen MH, et al. Non-pharmacological treatment of hypertension in primary health care: a 2-year open randomized controlled trial of lifestyle intervention against hypertension in eastern Finland. *J Hypertens.* 2002;20:2505-12.	No weight outcomes
Krempf M, Louvet JP, Allanic H, et al. Weight reduction and long-term maintenance after 18 months treatment with orlistat for obesity. *Int J Obes Relat Metab Disord.* 2003;27:591-7.	No weight outcomes
Kuller LH, Simkin-Silverman LR, Wing RR, et al. Women's Healthy Lifestyle Project—a randomized clinical trial: results at 54 months. *Circulation.* 2001;103:32-7.	No weight outcomes
Langford HG, Blaufox MD, Oberman A, et al. Dietary therapy slows the return of hypertension after stopping prolonged medication. *JAMA.* 1985;253:657-64.	No weight outcomes
Langford HG, Davis BR, Blaufox D, et al. Effect of drug and diet treatment of mild hypertension on diastolic blood pressure. *Hypertension.* 1991;17:210-7.	No weight outcomes
Lindgarde F. The effect of orlistat on body weight and coronary heart disease risk profile in obese patients: the Swedish Multimorbidity Study. *J Intern Med.* 2000;248:245-54.	No weight outcomes
Martin DP, Rhode PC, Dutton GR, et al. A primary care weight management intervention for low-income African-American women. *Obesity.* 2006;14:1412-20.	No weight outcomes
Martin PD, Dutton GR, Rhode PC, et al. Weight loss maintenance following a primary care intervention for low-income minority women. *Obesity.* 2008;16:2462-7.	No weight outcomes
Mayer-Davis EJ, D'Antonio AM, Smith SM, et al. Pounds Off With Empowerment (POWER): a clinical trial of weight management strategies for black and white adults with diabetes who live in medically underserved rural communities. *Am J Public Health.* 2004;94:1736-42.	No weight outcomes
Mensink M, Blaak EE, Corpeleijn E, et al. Lifestyle intervention according to general recommendations improves glucose tolerance. *Obes Res.* 2003;11:1588-96.	No weight outcomes
Mensink M, Corpeleijn E, Feskens EJ, et al. Study on Lifestyle-intervention and Impaired Glucose Tolerance Maastricht (SLIM): design and screening results. *Diabetes Res Clin Pract.* 2003;61:49-58.	No weight outcomes

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Reference	Reason for Exclusion
Miles JM, Leiter L, Hollander P, et al. Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. *Diabetes Care.* 2002;25:1123-8.	No weight outcomes
Mitsui T, Shimaoka K, Tsuzuku S, et al. Gentle exercise of 40 minutes with dietary counseling is effective in treating metabolic syndrome. *Tohoku J Exp Med.* 2008;215:355-61.	No weight outcomes
Mohanka M, Irwin M, Heckbert SR, et al. Serum lipoproteins in overweight/obese postmenopausal women: a one-year exercise trial. *Med Sci Sports Exerc.* 2006;38:231-9.	No weight outcomes
Moore H, Summerbell CD, Greenwood DC, et al. Improving management of obesity in primary care: cluster randomised trial. *BMJ.* 2003;327:1085.	No weight outcomes
Narayan KM, Hoskin M, Kozak D, et al. Randomized clinical trial of lifestyle interventions in Pima Indians: a pilot study. *Diabet Med.* 1998;15:66-72.	No weight outcomes
Park HA, Lee JS, Kuller LH, Cauley JA. Effects of weight control during the menopausal transition on bone mineral density. *J Clin Endocrinol Metab.* 2007;92:3809-15.	No weight outcomes
Perri MG, McAllister DA, Gange JJ, et al. Effects of four maintenance programs on the long-term management of obesity. *J Consult Clin Psychol.* 1988;56:529-34.	No weight outcomes
Pritchard DA, Hyndman J, Taba F. Nutritional counselling in general practice: a cost effective analysis. *J Epidemiol Community Health.* 1999;53:311-6.	No weight outcomes
Silva MN, Markland D, Minderico CS, et al. A randomized controlled trial to evaluate self-determination theory for exercise adherence and weight control: rationale and intervention description. *BMC Public Health.* 2008;8:234.	No weight outcomes
Silva MN, Vieira PN, Coutinho SR, et al. Using self-determination theory to promote physical activity and weight control: a randomized controlled trial in women. *J Behav Med.* 2010;33:110-22.	No weight outcomes
Simkin-Silverman LR, Wing RR, Boraz MA, Kuller LH. Lifestyle intervention can prevent weight gain during menopause: results from a 5-year randomized clinical trial. *Ann Behav Med.* 2003;26:212-20.	No weight outcomes
Simkin-Silverman LR, Wing RR, Boraz MA, et al. Maintenance of cardiovascular risk factor changes among middle-aged women in a lifestyle intervention trial. *Womens Health.* 1998;4:255-71.	No weight outcomes
Sjostrom L, Rissanen A, Andersen T, et al. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. *Lancet.* 1998;352:167-72.	No weight outcomes
Stevens VJ, Obarzanek E, Cook NR, et al. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Ann Intern Med.* 2001;134:1-11.	No weight outcomes
Stevens VJ, Corrigan SA, Obarzanek E, et al. Weight loss intervention in phase 1 of the Trials of Hypertension Prevention. *Arch Intern Med.* 1993;153:849-58.	No weight outcomes
Teixeira PJ, Silva MN, Coutinho SR, et al. Mediators of weight loss and weight loss maintenance in middle-aged women. *Obesity (Silver Spring).* 2010;18:725-35.	No weight outcomes
ter Bogt NC, Bemelmans WJ, Beltman FW, et al. Preventing weight gain: one-year results of a randomized lifestyle intervention. *Am J Prev Med.* 2009;37:270-7.	No weight outcomes
HOT Study Group. The Hypertension Optimal Treatment study (the HOT study). *Blood Press.* 1993;2:62-8.	No weight outcomes
Trials of Hypertention Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. *Arch Intern Med*. 1997;157:657-67.	No weight outcomes
Trials of Hypertension Prevention Collaborative Research Group. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels: results of the Trials of Hypertension Prevention, phase I. *JAMA.* 1992;267:1213-20.	No weight outcomes
Villareal DT, Miller BV III, Banks M, et al. Effect of lifestyle intervention on metabolic coronary heart disease risk factors in obese older adults. *Am J Clin Nutr.* 2006;84:1317-23.	No weight outcomes
Villareal DT, Banks M, Sinacore DR, et al. Effect of weight loss and exercise on frailty in obese older adults. *Arch Intern Med.* 2006;166:860-6.	No weight outcomes

Appendix D Table 2. Studies Excluded From Review for Key Question 2

Reference	Reason for Exclusion
Villareal DT, Shah K, Banks MR, et al. Effect of weight loss and exercise therapy on bone metabolism and mass in obese older adults: a one-year randomized controlled trial. *J Clin Endocrinol Metab.* 2008;93:2181-7.	No weight outcomes
Wassertheil-Smoller S, Langford HG, Blaufox MD, et al. Effective dietary intervention in hypertensives: sodium restriction and weight reduction. *J Am Diet Assoc.* 1985;85:423-30.	No weight outcomes
Werkman A, Hulshof PJ, Stafleu A, et al. Effect of an individually tailored one-year energy balance programme on body weight, body composition and lifestyle in recent retirees: a cluster randomised controlled trial. *BMC Public Health.* 2010;10:110.	No weight outcomes
Whelton PK, Hebert PR, Cutler J, et al. Baseline characteristics of participants in phase I of the Trials of Hypertension Prevention. *Ann Epidemiol*. 1992;2:295-310.	No weight outcomes
Wood PD, Stefanick ML, Dreon DM, et al. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N Engl J Med.* 1988;319:1173-9.	No weight outcomes
Woollard J, Burke V, Beilin LJ, et al. Effects of a general practice-based intervention on diet, body mass index and blood lipids in patients at cardiovascular risk. *J Cardiovasc Risk.* 2003;10:31-40.	No weight outcomes
Lakerveld J, Bot SD, Chinapaw MJ, et al. Primary prevention of diabetes mellitus type 2 and cardiovascular diseases using a cognitive behavior program aimed at lifestyle changes in people at risk: design of a randomized controlled trial. *BMC Endocr Disord.* 2008;8:6.	No weight or harms outcomes
Davey SG, Bracha Y, Svendsen KH, et al. Incidence of type 2 diabetes in the randomized Multiple Risk Factor Intervention Trial. *Ann Intern Med.* 2005;142:313-22	Not one of the specified interventions
Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract.* 2005;67:152-62.	Comparative effectiveness
Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. *Arch Intern Med.* 1559;168:1550-9.	Comparative effectiveness
Jacob S, Rabbia M, Meier MK, Hauptman J. Orlistat 120 mg improves glycaemic control in type 2 diabetic patients with or without concurrent weight loss. *Diabetes Obes Metab.* 2009;11:361-71.	Less than 12 months followup

Appendix D Table 3. Studies Excluded From Review for Key Question 3

Reference	Reason for Exclusion
Aadahl M, von Huth SL, Pisinger C, et al. Five-year change in physical activity is associated with changes in cardiovascular disease risk factors. *Prev Med.* 2009;48(4):326-31.	Does not meet design requirements in inclusion criteria
Acharya NV, Wilton LV, Shakir SA. Safety profile of orlistat: results of a prescription-event monitoring study. *Int J Obes.* 2006;30:1645-52.	Does not meet design requirements in inclusion criteria
Agurs-Collins TD, Kumanyika SK, Ten Have TR, Adams-Campbell LL. A randomized controlled trial of weight reduction and exercise for diabetes management in older African-American subjects. *Diabetes Care.* 1997;20:1503-11.	Less than 12 months followup
Akinson RL. Conjugated linoleic acid for altering body composition and treating obesity. In: Yurawecz MP, Mossoba MM, Kramer JK, et al, eds. *Advances in Conjugated Linoleic Acid Research.* Vol 1. Champaign, IL: AOCS Press; 1999:348-53.	Does not meet design requirements in inclusion criteria
Alhassan S, Kim S, Bersamin A, et al. Dietary adherence and weight loss success among overweight women: results from the A TO Z weight loss study. *Int J Obes.* 2008;32:985-91.	Comparative effectiveness
Allen P, Thompson JL, Herman CJ,, et al. Impact of periodic follow-up testing among urban American Indian women with impaired fasting glucose. *Preventing Chronic Disease.* 2008;5:A76.	Not one of the specified interventions
Andersen RE, Wadden TA, Bartlett SJ, et al. Effects of lifestyle activity vs structured aerobic exercise in obese women: a randomized trial. *JAMA.* 1999;281:335-40.	Comparative effectiveness
Anderson JW, Grant L, Gotthelf L, Stifler LT. Weight loss and long-term follow-up of severely obese individuals treated with an intense behavioral program. *Int J Obes.* 2007;31:488-93.	Does not meet design requirements in inclusion criteria
Anderssen SA, Carroll S, Urdal P, Holme I. Combined diet and exercise intervention reverses the metabolic syndrome in middle-aged males: results from the Oslo Diet and Exercise Study. *Scand J Med Sci Sports.* 2007;17:687-95.	No weight outcomes
Anderssen SA, Holme I, Urdal P, Hjermann I. Associations between central obesity and indexes of hemostatic, carbohydrate and lipid metabolism: results of a 1-year intervention from the Oslo Diet and Exercise Study. *Scand J Med Sci Sports.* 1998;8:109-15.	Does not include specified weight outcomes
Andersson K, Karlstrom B, Freden S, et al. A two-year clinical lifestyle intervention program for weight loss in obesity. *Food Nutr Res.* 2008;52.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Andrade AM, Coutinho SR, Silva MN, et al. The effect of physical activity on weight loss is mediated by eating self-regulation. *Patient Educ Couns*. 2010;79(3):320-6.	No weight outcomes
Annunziato RA, Timko CA, Crerand CE, et al. A randomized trial examining differential meal replacement adherence in a weight loss maintenance program after one-year follow-up. *Eat Behav.* 2009;10:176-83.	Comparative effectiveness
Lakerveld J, Bot SD, Chinapaw MJ, et al. Primary prevention of diabetes mellitus type 2 and cardiovascular diseases using a cognitive behavior program aimed at lifestyle changes in people at risk: design of a randomized controlled trial. *BMC Endocr Disord.* 2008;8:6.	No weight outcomes
Apfelbaum M, Vague P, Ziegler O, et al. Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. *Am J Med.* 1999;106:179-84.	Sibutramine intervention
Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA.* 2003;289:2083-93.	Not one of the specified interventions
Appel LJ, Espeland MA, Easter L, et al. Effects of reduced sodium intake on hypertension control in older individuals: results from the Trial of Nonpharmacologic Interventions in the Elderly (TONE). *Arch Intern Med.* 2001;161:685-93.	No weight outcomes
Arterburn D, DeLaet D, Schauer D. Obesity in adults. *Clin Evid (Online).* 2008.	Does not meet design requirements in inclusion criteria
Ash S, Reeves M, Bauer J, et al. A randomised control trial comparing lifestyle groups, individual counselling and written information in the management of weight and health outcomes over 12 months. *Int J Obes.* 2006;30:1557-64.	Comparative effectiveness
Ashley JM, St Jeor ST, Schrage JP, et al. Weight control in the physician's office. *Arch Intern Med.* 2001;161:1599-604.	Comparative effectiveness

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Reference	Reason for Exclusion
Ashutosh K, Methrotra K, Fragale-Jackson J. Effects of sustained weight loss and exercise on aerobic fitness in obese women. *J Sports Med Phys Fitness.* 1997;37:252-7.	Comparative effectiveness
Avenell A, Brown TJ, McGee MA, et al. What are the long-term benefits of weight reducing diets in adults? A systematic review of randomized controlled trials. *J Hum Nutr Diet.* 2004;17:317-35.	Does not meet design requirements in inclusion criteria
Babamoto KS, Sey KA, Camilleri AJ, et al. Improving diabetes care and health measures among Hispanics using community health workers: results from a randomized controlled trial. *Health Educ Behav.* 2009;36:113-26.	Less than 12 months followup
Bach DS, Rissanen AM, Mendel CM, et al. Absence of cardiac valve dysfunction in obese patients treated with sibutramine. *Obes Res.* 1999;7:363-9.	Sibutramine intervention
Bacon L, Keim NL, Van L, et al. Evaluating a "non-diet" wellness intervention for improvement of metabolic fitness, psychological well-being and eating and activity behaviors. *Int J Obes Relat Metab Disord.* 2002;26:854-65.	Comparative effectiveness
Bakris G, Calhoun D, Egan B, et al. Orlistat improves blood pressure control in obese subjects with treated but inadequately controlled hypertension. *J Hypertens.* 2002;20:2257-67.	High or differential attrition
Balducci S, Zanuso S, Nicolucci A, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutr Metab Cardiovasc Dis.* 2010;20:608-17.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Barr SI, McCarron DA, Heaney RP, et al. Effects of increased consumption of fluid milk on energy and nutrient intake, body weight, and cardiovascular risk factors in healthy older adults. *J Am Diet Assoc.* 2000;100:810-7.	Not one of the specified interventions
Bauer C, Fischer A, Keller U. Effect of sibutramine and of cognitive-behavioural weight loss therapy in obesity and subclinical binge eating disorder. *Diabetes Obes Metab.* 2006;8:289-95.	Less than 12 months followup
Beck-da-Silva L, Higginson L, Fraser M, et al. Effect of orlistat in obese patients with heart failure: a pilot study. *Congest Heart Fail.* 2005;11:118-23.	Less than 12 months followup
Bemelmans WJ, Broer J, de Vries JH, et al. Impact of Mediterranean diet education versus posted leaflet on dietary habits and serum cholesterol in a high risk population for cardiovascular disease. *Public Health Nutr.* 2000;3:273-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Bergstrom I, Lombardo C, Brinck J. Physical training decreases waist circumference in postmenopausal borderline overweight women. *Acta Obstet Gynecol Scand.* 2009;88:308-13.	Focus on patients in subgroups other than specified conditions
Bhargava A, Guthrie JF. Unhealthy eating habits, physical exercise and macronutrient intakes are predictors of anthropometric indicators in the Women's Health Trial Feasibility Study in Minority Populations. *Br J Nutr.* 2002;88:719-28.	Not one of the specified interventions
Blumenthal JA, Sherwood A, Gullette EC, et al. Exercise and weight loss reduce blood pressure in men and women with mild hypertension: effects on cardiovascular, metabolic, and hemodynamic functioning. *Arch Intern Med.* 2000;160:1947-58.	Less than 12 months followup
Bo S, Ciccone G, Baldi C, et al. Effectiveness of a lifestyle intervention on metabolic syndrome: a randomized controlled trial. *J Gen Intern Med.* 2007;22:1695-703.	Not one of the specified interventions
Bo S, Ciccone G, Guidi S, et al. Diet or exercise: what is more effective in preventing or reducing metabolic alterations? *Eur J Endocrinol.* 2008;159:685-91.	Not one of the specified interventions
Borg P, Kukkonen-Harjula K, Fogelholm M, Pasanen M. Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: a randomized trial. *Int J Obes Relat Metab Disord.* 2002;26:676-83.	Comparative effectiveness
Botomino A, Bruppacher R, Krahenbuhl S, Hersberger KE. Change of body weight and lifestyle of persons at risk for diabetes after screening and counselling in pharmacies. *Pharm World Sci.* 2008;30:222-6.	Does not meet design requirements in inclusion criteria
Bowen D, Clifford CK, Coates R, et al. The Women's Health Trial Feasibility Study in Minority Populations: design and baseline descriptions. *Ann Epidemiol.* 1996;6:507-19.	Not one of the specified interventions
Bowen J, Noakes M, Clifton PM. A high dairy protein, high-calcium diet minimizes bone turnover in overweight adults during weight loss. *J Nutr.* 2004;134:568-73.	Less than 12 months followup

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Reference	Reason for Exclusion
Bowerman S, Bellman M, Saltsman P, et al. Implementation of a primary care physician network obesity management program. *Obes Res.* 2001;9(Suppl 4):S321-5.	Less than 12 months followup
Bravata DM, Smith-Spangler C, Sundaram V, et al. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA.* 2007;298:2296-304.	Does not meet design requirements in inclusion criteria
Brinkworth GD, Noakes M, Keogh JB, et al. Long-term effects of a high-protein, low-carbohydrate diet on weight control and cardiovascular risk markers in obese hyperinsulinemic subjects. *Int J Obes Relat Metab Disord.* 2004;28:661-70.	Comparative effectiveness
Brinkworth GD, Noakes M, Parker B, et al. Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: one-year follow-up of a randomised trial. *Diabetologia.* 2004;47:1677-86.	Comparative effectiveness
Broom I, Hughes E, Dodson P, Reckless J. The role of orlistat in the treatment of obese patients with mild to moderate hypercholesterolaemia: consequences for coronary risk. *Br J Cardiol.* 2002;9:460-8.	Less than 12 months followup
Brownell KD. The LEARN Program for Weight Management. New Haven, CT: American Health Publishing Company; 2000.	Comparative effectiveness
Bryan J, Tiggemann M. The effect of weight-loss dieting on cognitive performance and psychological well-being in overweight women. *Appetite.* 2001;36:147-56.	Less than 12 months followup
Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA.* 2004;292:1724-37.	Does not meet design requirements in inclusion criteria
Burke V, Beilin LJ, Cutt HE, et al. A lifestyle program for treated hypertensives improved health-related behaviors and cardiovascular risk factors, a randomized controlled trial. *J Clin Epidemiol.* 2007;60:133-41.	No weight outcomes
Burke V, Mansour J, Beilin LJ, Mori TA. Long-term follow-up of participants in a health promotion program for treated hypertensives (ADAPT). *Nutr Metab Cardiovasc Dis.* 2008;18:198-206.	No weight outcomes
Burke V, Mori TA, Giangiulio N, et al. An innovative program for changing health behaviours. *Asia Pac J Clin Nutr.* 2002;11(Suppl 3):S586-97.	High or differential attrition
Caan B, Neuhouser M, Aragaki A, et al. Calcium plus vitamin D supplementation and the risk of postmenopausal weight gain. *Arch Intern Med.* 2007;167:893-902.	Not one of the specified interventions
Calle-Pascual AL, Rodriguez C, Camacho F, et al. Behaviour modification in obese subjects with type 2 diabetes mellitus. *Diabetes Res Clin Pract.* 1992;15:157-62.	Does not meet design requirements in inclusion criteria
Campbell PT, Campbell KL, Wener MH, et al. A yearlong exercise intervention decreases CRP among obese postmenopausal women. *Med Sci Sports Exerc.* 2009;41:1533-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Carr DB, Utzschneider KM, Boyko EJ, et al. A reduced-fat diet and aerobic exercise in Japanese Americans with impaired glucose tolerance decreases intra-abdominal fat and improves insulin sensitivity but not beta-cell function. *Diabetes.* 2005;54:340-7.	Comparative effectiveness
Carr LJ, Bartee RT, Dorozynski CM, et al. Eight-month follow-up of physical activity and central adiposity: results from an Internet-delivered randomized control trial intervention. *J Phys Act Health.* 2009;6:444-55.	Comparative effectiveness
Castaneda C, Layne JE, Munoz-Orians L, et al. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes Care.* 2002;25:2335-41.	Less than 12 months followup
Chang MW, Nitzke S, Brown R. Design and outcomes of a Mothers In Motion behavioral intervention pilot study. *J Nutr Educ Behav.* 2010;42(Suppl 3):S11-21.	Less than 12 months followup
Charles MA, Morange P, Eschwege E, et al. Effect of weight change and metformin on fibrinolysis and the von Willebrand factor in obese nondiabetic subjects: the BIGPRO1 study. *Diabetes Care.* 1998;21:1967-72.	No weight outcomes
Cheyette C. Weight No More: a randomised controlled trial for people with type 2 diabetes on insulin therapy. *Pract Diabetes Int.* 2007;24:450-6.	High or differential attrition
Chiasson JL, Lau DC, Leiter LA, et al. Fluoxetine has potential in obese NIDDM—multicenter Canadian trial. *Diabetes*. 1989;38(Suppl 2):A154.	Not one of the specified interventions
Clark M, Hampson SE, Avery L, Simpson R. Effects of a tailored lifestyle self-management intervention in patients with type 2 diabetes. *Br J Health Psychol.* 2004;9:365-79.	Not focused on behavioral or pharmacological interventions designed to promote weight loss

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Reference	Reason for Exclusion
Clarke KK, Freeland-Graves J, Klohe-Lehman DM, et al. Promotion of physical activity in low-income mothers using pedometers. *J Am Diet Assoc.* 2007;107:962-7.	Less than 12 months followup
Clifford PA, Tan SY, Gorsuch RL. Efficacy of a self-directed behavioral health change program: weight, body composition, cardiovascular fitness, blood pressure, health risk, and psychosocial mediating variables. *J Behav Med.* 1991;14:303-23.	Comparative effectiveness
Cocco G, Pandolfi S, Rousson V. Sufficient weight reduction decreases cardiovascular complications in diabetic patients with the metabolic syndrome: a randomized study of orlistat as an adjunct to lifestyle changes (diet and exercise). *Heart Drug.* 2005;5:68-74.	Less than 12 months followup
Coker RH, Williams RH, Yeo SE, et al. The impact of exercise training compared to caloric restriction on hepatic and peripheral insulin resistance in obesity. *J Clin Endocrinol Metab.* 2009;94:4258-66.	Less than 12 months followup
Corpeleijn E, Feskens EJ, Jansen EH, et al. Improvements in glucose tolerance and insulin sensitivity after lifestyle intervention are related to changes in serum fatty acid profile and desaturase activities: the SLIM study. *Diabetologia.* 2006;49:2392-401.	Not one of the specified interventions
Counterweight Project Team. Evaluation of the Counterweight Programme for obesity management in primary care: a starting point for continuous improvement. *Br J Gen Pract.* 2008;58:548-54.	Does not meet design requirements in inclusion criteria
Counterweight Project Team. Influence of body mass index on prescribing costs and potential cost savings of a weight management programme in primary care. *J Health Serv Res Policy.* 2008;13:158-66.	Does not meet design requirements in inclusion criteria
Cousins JH, Rubovits DS, Dunn JK, et al. Family versus individually oriented intervention for weight loss in Mexican American women. *Public Health Rep.* 1992;107:549-55.	Comparative effectiveness
Cuellar GE, Ruiz AM, Monsalve MC, Berber A. Six-month treatment of obesity with sibutramine 15 mg; a double-blind, placebo-controlled monocenter clinical trial in a Hispanic population. *Obes Res.* 2000;8:71-82.	Not on list of countries with HDI > 0.90
Culturally appropriate lifestyle interventions promote weight loss in rural dwelling people with type 2 diabetes. *Evid Based Healthc Public Health.* 2005;9:231-2.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dale KS, Mann JI, McAuley KA, et al. Sustainability of lifestyle changes following an intensive lifestyle intervention in insulin resistant adults: follow-up at 2-years. *Asia Pac J Clin Nutr.* 2009;18:114-20.	Comparative effectiveness
Dale KS, McAuley KA, Taylor RW, et al. Determining optimal approaches for weight maintenance: a randomized controlled trial. *Can Med Assoc J.* 2009;180:E39-46.	Comparative effectiveness
Davey SG, Bracha Y, Svendsen KH, et al. Incidence of type 2 diabetes in the randomized Multiple Risk Factor Intervention Trial. *Ann Intern Med.* 2005;142:313-22.	Not one of the specified interventions
Davies MJ, Heller S, Skinner TC, et al. Effectiveness of the Diabetes Education and Self Management for Ongoing and Newly Diagnosed (DESMOND) Programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. *BMJ.* 2008;336:491-5.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Davis BR, Blaufox MD, Oberman A, et al. Reduction in long-term antihypertensive medication requirements: effects of weight reduction by dietary intervention in overweight persons with mild hypertension. *Arch Intern Med.* 1993;153:1773-82.	No weight outcomes
de Waard F, Ramlau R, Mulders Y, et al. A feasibility study on weight reduction in obese postmenopausal breast cancer patients. *Eur J Cancer Prev.* 1993;2:233-8.	Focus on patients in subgroups other than specified conditions
de Wit LT, Mathus-Vliegen L, Hey C, et al. Open versus laparoscopic adjustable silicone gastric banding: a prospective randomized trial for treatment of morbid obesity. *Ann Surg.* 1999;230:800-5.	Not one of the specified interventions
Delahanty LM, Nathan DM. Implications of the Diabetes Prevention Program and Look AHEAD clinical trials for lifestyle interventions. *J Am Diet Assoc.* 2008;108(Suppl 1):S66-72.	Comparative effectiveness
Delecluse C, Colman V, Roelants M, et al. Exercise programs for older men: mode and intensity to induce the highest possible health-related benefits. *Prev Med.* 2004;39:823-33.	Less than 12 months followup
Dennis KE, Tomoyasu N, McCrone SH, et al. Self-efficacy targeted treatments for weight loss in postmenopausal women. *Sch Inq Nurs Pract.* 2001;15:259-76.	Comparative effectiveness

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Reference	Reason for Exclusion
Derosa G, Cicero AF, Murdolo G, et al. Efficacy and safety comparative evaluation of orlistat and sibutramine treatment in hypertensive obese patients. *Diabetes Obes Metab.* 2005;7:47-55.	Comparative effectiveness
Devine A, Prince RL, Bell R. Nutritional effect of calcium supplementation by skim milk powder or calcium tablets on total nutrient intake in postmenopausal women. *Am J Clin Nutr.* 1996;64:731-7.	Comparative effectiveness
Di Francesco V, Sacco T, Zamboni M, et al. Weight loss and quality of life improvement in obese subjects treated with sibutramine: a double-blind randomized multicenter study. *Ann Nutr Metab.* 2007;51:75-81.	Sibutramine intervention
Di Loreto C, Fanelli C, Lucidi P, et al. Validation of a counseling strategy to promote the adoption and the maintenance of physical activity by type 2 diabetic subjects. *Diabetes Care.* 2003;26:404-8.	Comparative effectiveness
Ditschuneit HH, Flechtner-Mors M, Johnson TD, Adler G. Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *Am J Clin Nutr.* 1999;69:198-204.	Comparative effectiveness
Djuric Z, DiLaura NM, Jenkins I, et al. Combining weight-loss counseling with the Weight Watchers plan for obese breast cancer survivors. *Obes Res.* 2002;10:657-65.	Focus on patients in subgroups other than specified conditions
Donnelly JE, Hill JO, Jacobsen DJ, et al. Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med.* 2003;163:1343-50.	High or differential attrition
Donnelly JE, Jacobsen DJ, Heelan KS, et al. The effects of 18 months of intermittent vs. continuous exercise on aerobic capacity, body weight and composition, and metabolic fitness in previously sedentary, moderately obese females. *Int J Obes Relat Metab Disord.* 2000;24:566-72.	Comparative effectiveness
Donnelly JE, Kirk EP, Jacobsen DJ, et al. Effects of 16 mo of verified, supervised aerobic exercise on macronutrient intake in overweight men and women: the Midwest Exercise Trial. *Am J Clin Nutr.* 2003;78:950-6.	High or differential attrition
Donnelly JE, Smith BK, Dunn L, et al. Comparison of a phone vs clinic approach to achieve 10% weight loss. *Int J Obes.* 2007;31:1270-6.	Less than 12 months followup
Due A, Larsen TM, Mu H, et al. Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease, and diabetes: a 6-mo randomized, controlled trial. *Am J Clin Nutr.* 2008;88:1232-41.	Less than 12 months followup
Dujovne CA, Zavoral JH, Rowe E, Mendel CM. Effects of sibutramine on body weight and serum lipids: a double-blind, randomized, placebo-controlled study in 322 overweight and obese patients with dyslipidemia. *Am Heart J.* 2001;142:489-97.	Sibutramine intervention
Dunn AL, Marcus BH, Kampert JB, et al. Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. *JAMA.* 1999;281:327-34.	Comparative effectiveness
Dunstan DW, Daly RM, Owen N, et al. Home-based resistance training is not sufficient to maintain improved glycemic control following supervised training in older individuals with type 2 diabetes. *Diabetes Care.* 2005;28:3-9.	Comparative effectiveness
Dutton GR, Davis MP, Welsch MA, Brantley PJ. Promoting physical activity for low-income minority women in primary care. *Am J Health Behavior.* 2007;31:622-31.	No weight outcomes
Dymek MP, Le Grange D, Neven K, Alverdy J. Quality of life after gastric bypass surgery: a cross-sectional study. *Obes Res.* 2002;10:1135-42.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dymek MP, Le Grange D, Neven K, Alverdy J. Quality of life and psychosocial adjustment in patients after Roux-en-Y gastric bypass: a brief report. *Obes Surg.* 2001;11:32-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dyson PA, Hammersley MS, Morris RJ, et al. The Fasting Hyperglycaemia Study, II: randomized controlled trial of reinforced healthy-living advice in subjects with increased but not diabetic fasting plasma glucose. *Metabolism.* 1997;46:50-5.	Not one of the specified interventions
Dzator JA, Hendrie D, Burke V, et al. A randomized trial of interactive group sessions achieved greater improvements in nutrition and physical activity at a tiny increase in cost. *J Clin Epidemiol.* 2004;57:610-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Early JL, Apovian CM, Aronne LJ, et al. Sibutramine plus meal replacement therapy for body weight loss and maintenance in obese patients. *Obesity.* 2007;15:1464-72.	Sibutramine intervention

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Reference	Reason for Exclusion
Eddy DM, Schlessinger L, Kahn R. Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. *Ann Intern Med.* 2005;143:251-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Eiben G, Lissner L. Health Hunters—an intervention to prevent overweight and obesity in young high-risk women. *Int J Obes.* 2006;30:691-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Elhayany A, Lustman A, Abel R, et al. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. *Diabetes Obes Metab.* 2010;12:204-9.	Comparative effectiveness
Elmer PJ, Obarzanek E, Vollmer WM, et al. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. *Ann Intern Med.* 2006;144:485-95.	Comparative effectiveness
Ely AC, Banitt A, Befort C, et al. Kansas primary care weighs in: a pilot randomized trial of a chronic care model program for obesity in 3 rural Kansas primary care practices. *J Rural Health.* 2008;24:125-32.	Less than 12 months followup
Eriksson KM, Westborg CJ, Eliasson MC. A randomized trial of lifestyle intervention in primary healthcare for the modification of cardiovascular risk factors. *Scand J Public Health.* 2006;34:453-61.	Not one of the specified interventions
Esposito K, Giugliano F, Di Palo C, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. *JAMA.* 2004;291:2978-84.	Comparative effectiveness
Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA.* 2004;292:1440-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Esposito K, Pontillo A, Di Palo C, et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. *JAMA.* 2003;289:1799-804.	Comparative effectiveness
Fabricatore AN, Wadden TA, Moore RH, et al. Predictors of attrition and weight loss success: results from a randomized controlled trial. *Behav Res Ther.* 2009;47:685-91.	Comparative effectiveness
Fanghanel G, Cortinas L, Sanchez-Reyes L, Berber A. A clinical trial of the use of sibutramine for the treatment of patients suffering essential obesity. *Int J Obes Relat Metab Disord.* 2000;24:144-50.	Less than 12 months followup
Fanghanel G, Cortinas L, Sanchez-Reyes L, et al. Safety and efficacy of sibutramine in overweight Hispanic patients with hypertension. *Adv Ther.* 2003;20:101-13.	Less than 12 months followup
Faria AN, Ribeiro Filho FF, Kohlmann NE, et al. Effects of sibutramine on abdominal fat mass, insulin resistance and blood pressure in obese hypertensive patients. *Diabetes Obes Metab.* 2005;7:246-53.	Less than 12 months followup
Faria AN, Ribeiro Filho FF, Lerario DD, et al. Effects of sibutramine on the treatment of obesity in patients with arterial hypertension. *Arq Bras Cardiol.* 2002;78:172-80.	Less than 12 months followup
Faulconbridge LF, Wadden TA, Berkowitz RI, et al. Changes in symptoms of depression with weight loss: results of a randomized trial. *Obesity.* 2009;17:1009-16.	No placebo in medication trial
Ferre R, Plana N, Merino J, et al. Effects of therapeutic lifestyle changes on peripheral artery tonometry in patients with abdominal obesity. *Nutr Metab Cardiovasc Dis.* 2010 Aug 11. [Epub ahead of print]	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Figueroa A, Going SB, Milliken LA, et al. Effects of exercise training and hormone replacement therapy on lean and fat mass in postmenopausal women. *J Gerontol A Biol Sci Med Sci.* 2003;58:266-70.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Finer N, Bloom SR, Frost GS, et al. Sibutramine is effective for weight loss and diabetic control in obesity with type 2 diabetes: a randomised, double-blind, placebo-controlled study. *Diabetes Obes Metab.* 2000;2:105-12.	Sibutramine intervention
Finkelstein EA, Linnan LA, Tate DF, Leese PJ. A longitudinal study on the relationship between weight loss, medical expenditures, and absenteeism among overweight employees in the WAY to Health study. *J Occup Environ Med.* 2009;51:1367-73.	Conducted primarily in a non-relevant setting
Finley CE, Barlow CE, Greenway FL, et al. Retention rates and weight loss in a commercial weight loss program. *Int J Obes (Lond).* 2007;31:292-8.	Does not meet design requirements in inclusion criteria

Appendix D Table 3. Studies Excluded From Review for Key Question 3

Reference	Reason for Exclusion
Flechtner-Mors M, Ditschuneit HH, Johnson TD, et al. Metabolic and weight loss effects of long-term dietary intervention in obese patients: four-year results. *Obes Res.* 2000;8:399-402.	Comparative effectiveness
Fleming RM. The effect of high-, moderate-, and low-fat diets on weight loss and cardiovascular disease risk factors. *Prev Cardiol.* 2002;5:110-8.	Comparative effectiveness
Flood A, Mitchell N, Jaeb M, et al. Energy density and weight change in a long-term weight-loss trial. *Int J Behav Nutr Phys Act.* 2009;6:57.	Study of overweight/obesity prevention
Focht BC, Rejeski WJ, Ambrosius WT, et al. Exercise, self-efficacy, and mobility performance in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum.* 2005;53:659-65.	Comparative effectiveness
Fogelholm M, Kukkonen-Harjula K, Nenonen A, Pasanen M. Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. *Arch Intern Med.* 2000;160:2177-84.	Comparative effectiveness
Fogelholm M, Kukkonen-Harjula K, Oja P. Eating control and physical activity as determinants of short-term weight maintenance after a very-low-calorie diet among obese women. *Int J Obes Relat Metab Disord.* 1999;23:203-10.	Comparative effectiveness
Fontana L, Villareal DT, Weiss EP, et al. Calorie restriction or exercise: effects on coronary heart disease risk factors: a randomized, controlled trial. *Am J Physiol Endocrinol Metab.* 2007;293:E197-202.	Comparative effectiveness
Fontbonne A, Diouf I, Baccara-Dinet M, et al. Effects of 1-year treatment with metformin on metabolic and cardiovascular risk factors in non-diabetic upper-body obese subjects with mild glucose anomalies: a post-hoc analysis of the BIGPRO1 trial. *Diabetes Metab.* 2009;35:385-91.	No weight outcomes
Fossati M, Amati F, Painot D, et al. Cognitive-behavioral therapy with simultaneous nutritional and physical activity education in obese patients with binge eating disorder. *Eat Weight Disord.* 2004;9:134-8.	Focus on patients in subgroups other than specified conditions
Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med.* 2009;169:1619-26.	Comparative effectiveness
Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med.* 2003;348:2082-90.	Comparative effectiveness
Foster-Schubert KE, McTiernan A, Frayo RS, et al. Human plasma ghrelin levels increase during a one-year exercise program. *J Clin Endocrinol Metab.* 2005;90:820-5.	No weight outcomes
Fujimoto WY, Jablonski KA, Bray GA, et al. Body size and shape changes and the risk of diabetes in the Diabetes Prevention Program. *Diabetes.* 2007;56:1680-5.	No weight outcomes
Gambineri A, Pelusi C, Genghini S, et al. Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome. *Clin Endocrinol.* 2004;60:241-9.	No weight outcomes
Gaullier JM, Halse J, Hoye K, et al. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. *Am J Clin Nutr.* 2004;79:1118-25.	Not one of the specified interventions
Gaullier JM, Halse J, Hoye K, et al. Supplementation with conjugated linoleic acid for 24 months is well tolerated by and reduces body fat mass in healthy, overweight humans. *J Nutr.* 2005;135:778-84.	Not one of the specified interventions
Ghroubi S, Elleuch H, Chikh T, et al. Physical training combined with dietary measures in the treatment of adult obesity: a comparison of two protocols. *Ann Phys Rehab Med.* 2009;52:394-413.	Not on list of countries with HDI > 0.90
Giugliano D, Quatraro A, Consoli G, et al. Metformin for obese, insulin-treated diabetic patients: improvement in glycaemic control and reduction of metabolic risk factors. *Eur J Clin Pharmacol.* 1993;44:107-12.	Less than 12 months followup
Glasgow RE, La Chance PA, Toobert DJ, et al. Long-term effects and costs of brief behavioural dietary intervention for patients with diabetes delivered from the medical office. *Patient Educ Couns.* 1997;32:175-84.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Glasgow RE, Nelson CC, Kearney KA, et al. Reach, engagement, and retention in an Internet-based weight loss program in a multi-site randomized controlled trial. *J Med Internet Res.* 2007;9:e11.	No weight outcomes
Godoy-Matos A, Carraro L, Vieira A, et al. Treatment of obese adolescents with sibutramine: a randomized, double-blind, controlled study. *J Clin Endocrinol Metab.* 2005;90:1460-5.	Focus on children or adolescents

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Reference	Reason for Exclusion
Gokcel A, Gumurdulu Y, Karakose H, et al. Evaluation of the safety and efficacy of sibutramine, orlistat and metformin in the treatment of obesity. *Diabetes Obes Metab.* 2002;4:49-55.	Comparative effectiveness
Gokcel A, Karakose H, Ertorer EM, et al. Effects of sibutramine in obese female subjects with type 2 diabetes and poor blood glucose control. *Diabetes Care.* 2001;24:1957-60.	Not on list of countries with HDI > 0.90
Gold BC, Burke S, Pintauro S, et al. Weight loss on the web: a pilot study comparing a structured behavioral intervention to a commercial program. *Obesity.* 2007;15:155-64.	Comparative effectiveness
Gotfredsen A, Westergren HH, Andersen T. Influence of orlistat on bone turnover and body composition. *Int J Obes Relat Metab Disord.* 2001;25:1154-60.	No weight outcomes
Greaves CJ, Middlebrooke A, O'Loughlin L, et al. Motivational interviewing for modifying diabetes risk: a randomised controlled trial. *Br J Gen Pract.* 2008;58:535-40.	Less than 12 months followup
Grimm RH Jr, Grandits GA, Cutler JA, et al. Relationships of quality-of-life measures to long-term lifestyle and drug treatment in the Treatment of Mild Hypertension Study. *Arch Intern Med.* 1997;157:638-48.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Guisado JA, Vaz FJ, Alarcon J, et al. Psychopathological status and interpersonal functioning following weight loss in morbidly obese patients undergoing bariatric surgery. *Obes Surg.* 2002;12:835-40.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Gunther CW, Legowski PA, Lyle RM, et al. Dairy products do not lead to alterations in body weight or fat mass in young women in a 1-y intervention. *Am J Clin Nutr.* 2005;81:751-6.	Study of overweight/obesity prevention
Gurka MJ, Wolf AM, Conaway MR, et al. Lifestyle intervention in obese patients with type 2 diabetes: impact of the patient's educational background. *Obesity.* 2006;14:1085-92.	Comparative effectiveness
Gustafson A, Khavjou O, Stearns SC, et al. Cost-effectiveness of a behavioral weight loss intervention for low-income women: the Weight-Wise Program. *Prev Med.* 2009;49:390-5.	Less than 12 months followup
Guy-Grand B, Drouin P, Eschwege E, et al. Effects of orlistat on obesity-related diseases—a six-month randomized trial. *Diabetes Obes Metab.* 2004;6:375-83.	Less than 12 months followup
Hainer V, Kunesova M, Bellisle F, et al. Psychobehavioral and nutritional predictors of weight loss in obese women treated with sibutramine. *Int J Obes (Lond).* 2005;29:208-16.	Less than 12 months followup
Hakala K, Maasilta P, Sovijarvi AR. Upright body position and weight loss improve respiratory mechanics and daytime oxygenation in obese patients with obstructive sleep apnoea. *Clin Physiol.* 2000;20:50-5.	Does not meet design requirements in inclusion criteria
Hall WD, Feng Z, George VA, et al. Low-fat diet: effect on anthropometrics, blood pressure, glucose, and insulin in older women. *Ethn Dis.* 2003;13:337-43.	Less than 12 months followup
Hansen D, Astrup A, Toubro S, et al. Predictors of weight loss and maintenance during 2 years of treatment by sibutramine in obesity: results from the European multi-centre STORM trial. *Int J Obes Rel Metab Disord.* 2001;25:496-501.	High or differential attrition
Hansen DL, Toubro S, Stock MJ, et al. The effect of sibutramine on energy expenditure and appetite during chronic treatment without dietary restriction. *Int J Obes Relat Metab Disord.* 1999;23:1016-24.	Sibutramine intervention
Harvey BJ, Gold BC, Lauber R, Starinski A. The impact of calcium and dairy product consumption on weight loss. *Obes Res.* 2005;13:1720-6.	Comparative effectiveness
Harvey-Berino J, Pintauro S, Buzzell P, et al. Does using the Internet facilitate the maintenance of weight loss? *Int J Obes Relat Metab Disord.* 2002;26:1254-60.	Comparative effectiveness
Harvey-Berino J, Pintauro S, Buzzell P, Gold EC. Effect of Internet support on the long-term maintenance of weight loss. *Obes Res.* 2004;12:320-9.	Comparative effectiveness
Harvey-Berino J, Pintauro SJ, Gold EC. The feasibility of using Internet support for the maintenance of weight loss. *Behav Modif.* 2002;26:103-16.	Less than 12 months followup
Haskell WL, Alderman EL, Fair JM, et al. Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease. *Circulation.* 1994;89:975-90.	Not one of the specified interventions
Haub MD, Simons TR, Cook CM, et al. Calcium-fortified beverage supplementation on body composition in postmenopausal women. *Nutr J.* 2005;4:21.	Not one of the specified interventions

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Reference	Reason for Exclusion
Hauner H, Meier M, Wendland G, et al. Weight reduction by sibutramine in obese subjects in primary care medicine: the SAT Study. *Exp Clin Endocrinol Diabetes.* 2004;112:201-7.	Sibutramine intervention
Hawley G, Horwath C, Gray A, et al. Sustainability of health and lifestyle improvements following a non-dieting randomised trial in overweight women. *Prev Med.* 2008;47:593-9.	Comparative effectiveness
Hays NP, Starling RD, Sullivan DH, et al. Effects of an ad libitum, high carbohydrate diet and aerobic exercise training on insulin action and muscle metabolism in older men and women. *J Gerontol A Biol Sci Med Sci.* 2006;61:299-304.	Comparative effectiveness
Hazenberg BP. Randomized, double-blind, placebo-controlled, multicenter study of sibutramine in obese hypertensive patients. *Cardiology.* 2000;94:152-8.	Sibutramine intervention
Hensrud DD. Dietary treatment and long-term weight loss and maintenance in type 2 diabetes. *Obes Res.* 2001;9(Suppl 4):S348-53.	Does not meet design requirements in inclusion criteria
Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med.* 2005;142:323-32.	No weight outcomes
Hermann LS, Kalen J, Katzman P, et al. Long-term glycaemic improvement after addition of metformin to insulin in insulin-treated obese type 2 diabetes patients. *Diabetes Obes Metab.* 2001;3:428-34.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Heshka S, Anderson JW, Atkinson RL, et al. Weight loss with self-help compared with a structured commercial program: a randomized trial. *JAMA.* 2003;289:1792-8.	Comparative effectiveness
Heymsfield SB, Segal KR, Hauptman J, et al. Effects of weight loss with orlistat on glucose tolerance and progression to type 2 diabetes in obese adults. *Arch Intern Med.* 2000;160:1321-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hivert MF, Langlois MF, Berard P, et al. Prevention of weight gain in young adults through a seminar-based intervention program. *Int J Obes.* 2007;31:1262-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hoeger KM, Kochman L, Wixom N, et al. A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertil Steri.* 2004;82:421-9.	High or differential attrition
Hooper L. Primary prevention of CVD: diet and weight loss. *Clin Evid (Online).* 2007.	Does not meet design requirements in inclusion criteria
Hope AA, Kumanyika SK, Shults J, Holmes WC. Changes in health-related quality of life among African-Americans in a lifestyle weight loss program. *Qual Life Res.* 2010;19:1025-33.	Does not meet design requirements in inclusion criteria
Howard BV, Manson JE, Stefanick ML, et al. Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. *JAMA.* 2006;295:39-49.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hsieh CJ, Wang PW, Liu RT, et al. Orlistat for obesity: benefits beyond weight loss. *Diabetes Res Clin Pract.* 2005;67:78-83.	Not on list of countries with HDI > 0.90
Hunter GR, Brock DW, Byrne NM, et al. Exercise training prevents regain of visceral fat for 1 year following weight loss. *Obesity.* 2010;18:690-5.	Comparative effectiveness
Jacob S, Rabbia M, Meier MK, Hauptman J. Orlistat 120 mg improves glycaemic control in type 2 diabetic patients with or without concurrent weight loss. *Diabetes Obes Metab.* 2009;11:361-71.	Less than 12 months followup
Jacobs DR, Sluik D, Rokling-Andersen MH, et al. Association of 1-y changes in diet pattern with cardiovascular disease risk factors and adipokines: results from the 1-y randomized Oslo Diet and Exercise Study. *Am J Clin Nutr.* 2009;89:509-17.	No weight outcomes
Jakicic JM, Jaramillo SA, Balasubramanyam A, et al. Effect of a lifestyle intervention on change in cardiorespiratory fitness in adults with type 2 diabetes: results from the Look AHEAD Study. *Int J Obes.* 2009;33:305-16.	Comparative effectiveness
Jakicic JM, Marcus BH, Gallagher KI, et al. Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *JAMA.* 2003;290:1323-30.	Comparative effectiveness
Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. *Arch Intern Med.* 1559;168:1550-9.	Comparative effectiveness
Jakicic JM, Otto AD, Lang W, et al. The effect of physical activity on 18-month weight change in overweight adults. *Obesity (Silver Spring).* 2011;19:100-9.	Comparative effectiveness

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Reference	Reason for Exclusion
Jakicic JM, Winters C, Lang W, Wing RR. Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *JAMA.* 1999;282:1554-60.	Comparative effectiveness
Jalkanen L. The effect of a weight reduction program on cardiovascular risk factors among overweight hypertensives in primary health care. *Scand J Soc Med.* 1991;19:66-71.	Other quality issues
James WP, Astrup A, Finer N, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. *Lancet.* 2000;356:2119-25.	Sibutramine intervention
Janssen I, Fortier A, Hudson R, Ross R. Effects of an energy-restrictive diet with or without exercise on abdominal fat, intermuscular fat, and metabolic risk factors in obese women. *Diabetes Care.* 2002;25:431-8.	Comparative effectiveness
Jarjou LM, Prentice A, Sawo Y, et al. Randomized, placebo-controlled, calcium supplementation study in pregnant Gambian women: effects on breast-milk calcium concentrations and infant birth weight, growth, and bone mineral accretion in the first year of life. *Am J Clin Nutr.* 2006;83:657-66.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Jarrett RJ, Keen H, Murrells T. Changes in blood pressure and body weight over ten years in men selected for glucose intolerance. *J Epidemiol Community Health.* 1987;41:145-51.	Comparative effectiveness
Jeffery RW, French SA. Preventing weight gain in adults: design, methods and one year results from the Pound of Prevention study. *Int J Obes Relat Metab Disord.* 1997;21:457-64.	Study of overweight/obesity prevention
Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr.* 2003;78:684-9.	Comparative effectiveness
Jehn ML, Patt MR, Appel LJ, Miller ER III. One year follow-up of overweight and obese hypertensive adults following intensive lifestyle therapy. *J Hum Nutr Diet.* 2006;19:349-54.	Comparative effectiveness
Jensen LB, Kollerup G, Quaade F, Sorensen OH. Bone minerals changes in obese women during a moderate weight loss with and without calcium supplementation. *J Bone Miner Res.* 2001;16:141-7.	Less than 12 months followup
Jirik-Babb P, Geliebter A. Comparison of psychological characteristics of binging and nonbinging obese, adult, female outpatients. *Eat Weight Disord.* 2003;8:173-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Jordan J, Scholze J, Matiba B, et al. Influence of sibutramine on blood pressure: evidence from placebo-controlled trials. *Int J Obes.* 2005;29:509-16.	Does not meet design requirements in inclusion criteria
Kajaste S, Brander PE, Telakivi T, et al. A cognitive-behavioral weight reduction program in the treatment of obstructive sleep apnea syndrome with or without initial nasal CPAP: a randomized study. *Sleep Med.* 2004;5:125-31.	Not one of the specified interventions
Kalter-Leibovici O, Younis-Zeidan N, Atamna A, et al. Lifestyle intervention in obese Arab women: a randomized controlled trial. *Arch Intern Med.* 2010;170:970-6.	Comparative effectiveness
Kamioka H, Nakamura Y, Okada S, et al. Effectiveness of comprehensive health education combining lifestyle education and hot spa bathing for male white-collar employees: a randomized controlled trial with 1-year follow-up. *J Epidemiol.* 2009;19:219-30.	Conducted primarily in a non-relevant setting
Kansanen M, Vanninen E, Tuunainen A, et al. The effect of a very low-calorie diet-induced weight loss on the severity of obstructive sleep apnoea and autonomic nervous function in obese patients with obstructive sleep apnoea syndrome. *Clin Physiol.* 1998;18:377-85.	Does not meet design requirements in inclusion criteria
Karhunen L, Franssila-Kallunki A, Rissanen P, et al. Effect of orlistat treatment on body composition and resting energy expenditure during a two-year weight-reduction programme in obese Finns. *Int J Obes Relat Metab Disord.* 2000;24:1567-72.	No weight outcomes
Katzer L, Bradshaw AJ, Horwath CC, et al. Evaluation of a "nondieting" stress reduction program for overweight women: a randomized trial. *Am J Health Promot.* 2008;22:264-74.	Comparative effectiveness
Kaukua JK, Pekkarinen TA, Rissanen AM. Health-related quality of life in a randomised placebo-controlled trial of sibutramine in obese patients with type II diabetes. *Int J Obes Relat Metab Disord.* 2004;28:600-5.	Sibutramine intervention

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Reference	Reason for Exclusion
Kawano M, Shono N, Yoshimura T, et al. Improved cardio-respiratory fitness correlates with changes in the number and size of small dense LDL: randomized controlled trial with exercise training and dietary instruction. *Intern Med.* 2009;48:25-32.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Keating GM, Jarvis B. Orlistat: in the prevention and treatment of type 2 diabetes mellitus. *Drugs.* 2120;61:2107-19.	Does not meet design requirements in inclusion criteria
Kelley DE, Bray GA, Pi-Sunyer FX, et al. Clinical efficacy of orlistat therapy in overweight and obese patients with insulin-treated type 2 diabetes: a 1-year randomized controlled trial. *Diabetes Care.* 2002;25:1033-41.	High or differential attrition
Keogh JB, Luscombe-Marsh ND, Noakes M, et al. Long-term weight maintenance and cardiovascular risk factors are not different following weight loss on carbohydrate-restricted diets high in either monounsaturated fat or protein in obese hyperinsulinaemic men and women. *Br J Nutr.* 2007;97:405-10.	Comparative effectiveness
Keranen AM, Savolainen MJ, Reponen AH, et al. The effect of eating behavior on weight loss and maintenance during a lifestyle intervention. *Prev Med.* 2009;49:32-8.	Comparative effectiveness
Kerr J, Patrick K, Norman G, et al. Randomized control trial of a behavioral intervention for overweight women: impact on depressive symptoms. *Depress Anxiety.* 2008;25:555-8.	No weight outcomes
Ketola E, Makela M, Klockars M. Individualised multifactorial lifestyle intervention trial for high-risk cardiovascular patients in primary care. *Br J Gen Pract.* 2001;51:291-4.	Not one of the specified interventions
Kim SH, Lee YM, Jee SH, Nam CM. Effect of sibutramine on weight loss and blood pressure: a meta-analysis of controlled trials. *Obes Res.* 2003;11:1116-23.	Does not meet design requirements in inclusion criteria
Kim SI, Kim HS. Effectiveness of mobile and Internet intervention in patients with obese type 2 diabetes. *Int J Med Inf.* 2008;77:399-404.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kim Y, Pike J, Adams H, et al. Telephone intervention promoting weight-related health behaviors. *Prev Med.* 2010;50:112-7.	Comparative effectiveness
Kirk EP, Jacobsen DJ, Gibson C, et al. Time course for changes in aerobic capacity and body composition in overweight men and women in response to long-term exercise: the Midwest Exercise Trial (MET). *Int J Obes Relat Metab Disord.* 2003;27:912-9.	High or differential attrition
Kirk SF, Harvey EL, McConnon A, et al. A randomised trial of an Internet weight control resource: the UK Weight Control Trial. *BMC Health Serv Res.* 2003;3:19.	No weight outcomes
Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet.* 2009;274:1677-86.	No weight outcomes
Kolotkin RL, Norquist JM, Crosby RD, et al. One-year health-related quality of life outcomes in weight loss trial participants: comparison of three measures. *Health Qual Life Outcomes.* 2009;7:53.	Not one of the specified interventions
Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract.* 2005;67:152-62.	Comparative effectiveness
Kostis JB, Wilson AC, Hooper WC, et al. Association of angiotensin-converting enzyme DD genotype with blood pressure sensitivity to weight loss. *Am Heart J.* 2002;144:625-9.	No weight outcomes
Kostis JB, Wilson AC, Shindler DM, et al. Persistence of normotension after discontinuation of lifestyle intervention in the trial of TONE. *Am J Hypertens.* 2002;15:732-4.	No weight outcomes
Krakoff J, Clark JM, Crandall JP, et al. Effects of metformin and weight loss on serum alanine aminotransferase activity in the Diabetes Prevention Program. *Obesity (Silver Spring).* 2010;18:1762-7.	No weight outcomes
Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med.* 2002;347:1483-92.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kukkonen-Harjula KT, Borg PT, Nenonen AM, Fogelholm MG. Effects of a weight maintenance program with or without exercise on the metabolic syndrome: a randomized trial in obese men. *Prev Med.* 2005;41:784-90.	Comparative effectiveness

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Reference	Reason for Exclusion
Kuller LH, Kinzel LS, Pettee KK, et al. Lifestyle intervention and coronary heart disease risk factor changes over 18 months in postmenopausal women: the Women On the Move through Activity and Nutrition (WOMAN study) clinical trial. *J Womens Health.* 2006;15:962-74.	Comparative effectiveness
Kuller LH, Kriska AM, Kinzel LS, et al. The clinical trial of Women On the Move through Activity and Nutrition (WOMAN) study. *Contemp Clin Trials.* 2006;28:370-81.	Comparative effectiveness
Kumanyika SK, Cook NR, Cutler JA, et al. Sodium reduction for hypertension prevention in overweight adults: further results from the Trials of Hypertension Prevention phase II. *J Hum Hypertens.* 2005;19:33-45.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kumanyika SK, Shults J, Fassbender J, et al. Outpatient weight management in African-Americans: the Healthy Eating and Lifestyle Program (HELP) study. *Prev Med.* 2005;41:488-502.	Comparative effectiveness
Kumanyika SK, Wadden TA, Shults J, et al. Trial of family and friend support for weight loss in African American adults. *Arch Intern Med.* 2009;169:1795-804.	Comparative effectiveness
Laaksonen DE, Laitinen T, Schonberg J, et al. Weight loss and weight maintenance, ambulatory blood pressure and cardiac autonomic tone in obese persons with the metabolic syndrome. *J Hypertens.* 2003;21:371-8.	No weight outcomes
Laaksonen DE, Lindstrom J, Lakka TA, et al. Physical activity in the prevention of type 2 diabetes: the Finnish Diabetes Prevention Study. *Diabetes.* 2005;54:158-65.	No weight outcomes
Lally P, Chipperfield A, Wardle J. Healthy habits: efficacy of simple advice on weight control based on a habit-formation model. *Int J Obes (Lond).* 2008;32:700-7.	Less than 12 months followup
Larsen TM, Dalskov S, van Baak M, et al. The Diet, Obesity and Genes (Diogenes) dietary study in eight European countries—a comprehensive design for long-term intervention. *Obes Rev.* 2009;76-91.	Comparative effectiveness
Lasser VI, Raczynski JM, Stevens VJ, et al. Trials of Hypertension Prevention, phase II: structure and content of the weight loss and dietary sodium reduction interventions. *Ann Epidemiol.* 1995;5:156-64.	No weight outcomes
Laws R; Counterweight Project Team. A new evidence-based model for weight management in primary care: the Counterweight Programme. *J Hum Nutr Diet.* 2004;17:191-208.	Does not meet design requirements in inclusion criteria
Layman DK, Evans EM, Erickson D, et al. A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *J Nutr.* 2009;139:514-21.	Comparative effectiveness
Leermakers EA, Perri MG, Shigaki CL, Fuller PR. Effects of exercise-focused versus weight-focused maintenance programs on the management of obesity. *Addict Behav.* 1999;24:219-27.	Comparative effectiveness
Lehtovirta M, Forsen B, Gullstrom M, et al. Metabolic effects of metformin in patients with impaired glucose tolerance. *Diabet Med.* 2001;18:578-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Leibbrand R, Fichter MM. Maintenance of weight loss after obesity treatment: is continuous support necessary? *Behav Res Ther.* 2002;40:1275-89.	Focus on patients in subgroups other than specified conditions
Leinum CJ, Dopp JM, Morgan BJ. Sleep-disordered breathing and obesity: pathophysiology, complications, and treatment. *Nutr Clin Pract.* 2009;24:675-87.	Does not meet design requirements in inclusion criteria
Lejeune MP, Kovacs EM, Westerterp-Plantenga MS. Additional protein intake limits weight regain after weight loss in humans. *Br J Nutr.* 2005;93:281-9.	Less than 12 months followup
Liao D, Asberry PJ, Shofer JB, et al. Improvement of BMI, body composition, and body fat distribution with lifestyle modification in Japanese Americans with impaired glucose tolerance. *Diabetes Care.* 2002;25:1504-10.	Comparative effectiveness
Lien LF, Brown AJ, Ard JD, et al. Effects of PREMIER lifestyle modifications on participants with and without the metabolic syndrome. *Hypertension.* 2007;50:609-16.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Ligibel JA, Giobbie-Hurder A, Olenczuk D, et al. Impact of a mixed strength and endurance exercise intervention on levels of adiponectin, high molecular weight adiponectin and leptin in breast cancer survivors. *Cancer Causes Control.* 2009;20:1523-8.	Less than 12 months followup
Lindahl B, Nilsson TK, Jansson JH, et al. Improved fibrinolysis by intense lifestyle intervention: a randomized trial in subjects with impaired glucose tolerance. *J Intern Med.* 1999;246:105-12.	Not primary care feasible or referable

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Reference	Reason for Exclusion
Linde JA, Jeffery RW, Finch EA, et al. Are unrealistic weight loss goals associated with outcomes for overweight women? *Obes Res.* 2004;12:569-76.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Lindegarde F. Orlistat with diet was effective and safe for weight loss and coronary risk reduction in obesity. *Evid Based Med.* 2001;6:54.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Lindholm A, Bixo M, Bjorn I, et al. Effect of sibutramine on weight reduction in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Fertil Steril.* 2008;89:1221-8.	Less than 12 months followup
Lindholm LH, Ekbom T, Dash C, et al. The impact of health care advice given in primary care on cardiovascular risk. *BMJ.* 1995;310:1105-9.	Comparative effectiveness
Lindstrom J, Eriksson JG, Valle TT, et al. Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish Diabetes Prevention Study: results from a randomized clinical trial. *J Am Soc Nephrol.* 2003;14:S108-13.	No weight outcomes
Lindström J, Ilanne PP, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet.* 2006;368:1673-19.	No weight outcomes
Lindstrom J, Peltonen M, Eriksson JG, et al. High-fibre, low-fat diet predicts long-term weight loss and decreased type 2 diabetes risk: the Finnish Diabetes Prevention Study. *Diabetologia.* 2006;49:912-20.	No weight outcomes
Littman AJ, Vitiello MV, Foster-Schubert K, et al. Sleep, ghrelin, leptin and changes in body weight during a 1-year moderate-intensity physical activity intervention. *Int J Obes.* 2007;31:466-75.	No weight outcomes
Logue E, Sutton K, Jarjoura D, et al. Transtheoretical model-chronic disease care for obesity in primary care: a randomized trial. *Obes Res.* 2005;13:917-27.	Comparative effectiveness
Logue EE, Jarjoura DG, Sutton KS, et al. Longitudinal relationship between elapsed time in the action stages of change and weight loss. *Obes Res.* 2004;12:1499-508.	Does not meet design requirements in inclusion criteria
Lojander J, Mustajoki P, Ronka S, et al. A nurse-managed weight reduction programme for obstructive sleep apnoea syndrome. *J Intern Med.* 1998;244:251-5.	Does not meet design requirements in inclusion criteria
Lombard CB, Deeks AA, Ball K, et al. Weight, physical activity and dietary behavior change in young mothers: short term results of the HELP-HER cluster randomized controlled trial. *Nutr J.* 2009;8:17.	Less than 12 months followup
Bray G, Gregg E, et al; Look AHEAD Research Group. Baseline characteristics of the randomised cohort from the Look AHEAD (Action for Health in Diabetes) study. *Diabetes Vasc Dis Res.* 2006;3:202-15.	Comparative effectiveness
Wadden TA, West DS, et al; Look AHEAD Research Group. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity.* 2006;14:737-52.	Comparative effectiveness
Lucas CP, Boldrin MN, Reaven GM. Effect of orlistat added to diet (30% of calories from fat) on plasma lipids, glucose, and insulin in obese patients with hypercholesterolemia. *Am J Cardiol.* 2003;91:961-4.	Comparative effectiveness
Lucas KH, Kaplan-Machlis B. Orlistat—a novel weight loss therapy. *Ann Pharmacother.* 2001;35:314-28.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Major GC, Alarie F, Dore J, et al. Supplementation with calcium + vitamin D enhances the beneficial effect of weight loss on plasma lipid and lipoprotein concentrations. *Am J Clin Nutr.* 2007;85:54-9.	Not one of the specified interventions
Malone DC, Raebel MA, Porter JA, et al. Cost-effectiveness of sibutramine in the LOSE Weight Study: evaluating the role of pharmacologic weight-loss therapy within a weight management program. *J Manag Care Pharm.* 2005;11:458-68.	Comparative effectiveness
Malone M, Alger-Mayer S. Binge status and quality of life after gastric bypass surgery: a one-year study. *Obes Res.* 2004;12:473-81.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Manini TM, Newman AB, Fielding R, et al. Effects of exercise on mobility in obese and nonobese older adults. *Obesity (Silver Spring).* 2010;18:1168-75.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Manning RM, Jung RT, Leese GP, Newton RW. The comparison of four weight reduction strategies aimed at overweight patients with diabetes mellitus: four-year follow-up. *Diabet Med.* 1998;15:497-502.	Comparative effectiveness

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Reference	Reason for Exclusion
Marinilli PA, Gorin AA, Raynor HA, et al. Successful weight-loss maintenance in relation to method of weight loss. *Obesity.* 2008;16:2456-61.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Marshall NS, Grunstein RR. Losing weight in moderate to severe obstructive sleep apnoea. *BMJ.* 2009;339:b4363.	Conducted primarily in a non-relevant setting
Maruthur NM, Wang NY, Appel LJ. Lifestyle interventions reduce coronary heart disease risk: results from the PREMIER trial. *Circulation.* 2009;119:2026-31.	Not one of the specified interventions
Mata J, Silva MN, Vieira PN, et al. Motivational "spill-over" during weight control: increased self-determination and exercise intrinsic motivation predict eating self-regulation. *Health Psychol.* 2009;28:709-16.	No weight outcomes
Mathus-Vliegen EM; Balance Study Group. Long-term maintenance of weight loss with sibutramine in a GP setting following a specialist guided very-low-calorie diet: a double-blind, placebo-controlled, parallel group study. *Eur J Clin Nutr.* 2005;59(Suppl 1):S31-8.	Sibutramine intervention
Matvienko OA, Hoehns JD. A lifestyle intervention study in patients with diabetes or impaired glucose tolerance: translation of a research intervention into practice. *J Am Board Fam Med.* 2009;22:535-43.	Does not meet design requirements in inclusion criteria
McConnon A, Kirk SF, Cockroft JE, et al. The Internet for weight control in an obese sample: results of a randomised controlled trial. *BMC Health Serv Res.* 2007;7:206.	High or differential attrition
McConnon A, Kirk SF, Ransley JK. Process evaluation of an Internet-based resource for weight control: use and views of an obese sample. *J Nutr Educ Behav.* 2009;41:261-7.	No weight outcomes
McLaughlin T, Carter S, Lamendola C, et al. Clinical efficacy of two hypocaloric diets that vary in overweight patients with type 2 diabetes: comparison of moderate fat versus carbohydrate reductions. *Diabetes Care.* 2007;30:1877-9.	Comparative effectiveness
McMahon FG, Fujioka K, Singh BN, et al. Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. *Arch Intern Med.* 2000;160:2185-91.	Sibutramine intervention
McMahon FG, Weinstein SP, Rowe E, et al. Sibutramine is safe and effective for weight loss in obese patients whose hypertension is well controlled with angiotensin-converting enzyme inhibitors. *J Hum Hypertens.* 2002;16:5-11.	Sibutramine intervention
McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low fat, low-energy diet for weight loss in overweight adults. *Int J Obes Relat Metab Disord.* 2001;25:1503-11.	Comparative effectiveness
McNulty SJ, Ur E, Williams G. A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. *Diabetes Care.* 2003;26:125-31.	Sibutramine intervention
McTiernan A, Sorensen B, Irwin ML, et al. Exercise effect on weight and body fat in men and women. *Obesity.* 2007;15:1496-512.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Meenan RT, Vogt TM, Williams AE, et al. Economic evaluation of a worksite obesity prevention and intervention trial among hotel workers in Hawaii. *J Occup Environ Med.* 2010;52(Suppl 1):S8-13.	Conducted primarily in a non-relevant setting
Mengham LH, Morris BF, Palmer CR, White AJ. Is intensive dietetic intervention effective for overweight patients with diabetes mellitus? A randomised controlled trial in a general practice. *Pract Diab Int.* 1999;16:8.	Comparative effectiveness
Menon T, Quaddus S, Cohen L. Revision of failed vertical banded gastroplasty to non-resectional Scopinaro biliopancreatic diversion: early experience. *Obes Surg.* 2006;16:1420-4.	Comparative effectiveness
Messerli-Burgy N, Znoj H, Laederach K. Eating behavior, emotional regulation, and coping strategies in obese patients following a comprehensive weight reduction program. *Verhaltenstherapie.* 2007;17:56.	Does not meet design requirements in inclusion criteria
Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum.* 2004;50:1501-10.	Comparative effectiveness
Micic D, Ivkovic-Lazar T, Dragojevic R, et al. Orlistat, a gastrointestinal lipase inhibitor, in therapy of obesity with concomitant hyperlipidemia. *Med Pregl.* 1999;52:323-33.	Less than 12 months followup

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Reference	Reason for Exclusion
Molenaar EA, van Ameijden EJ, Vergouwe Y, et al. Effect of nutritional counselling and nutritional plus exercise counselling in overweight adults: a randomized trial in multidisciplinary primary care practice. *Fam Pract.* 2010;27:143-50.	High or differential attrition
Molitch ME, Fujimoto W, Hamman RF, et al. The Diabetes Prevention Program and its global implications. *J Am Soc Nephrol.* 2003;14(Suppl 2):S103-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Morgan PJ, Lubans DR, Collins CE, et al. 12-Month outcomes and process evaluation of the SHED-IT RCT: an Internet-based weight loss program targeting men. *Obesity (Silver Spring).* 2011;19:142-51.	Conducted primarily in a non-relevant setting
Muls E, Kolanowski J, Scheen A, Van Gaal L. The effects of orlistat on weight and on serum lipids in obese patients with hypercholesterolemia: a randomized, double-blind, placebo-controlled, multicentre study. *Int J Obes Relat Metab Disord.* 2001;25:1713-21.	Less than 12 months followup
Multiple Risk Factor Intervention Trial Research Group. Multiple Risk Factor Intervention Trial: risk factor changes and mortality results. *JAMA.* 1982;248:1465-77	Not one of the specified interventions
Munsch S, Biedert E, Keller U. Evaluation of a lifestyle change programme for the treatment of obesity in general practice. *Swiss Med Wkly.* 2003;133:148-54.	High or differential attrition
Murawski ME. Problem solving and the management of obesity in women from underserved rural settings. *Dissert Abstr Int B Sci Eng*. 2008;69:690.	Comparative effectiveness
Nahmias J, Kirschner M, Karetzky MS. Weight loss and OSA and pulmonary function in obesity. *N J Med.* 1993;90:48-53.	Does not meet design requirements in inclusion criteria
Nakata Y, Ohkawara K, Lee DJ, et al. Effects of additional resistance training during diet-induced weight loss on bone mineral density in overweight premenopausal women. *J Bone Miner Metab.* 2008;26:172-7.	Less than 12 months followup
Nanchahal K, Townsend J, Letley L, et al. Weight-management interventions in primary care: a pilot randomised controlled trial. *Br J Gen Pract.* 2009;59:e157-66.	Less than 12 months followup
Nauta H, Hospers H, Jansen A. One-year follow-up effects of two obesity treatments on psychological well-being and weight. *Br J Health Psychol.* 2001;6:271-84.	Comparative effectiveness
Neaton JD, Grimm RH Jr, Cutler JA. Recruitment of participants for the Multiple Risk Factor Intervention Trial (MRFIT). *Control Clin Trials.* 1987;8:S41-53.	Not one of the specified interventions
Nelson MS, Robbins AS, Thornton JA. An intervention to reduce excess body weight in adults with or at risk for type 2 diabetes. *Mil Med.* 2006;171:409-14.	Less than 12 months followup
Nicklas BJ, Ambrosius W, Messier SP, et al. Diet-induced weight loss, exercise, and chronic inflammation in older, obese adults: a randomized controlled clinical trial. *Am J Clin Nutr.* 2004;79:544-51.	Comparative effectiveness
Nowson CA, Worsley A, Margerison C, et al. Blood pressure change with weight loss is affected by diet type in men. *Am J Clin Nutr.* 2005;81:983-9.	Comparative effectiveness
Ockene IS, Hebert JR, Ockene JK, et al. Effect of physician-delivered nutrition counseling training and an office-support program on saturated fat intake, weight, and serum lipid measurements in a hyperlipidemic population: Worcester Area Trial for Counseling in Hyperlipidemia (WATCH). *Arch Intern Med.* 1999;159:725-31.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Olson TP, Dengel DR, Leon AS, Schmitz KH. Changes in inflammatory biomarkers following one-year of moderate resistance training in overweight women. *Int J Obes (Lond).* 2007;31:996-1003.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Olson TP, Dengel DR, Leon AS, Schmitz KH. Moderate resistance training and vascular health in overweight women. *Med Sci Sports Exerc.* 2006;38:1558-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Osei-Assibey G, Kyrou I, Adi Y, et al. Dietary and lifestyle interventions for weight management in adults from minority ethnic/non-white groups: a systematic review. *Obes Rev.* 2010;11:769-76.	Does not meet design requirements in inclusion criteria
Ost LG, Gotestam KG. Behavioral and pharmacological treatments for obesity: an experimental comparison. *Addict Behav.* 1976;1:331-8.	Precedes search period
Ostbye T, Krause KM, Lovelady CA, et al. Active Mothers Postpartum: a randomized controlled weight-loss intervention trial. *Am J Prev Med.* 2009;37:173-80.	Less than 12 months followup
O'Toole ML, Sawicki MA, Artal R. Structured diet and physical activity prevent postpartum weight retention. *J Womens Health (Larchmt).* 2003;12:991-8.	Comparative effectiveness

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Reference	Reason for Exclusion
Page RC, Harnden KE, Cook JT, Turner RC. Can life-styles of subjects with impaired glucose tolerance be changed? A feasibility study. *Diabet Med.* 1992;9:562-6.	Not one of the specified interventions
Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care.* 1997;20:537-44.	Not on list of countries with HDI > 0.90
Papalazarou A, Yannakoulia M, Kavouras SA, et al. Lifestyle intervention favorably affects weight loss and maintenance following obesity surgery. *Obesity (Silver Spring).* 2010;18:1348-53.	Comparative effectiveness
Park SK, Park JH, Kwon YC, et al. The effect of combined aerobic and resistance exercise training on abdominal fat in obese middle-aged women. *J Physiol Anthropol Appl Human Sci.* 2003;22:129-35.	Does not meet design requirements in inclusion criteria
Pasquali R, Colella P, Cirignotta F, et al. Treatment of obese patients with obstructive sleep apnea syndrome (OSAS): effect of weight loss and interference of otorhinolaryngoiatric pathology. *Int J Obes.* 1990;14:207-17.	Does not meet design requirements in inclusion criteria
Paul-Ebhohimhen V, Avenell A. A systematic review of the effectiveness of group versus individual treatments for adult obesity. *Obesity Facts.* 2009;2:17-24.	Does not meet design requirements in inclusion criteria
Perreault L, Kahn SE, Christophi CA, et al. Regression from pre-diabetes to normal glucose regulation in the Diabetes Prevention Program. *Diabetes Care.* 2009;32:1583-8.	No weight outcomes
Perreault L, Ma Y, Dagogo-Jack S, et al. Sex differences in diabetes risk and the effect of intensive lifestyle modification in the Diabetes Prevention Program. *Diabetes Care.* 2008;31:1416-21.	No weight outcomes
Perri MG, Limacher MC, Durning PE, et al. Extended-care programs for weight management in rural communities: the Treatment of Obesity in Underserved Rural Settings (TOURS) randomized trial. *Arch Intern Med.* 2008;168:2347-54.	Comparative effectiveness
Perrio MJ, Wilton LV, Shakir SA. The safety profiles of orlistat and sibutramine: results of prescription-event monitoring studies in England. *Obesity.* 2007;15:2712-22.	Does not meet design requirements in inclusion criteria
Petrofsky J, Batt J, Berk L, et al. The effect of an aerobic dance and diet program on cardiovascular fitness, body composition, and weight loss in women. *J Appl Res.* 2008;8:179-88.	Less than 12 months followup
Phelan S, Wadden TA, Berkowitz RI, et al. Impact of weight loss on the metabolic syndrome. *Int J Obes.* 2007;31:1442-8.	Does not meet design requirements in inclusion criteria
Philippou E, Neary NM, Chaudhri O, et al. The effect of dietary glycemic index on weight maintenance in overweight subjects: a pilot study. *Obesity.* 2009;17:396-401.	Comparative effectiveness
Pinkston MM, Poston WS, Reeves RS, et al. Does metabolic syndrome mitigate weight loss in overweight Mexican American women treated for 1-year with orlistat and lifestyle modification? *Eat Weight Disord.* 2006;11:e35-41.	No placebo in medication trial
Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the Look AHEAD trial. *Diabetes Care.* 2007;30:1374-83.	Comparative effectiveness
Porter JA, Raebel MA, Conner DA, et al. The Long-term Outcomes of Sibutramine Effectiveness on Weight (LOSE Weight) study: evaluating the role of drug therapy within a weight management program in a group-model health maintenance organization. *Am J Manag Care.* 2004;10:369-76.	No placebo in medication trial
Poston WS, Haddock CK, Olvera NE, et al. Evaluation of a culturally appropriate intervention to increase physical activity. *Am J Health Behav.* 2001;25:396-406.	Not one of the specified interventions
Poston WS, Haddock CK, Pinkston MM, et al. Evaluation of a primary care-oriented brief counselling intervention for obesity with and without orlistat. *J Intern Med.* 2006;260:388-98.	Does not meet design requirements in inclusion criteria
Poston WS, Reeves RS, Haddock CK, et al. Weight loss in obese Mexican Americans treated for 1-year with orlistat and lifestyle modification. *Int J Obes Relat Metab Disord.* 2003;27:1486-93.	No placebo in medication trial
Potteiger JA, Jacobsen DJ, Donnelly JE, Hill JO. Glucose and insulin responses following 16 months of exercise training in overweight adults: the Midwest Exercise Trial. *Metab.* 2003;52:1175-81.	High or differential attrition

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Reference	Reason for Exclusion
Potteiger JA, Kirk EP, Jacobsen DJ, Donnelly JE. Changes in resting metabolic rate and substrate oxidation after 16 months of exercise training in overweight adults. *Int J Sport Nutr Exerc Metab.* 2008;18:79-95.	High or differential attrition
Pritchard JE, Nowson CA, Wark JD. A worksite program for overweight middle-aged men achieves lesser weight loss with exercise than with dietary change. *J Am Diet Assoc.* 1997;97:37-42.	Conducted primarily in a non-relevant setting
Promrat K, Kleiner DE, Niemeier HM, et al. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. *Hepatology.* 2010;51:121-9.	Focus on patients in subgroups other than specified conditions
Proper KI, Hildebrandt VH, Van der Beek AJ, et al. Effect of individual counseling on physical activity fitness and health: a randomized controlled trial in a workplace setting. *Am J Prev Med.* 2003;24:218-26.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Provencher V, Begin C, Tremblay A, et al. Health-at-every-size and eating behaviors: 1-year follow-up results of a size acceptance intervention. *J Am Diet Assoc.* 2009;109:1854-61.	Not one of the specified interventions
Racette SB, Deusinger SS, Inman CL, et al. Worksite Opportunities for Wellness (WOW): effects on cardiovascular disease risk factors after 1 year. *Prev Med.* 2009;49:108-14.	Conducted primarily in a non-relevant setting
Racette SB, Weiss EP, Obert KA, et al. Modest lifestyle intervention and glucose tolerance in obese African Americans. *Obes Res.* 2001;9:348-55.	Comparative effectiveness
Racette SB, Weiss EP, Villareal DT, et al. One year of caloric restriction in humans: feasibility and effects on body composition and abdominal adipose tissue. *J Gerontol A Biol Sci Med Sci.* 2006;61:943-50.	Comparative effectiveness
Ramachandran A, Snehalatha C, Mary S, et al. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia.* 2006;49:289-97.	Not on list of countries with HDI > 0.90
Ramirez EM, Rosen JC. A comparison of weight control and weight control plus body image therapy for obese men and women. *J Consult Clin Psychol.* 2001;69:440-6.	Comparative effectiveness
Randomised trial of jejunoileal bypass versus medical treatment in morbid obesity. *Lancet.* 1979;2:1255-8.	Not one of the specified interventions
Rapoport L, Clark M, Wardle J. Evaluation of a modified cognitive-behavioural programme for weight management. *Int J Obes Relat Metab Disord.* 2000;24:1726-37.	Comparative effectiveness
Ratner RE; Diabetes Prevention Program. An update on the Diabetes Prevention Program. *Endocr Pract.* 2006; 12(Suppl 1):20-4.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Razquin C, Martinez JA, Martinez-Gonzalez MA, et al. A 3 years follow-up of a Mediterranean diet rich in virgin olive oil is associated with high plasma antioxidant capacity and reduced body weight gain. *Eur J Clin Nutr.* 2009;63:1387-93.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Reaven G, Segal K, Hauptman J, et al. Effect of orlistat-assisted weight loss in decreasing coronary heart disease risk in patients with syndrome X. *Am J Cardiol.* 2001;87:827-31.	Other quality issues
Redmon JB, Bertoni AG, Connelly S, et al. Effect of the Look AHEAD study intervention on medication use and related cost to treat cardiovascular disease risk factors in individuals with type 2 diabetes. *Diabetes Care.* 2010;33:1153-8.	Comparative effectiveness
Redmon JB, Raatz SK, Reck KP, et al. One-year outcome of a combination of weight loss therapies for subjects with type 2 diabetes: a randomized trial. *Diabetes Care.* 2003;26:2505-11.	Not one of the specified interventions
Redmon JB, Reck KP, Raatz SK, et al. Two-year outcome of a combination of weight loss therapies for type 2 diabetes. *Diabetes Care.* 2005;28:1311-5.	Comparative effectiveness
Reid IR, Horne A, Mason B, et al. Effects of calcium supplementation on body weight and blood pressure in normal older women: a randomized controlled trial. *J Clin Endocrinol Metab.* 2005;90:3824-9.	Not one of the specified interventions
Rejeski WJ, Focht BC, Messier SP, et al. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol.* 2002;21:419-26.	Comparative effectiveness
Renzaho AM, Mellor D, Boulton K, Swinburn B. Effectiveness of prevention programmes for obesity and chronic diseases among immigrants to developed countries—a systematic review. *Public Health Nutr.* 2010;13:438-50.	Does not meet design requirements in inclusion criteria

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Reference	Reason for Exclusion
Ricci TA, Chowdhury HA, Heymsfield SB, et al. Calcium supplementation suppresses bone turnover during weight reduction in postmenopausal women. *J Bone Miner Res.* 1998;13:1045-50.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Rimmer JH, Rauworth A, Wang E, et al. A randomized controlled trial to increase physical activity and reduce obesity in a predominantly African American group of women with mobility disabilities and severe obesity. *Prev Med.* 2009;48:473-9.	Less than 12 months followup
Rissanen P, Vahtera E, Krusius T, et al. Weight change and blood coagulability and fibrinolysis in healthy obese women. *Int J Obes Relat Metab Disord.* 2001;25:212-8.	No weight outcomes
Rock CL, Flatt SW, Sherwood NE, et al. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *JAMA.* 2010;304:1803-10.	Comparative effectiveness
Rock CL, Pakiz B, Flatt SW, Quintana EL. Randomized trial of a multifaceted commercial weight loss program. *Obesity.* 2007;15:939-49.	Comparative effectiveness
Rosenfalck AM, Hendel H, Rasmussen MH, et al. Minor long-term changes in weight have beneficial effects on insulin sensitivity and beta-cell function in obese subjects. *Diabetes Obes Metab.* 2002;4:19-28.	No weight outcomes
Ross R, Blair SN, Godwin M, et al. Prevention and Reduction of Obesity through Active Living (PROACTIVE): rationale, design and methods. *Br J Sports Med.* 2009;43:57-63.	No weight outcomes
Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obes Res.* 2004;12:789-98.	Comparative effectiveness
Rothacker DQ, Staniszewski BA, Ellis PK. Liquid meal replacement vs traditional food: a potential model for women who cannot maintain eating habit change. *J Am Diet Assoc.* 2001;101:345-7.	Comparative effectiveness
Rothert K, Strecher VJ, Doyle LA, et al. Web-based weight management programs in an integrated health care setting: a randomized, controlled trial. *Obesity.* 2006;14:266-72.	Less than 12 months followup
Ryan DH, Johnson WD, Myers VH, et al. Nonsurgical weight loss for extreme obesity in primary care settings: results of the Louisiana Obese Subjects Study. *Arch Intern Med.* 2010;170:146-54.	No placebo in medication trial
Sabbioni ME, Dickson MH, Eychmuller S, et al. Intermediate results of health related quality of life after vertical banded gastroplasty. *Int J Obes Relat Metab Disord.* 2002;26:277-80.	Not one of the specified interventions
Saccone A, Israel A. Effects of experimenter versus significant other-controlled reinforcement and choice of target behavior on weight loss. *Behav Ther*. 1978;9:271-8.	Precedes search period
Salas SJ, Fernández BJ, Ros E, et al. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. *Arch Intern Med.* 2008;168:2449-58.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Samaras K, Ashwell S, Mackintosh AM, et al. Will older sedentary people with non-insulin-dependent diabetes mellitus start exercising? A health promotion model. *Diabetes Res Clin Pract.* 1997;37:121-8.	Not one of the specified interventions
Sampol G, Munoz X, Sagales MT, et al. Long-term efficacy of dietary weight loss in sleep apnoea/hypopnoea syndrome. *Eur Respir J.* 1998;12:1156-9.	Does not meet design requirements in inclusion criteria
Samsa GP, Kolotkin RL, Williams GR, et al. Effect of moderate weight loss on health-related quality of life: an analysis of combined data from 4 randomized trials of sibutramine vs placebo. *Am J Manag Care.* 2001;7:875-83.	Does not meet design requirements in inclusion criteria
Sanchez-Reyes L, Fanghanel G, Yamamoto J, et al. Use of sibutramine in overweight adult Hispanic patients with type 2 diabetes mellitus: a 12-month, randomized, double-blind, placebo-controlled clinical trial. *Clin Ther.* 2004;26:1427-35.	Not on list of countries with HDI > 0.90
Sarac S, Sarac F. Cardiac valve evaluation and adipokine levels in obese women treated with sibutramine. *Anadolu Kardiyoloji Dergisi.* 2010;10:226-32.	Does not meet design requirements in inclusion criteria
Sarwer DB, von Sydow GA, Vetter ML, Wadden TA. Behavior therapy for obesity: where are we now? *Curr Opin Endocr Diabetes Obes.* 2009;16:347-52.	Does not meet design requirements in inclusion criteria
Sbrocco T, Nedegaard RC, Stone JM, Lewis EL. Behavioral choice treatment promotes continuing weight loss: preliminary results of a cognitive-behavioral decision-based treatment for obesity. *J Consult Clin Psychol.* 1999;67:260-6.	Comparative effectiveness

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Reference	Reason for Exclusion
Schmitz KH, Hannan PJ, Stovitz SD, et al. Strength training and adiposity in premenopausal women: Strong, Healthy, and Empowered study. *Am J Clin Nutr.* 2007;86:566-72.	No weight outcomes
Schuler G, Hambrecht R, Schlierf G, et al. Regular physical exercise and low-fat diet: effects on progression of coronary artery disease. *Circulation.* 1992;86:1-11.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Schuster RJ, Tasosa J, Terwoord NA. Translational research—implementation of NHLBI Obesity Guidelines in a primary care community setting: the Physician Obesity Awareness Project. *J Nutr Health Aging.* 2008;12:S764-9.	Comparative effectiveness
Serrano-Rios M, Melchionda N, Moreno-Carretero E. Role of sibutramine in the treatment of obese type 2 diabetic patients receiving sulphonylurea therapy. *Diabetes Med.* 2002;19:119-24.	Sibutramine intervention
Shapses SA, Heshka S, Heymsfield SB. Effect of calcium supplementation on weight and fat loss in women. *J Clin Endocrinol Metab.* 2004;89:632-7.	Not one of the specified interventions
Shea MK, Houston DK, Nicklas BJ, et al. The effect of randomization to weight loss on total mortality in older overweight and obese adults: the ADAPT study. *J Gerontol A Biol Sci Med Sci.* 2010;65:519-25.	Comparative effectiveness
Sherwood NE, Jeffery RW, Pronk NP, et al. Mail and phone interventions for weight loss in a managed-care setting: Weigh-To-Be 2-year outcomes. *Int J Obes.* 2006;30:1565-73.	High or differential attrition
Short KR, Vittone JL, Bigelow ML, et al. Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. *Diabetes.* 2003;52:1888-96.	Less than 12 months followup
Siegel JM, Prelip ML, Erausquin JT, Kim SA. A worksite obesity intervention: results from a group-randomized trial. *Am J Public Health.* 2010;100:327-33.	Conducted primarily in a non-relevant setting
Silva MN, Markland D, Carraca EV, et al. Exercise autonomous motivation predicts three-year weight loss in women. *Med Sci Sports Exerc.* 2011;43:728-37.	Study of overweight/obesity prevention
Simmons D, Rush E, Crook N; Te Wai o Rona Diabetes Prevention Strategy Team. Development and piloting of a community health worker-based intervention for the prevention of diabetes among New Zealand Maori in Te Wai o Rona: Diabetes Prevention Strategy. *Public Health Nutr.* 2008;11:1318-25.	Focus on patients in subgroups other than specified conditions
Sircar AR, Kumar A, Lal M. Clinical evaluation of sibutramine in obese type 2 diabetic patients refractory to dietary management. *J Assoc Physicians India.* 2001;49:885-8.	Less than 12 months followup
Sjostrom L. Analysis of the XENDOS study (Xenical in the Prevention of Diabetes in Obese Subjects). *Endocr Pract.* 2006;12(Suppl 1):31-3.	No weight outcomes
Skender ML, Goodrick GK, Del Junco DJ, et al. Comparison of 2-year weight loss trends in behavioral treatments of obesity: diet, exercise, and combination interventions. *J Am Diet Assoc.* 1996;96:342-6.	Comparative effectiveness
Skinner TC, Carey ME, Cradock S, et al. Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND): process modelling of pilot study. *Patient Educ Couns.* 2006;64:369-77.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE—a randomized controlled study. *Arch Intern Med.* 2004;164:31-9.	Less than 12 months followup
Smith IG, Goulder MA. Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. *J Fam Pract.* 2001;50:505-12.	Sibutramine intervention
Smith PL, Gold AR, Meyers DA, et al. Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med.* 1985;103:850-5.	Less than 12 months followup
Southard BH, Southard DR, Nuckolls J. Clinical trial of an Internet-based case management system for secondary prevention of heart disease. *J Cardiopulm Rehabil.* 2003;23:341-8.	Less than 12 months followup
Sramek JJ, Leibowitz MT, Weinstein SP, et al. Efficacy and safety of sibutramine for weight loss in obese patients with hypertension well controlled by beta-adrenergic blocking agents: a placebo-controlled, double-blind, randomised trial. *J Hum Hypertens.* 2002;16:13-9.	Less than 12 months followup
Stahre L, Hallstrom T. A short-term cognitive group treatment program gives substantial weight reduction up to 18 months from the end of treatment: a randomized controlled trial. *Eat Weight Disord.* 2005;10:51-8.	High or differential attrition

Appendix D Table 3. Studies Excluded From Review for Key Question 3

Reference	Reason for Exclusion
Stefanick ML, Mackey S, Sheehan M, et al. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. *N Engl J Med.* 1998;339:12-20.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Stenius-Aarniala B, Poussa T, Kvarnstrom J, et al. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ.* 2000;320:827-32.	Comparative effectiveness
Stensel DJ, Brooke-Wavell K, Hardman AE, et al. The influence of a 1-year programme of brisk walking on endurance fitness and body composition in previously sedentary men aged 42-59 years. *Eur J Appl Physiol Occup Physiol.* 1994;68:531-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Stern L, Iqbal N, Seshadri P, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med.* 2004;140:778-85.	Comparative effectiveness
Stuart RB. A three-dimensional program for the treatment of obesity. *Behav Res Ther.* 1971;9:177-86.	Precedes search period
Sun Q, Townsend MK, Okereke OI, et al. Adiposity and weight change in mid-life in relation to healthy survival after age 70 in women: prospective cohort study. *BMJ.* 2009;339:b3796.	Does not meet design requirements in inclusion criteria
Suratt PM, McTier RF, Findley LJ, et al. Effect of very-low-calorie diets with weight loss on obstructive sleep apnea. *Am J Clin Nutr.* 1992;56:S182-4.	Does not meet design requirements in inclusion criteria
Svendsen M, Helgeland M, Tonstad S. The long-term influence of orlistat on dietary intake in obese subjects with components of metabolic syndrome. *J Hum Nutr Diet.* 2009;22:55-63.	No weight outcomes
Svetkey LP, Pollak KI, Yancy WS Jr, et al. Hypertension Improvement Project: randomized trial of quality improvement for physicians and lifestyle modification for patients. *Hypertension.* 2009;54:1226-33.	Not one of the specified interventions
Swinburn BA, Metcalf PA, Ley SJ. Long-term (5-year) effects of a reduced-fat diet intervention in individuals with glucose intolerance. *Diabetes Care.* 2001;24:619-24.	Conducted primarily in a non-relevant setting
Swinburn BA, Woollard GA, Chang EC, Wilson MR. Effects of reduced-fat diets consumed ad libitum on intake of nutrients, particularly antioxidant vitamins. *J Am Diet Assoc.* 1999;99:1400-5.	Conducted primarily in a non-relevant setting
Tanco S, Linden W, Earle T. Well-being and morbid obesity in women: a controlled therapy evaluation. *Int J Eat Disord.* 1998;23:325-39.	Less than 12 months followup
Tanumihardjo SA, Valentine AR, Zhang Zet al. Strategies to increase vegetable or reduce energy and fat intake induce weight loss in adults. *Exp Biol Med.* 2009;234:542-52.	Comparative effectiveness
Tate DF, Jackvony EH, Wing RR. A randomized trial comparing human e-mail counseling, computer-automated tailored counseling, and no counseling in an Internet weight loss program. *Arch Intern Med.* 2006;166:1620-5.	Less than 12 months followup
Tate DF, Jackvony EH, Wing RR. Effects of Internet behavioral counseling on weight loss in adults at risk for type 2 diabetes: a randomized trial. *JAMA.* 2003;289:1833-6.	Comparative effectiveness
Tate DF, Jeffery RW, Sherwood NE, Wing RR. Long-term weight losses associated with prescription of higher physical activity goals: are higher levels of physical activity protective against weight regain? *Am J Clin Nutr.* 2007;85:954-9.	Comparative effectiveness
Tate DF, Wing RR, Winett RA. Using Internet technology to deliver a behavioral weight loss program. *JAMA.* 2001;285:1172-7.	Less than 12 months followup
Teixeira PJ, Going SB, Houtkooper LB, et al. Resistance training in postmenopausal women with and without hormone therapy. *Med Sci Sports Exerc.* 2003;35:555-62.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
ODES Investigators. The Oslo Diet and Exercise Study (ODES): design and objectives. *Control Clin Trials.* 1993;14:229-43.	No weight outcomes
Thomas TR, Warner SO, Dellsperger KC, et al. Exercise and the metabolic syndrome with weight regain. *J Appl Physiol.* 2010;109:3-10.	Comparative effectiveness
Thompson WG, Rostad HN, Janzow DJ, et al. Effect of energy-reduced diets high in dairy products and fiber on weight loss in obese adults. *Obes Res.* 2005;13:1344-53.	Comparative effectiveness
Tiikkainen M, Bergholm R, Rissanen A, et al. Effects of equal weight loss with orlistat and placebo on body fat and serum fatty acid composition and insulin resistance in obese women. *Am J Clin Nutr.* 2004;79:22-30.	Less than 12 months followup

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Reference	Reason for Exclusion
Tinker LF, Bonds DE, Margolis KL, et al. Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: the Women's Health Initiative randomized controlled dietary modification trial. *Arch Intern Med.* 2008;168:1500-11.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Toft U, Kristoffersen L, Ladelund S, et al. The effect of adding group-based counselling to individual lifestyle counselling on changes in dietary intake: the Inter99 Study—a randomized controlled trial. *Int J Behav Nutr Phys Act.* 2008;5:59.	No weight outcomes
Toobert DJ, Glasgow RE, Radcliffe JL. Physiologic and related behavioral outcomes from the Women's Lifestyle Heart Trial. *Ann Behav Med.* 2000;22:1-9.	Focus on patients in subgroups other than specified conditions
Toplak H, Ziegler O, Keller U, et al. X-PERT: weight reduction with orlistat in obese subjects receiving a mildly or moderately reduced-energy diet—early response to treatment predicts weight maintenance. *Diabetes Obes Metab.* 2005;7:699-708.	Comparative effectiveness
What is TOPS (Take Off Pounds Sensibly). Milwaukee, WI: TOPS Club, Inc; 2011. http://www.tops.org/TOPSInformation/AboutTOPS.aspx	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Trento M, Passera P, Tomalino M, et al. Group visits improve metabolic control in type 2 diabetes: a 2-year follow-up. *Diabetes Care.* 2001;24:995-1000.	Comparative effectiveness
Trolle B, Flyvbjerg A, Kesmodel U, Lauszus FF. Efficacy of metformin in obese and non-obese women with polycystic ovary syndrome: a randomized, double-blinded, placebo-controlled cross-over trial. *Hum Reprod.* 2007;22:2967-73.	Less than 12 months followup
Tsai AG, Wadden TA, Rogers MA, et al. A primary care intervention for weight loss: results of a randomized controlled pilot study. *Obesity (Silver Spring).* 2010;18:1614-8.	Comparative effectiveness
Tsai AG, Wadden TA. Treatment of obesity in primary care practice in the United States: a systematic review. *J Gen Intern Med.* 2009;24:1073-9.	Does not meet design requirements in inclusion criteria
Tseng MC, Lee MB, Chen SY, et al. Response of Taiwanese obese binge eaters to a hospital-based weight reduction program. *J Psychosom Res.* 2004;57:279-85.	Focus on patients in subgroups other than specified conditions
Turnin MC, Bourgeois O, Cathelineau G, et al. Multicenter randomized evaluation of a nutritional education software in obese patients. *Diabetes Metab.* 2001;27:139-47.	Comparative effectiveness
Tuthill A, Quinn A, McColgan D, et al. A prospective randomized controlled trial of lifestyle intervention on quality of life and cardiovascular risk score in patients with obesity and type 2 diabetes. *Diabetes Obes Metab.* 2007;9:917-9.	Less than 12 months followup
Uusi-Rasi K, Rauhio A, Kannus P, et al. Three-month weight reduction does not compromise bone strength in obese premenopausal women. *Bone.* 2010;46:1286-93.	Does not meet design requirements in inclusion criteria
Van Aggel-Leijssen DP, Saris WH, Hul GB, van Baak MA. Long-term effects of low-intensity exercise training on fat metabolism in weight-reduced obese men. *Metab.* 2002;51:1003-10.	Comparative effectiveness
Van Aggel-Leijssen DP, Saris WH, Hul GB, van Baak MA. Short-term effects of weight loss with or without low-intensity exercise training on fat metabolism in obese men. *Am J Clin Nutr.* 2001;73:523-31.	Comparative effectiveness
Van Aggel-Leijssen DP, Saris WH, Wagenmakers AJ, et al. The effect of low-intensity exercise training on fat metabolism of obese women. *Obes Res.* 2001;9:86-96.	Comparative effectiveness
Van Aggel-Leijssen DP, Saris WH, Wagenmakers AJ, et al. Effect of exercise training at different intensities on fat metabolism of obese men. *J Appl Physiol.* 2002;92:1300-9.	Comparative effectiveness
Van Gaal LF, Broom JI, Enzi G, Toplak H. Efficacy and tolerability of orlistat in the treatment of obesity: a 6-month dose-ranging study. *Eur J Clin Pharmacol.* 1998;54:125-32.	Less than 12 months followup
van Sluijs EM, van Poppel MN, Twisk JW, et al. Effect of a tailored physical activity intervention delivered in general practice settings: results of a randomized controlled trial. *Am J Public Health.* 2005;95:1825-31.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
van Wier MF, Ariens GA, Dekkers JC, et al. ALIFE@Work: a randomised controlled trial of a distance counselling lifestyle programme for weight control among an overweight working population. *BMC Public Health.* 2006;6:140.	Less than 12 months followup
van Wier MF, Ariens GA, Dekkers JC, et al. Phone and e-mail counselling are effective for weight management in an overweight working population: a randomized controlled trial. *BMC Public Health.* 2009;9:6.	Less than 12 months followup

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Reference	Reason for Exclusion
VanWormer JJ, Martinez AM, Benson GA, et al. Telephone counseling and home telemonitoring: the Weigh By Day Trial. *Am J Health Behavior.* 2009;33:445-54.	Comparative effectiveness
Velthuis MJ, Schuit AJ, Peeters PH, Monninkhof EM. Exercise program affects body composition but not weight in postmenopausal women. *Menopause.* 2009;16:777-84.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Venditti EM, Bray GA, Carrion-Petersen ML, et al. First versus repeat treatment with a lifestyle intervention program: attendance and weight loss outcomes. *Int J Obes.* 2008;32:1537-44.	No weight outcomes
Veverka DV, Anderson J, Auld GW, et al. Use of the stages of change model in improving nutrition and exercise habits in enlisted Air Force men. *Mil Med.* 2003;168:373-9.	Less than 12 months followup
Vidgren HM, Agren JJ, Valve RS, et al. The effect of orlistat on the fatty acid composition of serum lipid fractions in obese subjects. *Clin Pharmacol Ther.* 1999;66:315-22.	No weight outcomes
Villareal DT, Banks MR, Patterson BW, et al. Weight loss therapy improves pancreatic endocrine function in obese older adults. *Obesity.* 2008;16:1349-54.	No weight outcomes
Villareal DT, Fontana L, Weiss EP, et al. Bone mineral density response to caloric restriction-induced weight loss or exercise-induced weight loss: a randomized controlled trial. *Arch Intern Med.* 2006;166:2502-10.	Comparative effectiveness
Vissers D, Verrijken A, Mertens I, et al. Effect of long-term whole body vibration training on visceral adipose tissue: a preliminary report. *Obesity Facts.* 2010;3:93-100.	Other quality issues
Volpe SL, Kobusingye H, Bailur S, Stanek E. Effect of diet and exercise on body composition, energy intake and leptin levels in overweight women and men. *J Am Coll Nutr.* 2008;27:195-208.	Comparative effectiveness
von Huth SL, Ladelund S, Borch-Johnsen K, Jorgensen T. A randomized multifactorial intervention study for prevention of ischaemic heart disease (Inter99): the long-term effect on physical activity. *Scand J Public Health.* 2008;36:380-8.	No weight outcomes
Wadden TA, Berkowitz RI, Sarwer DB, et al. Benefits of lifestyle modification in the pharmacologic treatment of obesity: a randomized trial. *Arch Intern Med.* 2001;161:218-27.	Comparative effectiveness
Wadden TA, Berkowitz RI, Womble LG, et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity. *N Engl J Med.* 2005;353:2111-20.	No placebo in medication trial
Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD Study: factors associated with success. *Obesity.* 2009;17:713-22.	Comparative effectiveness
Wardle J, Rogers P, Judd P, et al. Randomized trial of the effects of cholesterol-lowering dietary treatment on psychological function. *Am J Med.* 2000;108:547-53.	Less than 12 months followup
Waring ME, Roberts MB, Parker DR, Eaton CB. Documentation and management of overweight and obesity in primary care. *J Am Board Fam Med.* 2009;22:544-52.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Warren M, Schmitz KH. Safety of strength training in premenopausal women: musculoskeletal injuries from a two-year randomized trial. *Am J Health Promot.* 2009;23:309-14.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Warziski MT, Sereika SM, Styn MA, et al. Changes in self-efficacy and dietary adherence: the impact on weight loss in the PREFER study. *J Behav Med.* 2008;31:81-92.	Comparative effectiveness
Wassertheil-Smoller S, Oberman A, Blaufox MD, et al. The Trial of Antihypertensive Interventions and Management (TAIM) study: final results with regard to blood pressure, cardiovascular risk, and quality of life. *Am J Hypertens.* 1992;5:37-44.	No weight outcomes
Wee CC, Davis RB, Phillips RS. Stage of readiness to control weight and adopt weight control behaviors in primary care. *J Gen Intern Med.* 2005;20:410-5.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Weiner R, Bockhorn H, Rosenthal R, Wagner D. A prospective randomized trial of different laparoscopic gastric banding techniques for morbid obesity. *Surg Endosc.* 2001;15:63-8.	Not one of the specified interventions
Weiss EP, Racette SB, Villareal DT, et al. Improvements in glucose tolerance and insulin action induced by increasing energy expenditure or decreasing energy intake: a randomized controlled trial. *Am J Clin Nutr.* 2006;84:1033-42.	Comparative effectiveness

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Reference	Reason for Exclusion
West DS, DiLillo V, Bursac Z, et al. Motivational interviewing improves weight loss in women with type 2 diabetes. *Diabetes Care.* 2007;30:1081-7.	Comparative effectiveness
Whittemore R, Melkus G, Wagner J, et al. Translating the Diabetes Prevention Program to primary care: a pilot study. *Nurs Res.* 2009;58:2-12.	Less than 12 months followup
Williamson DA, Martin CK, Anton SD, et al. Is caloric restriction associated with development of eating-disorder symptoms? Results from the CALERIE trial. *Health Psychol.* 2008;27(Suppl 1):S32-42.	Comparative effectiveness
Williamson DA, Rejeski J, Lang W, et al. Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. *Arch Intern Med.* 2009;169:163-71.	Comparative effectiveness
Williamson DF. Re: randomized trial of weight loss and total mortality. *J Gerontol A Biol Sci Med Sci.* 2010;65:904.	Does not meet design requirements in inclusion criteria
Wing RR, Anglin K. Effectiveness of a behavioral weight control program for blacks and whites with NIDDM. *Diabetes Care.* 1996;19:409-13.	Comparative effectiveness
Wing RR, Creasman JM, West DS, et al. Improving urinary incontinence in overweight and obese women through modest weight loss. *Obstetrics Gynecol.* 2010;116:284-92.	Comparative effectiveness
Wing RR, Epstein LH, Paternostro-Bayles M, et al. Exercise in a behavioural weight control programme for obese patients with type 2 (non-insulin-dependent) diabetes. *Diabetologia.* 1988;31:902-9.	Comparative effectiveness
Wing RR, Tate DF, Gorin AA, et al. STOP regain: are there negative effects of daily weighing? *J Consult Clin Psychol.* 2007;75:652-6.	No weight outcomes
Wing RR, Tate DF, Gorin AA, et al. A self-regulation program for maintenance of weight loss. *New Engl J Med.* 2006;355:1563-71.	Comparative effectiveness
Wing RR, Venditti E, Jakicic JM, et al. Lifestyle intervention in overweight individuals with a family history of diabetes. *Diabetes Care.* 1998;21:350-9.	Comparative effectiveness
Wing RR, West DS, Grady D, et al. Effect of weight loss on urinary incontinence in overweight and obese women: results at 12 and 18 months. *J Urol.* 2010;184:1005-10.	Comparative effectiveness
Wing RR. Behavioral approaches to the treatment of obesity. In: Bray G, Bouchard C, James WP, eds. *Handbook of Obesity*. New York: Marcel Dekker; 1998:855-73.	Does not meet design requirements in inclusion criteria
Wing RR. Behavioral weight control. In: Wadden TA, Stunkard AJ, eds. *Handbook of Obesity Treatment*. New York: Guilford Press; 2002:301-16.	Does not meet design requirements in inclusion criteria
Wirth A, Krause J. Long-term weight loss with sibutramine: a randomized controlled trial. *JAMA.* 2001;286:1331-9.	Sibutramine intervention
Wister A, Loewen N, Kennedy-Symonds H, et al. One-year follow-up of a therapeutic lifestyle intervention targeting cardiovascular disease risk. *Can Med Assoc J.* 2007;177:859-65.	Not one of the specified interventions
Wolf AM, Conaway MR, Crowther JQ, et al. Translating lifestyle intervention to practice in obese patients with type 2 diabetes: Improving Control with Activity and Nutrition (ICAN) study. *Diabetes Care.* 2004;27:1570-6.	Comparative effectiveness
Wolf AM, Siadaty MS, Crowther JQ, et al. Impact of lifestyle intervention on lost productivity and disability: improving control with activity and nutrition. *J Occup Environ Med.* 2009;51:139-45.	Comparative effectiveness
Womble LG, Wadden TA, McGuckin BG. A randomized controlled trial of a commercial Internet weight loss program. *Obes Res.* 2004;12:1011-8.	Comparative effectiveness
Wong SY, Lau EM, Lau WW, Lynn HS. Is dietary counselling effective in increasing dietary calcium, protein and energy intake in patients with osteoporotic fractures? A randomized controlled clinical trial. *J Hum Nutr Diet.* 2004;17:359-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Woo J, Sea MM, Tong P, et al. Effectiveness of a lifestyle modification programme in weight maintenance in obese subjects after cessation of treatment with orlistat. *J Eval Clin Pract.* 2007;13:853-9.	Less than 12 months followup
Wosje KS, Kalkwarf HJ. Lactation, weaning, and calcium supplementation: effects on body composition in postpartum women. *Am J Clin Nutr.* 2004;80:423-9.	Not one of the specified interventions
Wright AD, Cull CA, MacLeod KM, et al. Hypoglycemia in type 2 diabetic patients randomized to and maintained on monotherapy with diet, sulfonylurea, metformin, or insulin for 6 years from diagnosis: UKPDS73. *J Diabetes Complications.* 2006;20:395-401.	Comparative effectiveness

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Reference	Reason for Exclusion
Wylie-Rosett J, Swencionis C, Ginsberg M, et al. Computerized weight loss intervention optimizes staff time: the clinical and cost results of a controlled clinical trial conducted in a managed care setting. *J Am Diet Assoc.* 2001;101:1155-62.	Comparative effectiveness
Yancey AK, McCarthy WJ, Harrison GG, et al. Challenges in improving fitness: results of a community-based, randomized, controlled lifestyle change intervention. *J Womens Health.* 2006;15:412-29.	Not one of the specified interventions
Yassine HN, Marchetti CM, Krishnan RK, et al. Effects of exercise and caloric restriction on insulin resistance and cardiometabolic risk factors in older obese adults—a randomized clinical trial. *J Gerontol A Biol Sci Med Sci.* 2009;64:90-5.	Comparative effectiveness
Yates T, Davies M, Gorely T, et al. Effectiveness of a pragmatic education program designed to promote walking activity in individuals with impaired glucose tolerance: a randomized controlled trial. *Diabetes Care.* 2009;32:1404-10.	Not one of the specified interventions
Yeh MC, Rodriguez E, Nawaz H, et al. Technical skills for weight loss: 2-y follow-up results of a randomized trial. *Int J Obes Relat Metab Disord.* 2003;27:1500-6.	Comparative effectiveness
Zannad F, Gille B, Grentzinger A, et al. Effects of sibutramine on ventricular dimensions and heart valves in obese patients during weight reduction. *Am Heart J.* 2002;144:508-15.	Sibutramine intervention
Zavoral JH. Treatment with orlistat reduces cardiovascular risk in obese patients. *J Hypertens.* 1998;16:2013-7.	Other quality issues
Zemel MB, Richards J, Mathis S, et al. Dairy augmentation of total and central fat loss in obese subjects. *Int J Obes.* 2005;29:391-7.	Not one of the specified interventions
Zemel MB, Richards J, Milstead A, Campbell P. Effects of calcium and dairy on body composition and weight loss in African-American adults. *Obes Res.* 2005;13:1218-25.	Less than 12 months followup
Zemel MB, Thompson W, Milstead Aet al. Calcium and dairy acceleration of weight and fat loss during energy restriction in obese adults. *Obes Res.* 2004;12:582-90.	Comparative effectiveness

Appendix D Table 4. Studies Excluded From Review for Key Question 4

Reference	Reason for Exclusion
Aadahl M, von Huth SL, Pisinger C, et al. Five-year change in physical activity is associated with changes in cardiovascular disease risk factors: the Inter99 study. *Prev Med.* 2009;48(4):326-31.	Does not meet design requirements in inclusion criteria
Agurs-Collins TD, Kumanyika SK, Ten Have TR, Adams-Campbell LL. A randomized controlled trial of weight reduction and exercise for diabetes management in older African-American subjects. *Diabetes Care.* 1997;20:1503-11.	No harms outcomes
Akinson RL. Conjugated linoleic acid for altering body composition and treating obesity. In: Yurawecz MP, Mossoba MM, Kramer JK, et al, eds. *Advances in Conjugated Linoleic Acid Research.* vol 1. Champaign, IL: AOCS Press; 1999:348-53.	Does not meet design requirements in inclusion criteria
Alhassan S, Kim S, Bersamin A, et al. Dietary adherence and weight loss success among overweight women: results from the A TO Z weight loss study. *Int J Obes.* 2008;32:985-91.	Comparative effectiveness
Allen P, Thompson JL, Herman CJ, et al. Impact of periodic follow-up testing among urban American Indian women with impaired fasting glucose. *Prev Chron Dis.* 2008;5:A76.	Not one of the specified interventions
Andersen RE, Wadden TA, Bartlett SJ, et al. Effects of lifestyle activity vs structured aerobic exercise in obese women: a randomized trial. *JAMA.* 1999;281:335-40.	Comparative effectiveness
Anderson JW, Grant L, Gotthelf L, Stifler LT. Weight loss and long-term follow-up of severely obese individuals treated with an intense behavioral program. *Int J Obes.* 2007;31:488-93.	No harms outcomes
Anderssen SA, Carroll S, Urdal P, Holme I. Combined diet and exercise intervention reverses the metabolic syndrome in middle-aged males: results from the Oslo Diet and Exercise Study. *Scand J Med Sci Sports.* 2007;17:687-95.	No harms outcomes
Anderssen SA, Holme I, Urdal P, Hjermann I. Associations between central obesity and indexes of hemostatic, carbohydrate and lipid metabolism: results of a 1-year intervention from the Oslo Diet and Exercise Study. *Scand J Med Sci Sports.* 1998;8:109-15.	No harms outcomes
Andersson K, Karlstrom B, Freden S, et al. A two-year clinical lifestyle intervention program for weight loss in obesity. *Food Nutr Res.* 2008;52.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Andrade AM, Coutinho SR, Silva MN, et al. The effect of physical activity on weight loss is mediated by eating self-regulation. *Patient Educ Couns*. 2010;79(3):320-6.	No harms outcomes
Annunziato RA, Timko CA, Crerand CE, et al. A randomized trial examining differential meal replacement adherence in a weight loss maintenance program after one-year follow-up. *Eat Behav.* 2009;10:176-83.	Comparative effectiveness
Apfelbaum M, Vague P, Ziegler O, et al. Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. *Am J Med.* 1999;106:179-84.	Sibutramine intervention
Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA.* 2003;289:2083-93.	Not one of the specified interventions
Appel LJ, Espeland MA, Easter L, et al. Effects of reduced sodium intake on hypertension control in older individuals: results from the Trial of Nonpharmacologic Interventions in the Elderly (TONE). *Arch Intern Med.* 2001;161:685-93.	No harms outcomes
Arterburn D, DeLaet D, Schauer D. Obesity in adults. *Clin Evid (Online).* 2008.	Does not meet design requirements in inclusion criteria
Ash S, Reeves M, Bauer J, et al. A randomised control trial comparing lifestyle groups, individual counselling and written information in the management of weight and health outcomes over 12 months. *Int J Obes.* 2006;30:1557-64.	Comparative effectiveness
Ashley JM, St Jeor ST, Schrage JP, et al. Weight control in the physician's office. *Arch Intern Med.* 2001;161:1599-604.	Comparative effectiveness
Ashutosh K, Methrotra K, Fragale-Jackson J. Effects of sustained weight loss and exercise on aerobic fitness in obese women. *J Sports Med Phys Fitness.* 1997;37:252-7.	Comparative effectiveness
Avenell A, Brown TJ, McGee MA, et al. What are the long-term benefits of weight reducing diets in adults? A systematic review of randomized controlled trials. *J Hum Nutr Diet.* 2004;17:317-35.	Does not meet design requirements in inclusion criteria

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Reference	Reason for Exclusion
Babamoto KS, Sey KA, Camilleri AJ, et al. Improving diabetes care and health measures among Hispanics using community health workers: results from a randomized controlled trial. *Health Educ Behav.* 2009;36:113-26.	No harms outcomes
Bach DS, Rissanen AM, Mendel CM, et al. Absence of cardiac valve dysfunction in obese patients treated with sibutramine. *Obes Res.* 1999;7:363-9.	Sibutramine intervention
Bacon L, Keim NL, Van L, et al. Evaluating a "non-diet" wellness intervention for improvement of metabolic fitness, psychological well-being and eating and activity behaviors. *Int J Obes Relat Metab Disord.* 2002;26:854-65.	Comparative effectiveness
Balducci S, Zanuso S, Nicolucci A, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutr Metab Cardiovasc Dis.* 2010;20:608-17.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Barba M, Schunemann HJ, Sperati F, et al. The effects of metformin on endogenous androgens and SHBG in women: a systematic review and meta-analysis. *Clin Endocrinol (Oxf).* 2009;70:661-70.	No harms outcomes
Barr SI, McCarron DA, Heaney RP, et al. Effects of increased consumption of fluid milk on energy and nutrient intake, body weight, and cardiovascular risk factors in healthy older adults. *J Am Diet Assoc.* 2000;100:810-7.	Not one of the specified interventions
Bauer C, Fischer A, Keller U. Effect of sibutramine and of cognitive-behavioural weight loss therapy in obesity and subclinical binge eating disorder. *Diabetes Obes Metab.* 2006;8:289-95.	No harms outcomes
Beck-da-Silva L, Higginson L, Fraser M, et al. Effect of orlistat in obese patients with heart failure: a pilot study. *Congest Heart Fail.* 2005;11:118-23.	Focus on patients with obesity secondary to genetic or medical conditions, or medically induced weight gain
Bemelmans WJ, Broer J, de Vries JH, et al. Impact of Mediterranean diet education versus posted leaflet on dietary habits and serum cholesterol in a high risk population for cardiovascular disease. *Public Health Nutr.* 2000;3:273-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Bergstrom I, Lombardo C, Brinck J. Physical training decreases waist circumference in postmenopausal borderline overweight women. *Acta Obstet Gynecol Scand.* 2009;88:308-13.	Focus on patients in subgroups other than specified conditions
Berven G, Bye A, Hals O, et al. Safety of conjugated linoleic acid (CLA) in overweight or obese human volunteers. *Eur J Lipid Sci Tech*. 2009;102:455-62.	Not one of the specified interventions
Bhargava A, Guthrie JF. Unhealthy eating habits, physical exercise and macronutrient intakes are predictors of anthropometric indicators in the Women's Health Trial Feasibility Study in Minority Populations. *Br J Nutr.* 2002;88:719-28.	Not one of the specified interventions
Blankson H, Stakkestad JA, Fagertun H, et al. Conjugated linoleic acid reduces body fat mass in overweight and obese humans. *J Nutr.* 2000;130:2943-8.	Not one of the specified interventions
Blumenthal JA, Sherwood A, Gullette EC, et al. Exercise and weight loss reduce blood pressure in men and women with mild hypertension: effects on cardiovascular, metabolic, and hemodynamic functioning. *Arch Intern Med.* 2000;160:1947-58.	No harms outcomes
Bo S, Ciccone G, Baldi C, et al. Effectiveness of a lifestyle intervention on metabolic syndrome: a randomized controlled trial. *J Gen Intern Med.* 2007;22:1695-703.	Not one of the specified interventions
Bo S, Ciccone G, Guidi S, et al. Diet or exercise: what is more effective in preventing or reducing metabolic alterations? *Eur J Endocrinol.* 2008;159:685-91.	Not one of the specified interventions
Borg P, Kukkonen-Harjula K, Fogelholm M, Pasanen M. Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: a randomized trial. *Int J Obes Relat Metab Disord.* 2002;26:676-83.	Comparative effectiveness
Botomino A, Bruppacher R, Krahenbuhl S, Hersberger KE. Change of body weight and lifestyle of persons at risk for diabetes after screening and counselling in pharmacies. *Pharm World Sci.* 2008;30:222-6.	Does not meet design requirements in inclusion criteria
Bowen D, Clifford CK, Coates R, et al. The Women's Health Trial Feasibility Study in Minority Populations: design and baseline descriptions. *Ann Epidemiol.* 1996;6:507-19.	Not one of the specified interventions
Bowen J, Noakes M, Clifton PM. A high dairy protein, high-calcium diet minimizes bone turnover in overweight adults during weight loss. *J Nutr.* 2004;134:568-73.	No harms outcomes

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Reference	Reason for Exclusion
Bowerman S, Bellman M, Saltsman P, et al. Implementation of a primary care physician network obesity management program. *Obes Res.* 2001;9(Suppl 4):S321-5.	No harms outcomes
Bravata DM, Smith-Spangler C, Sundaram V, et al. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA.* 2007;298:2296-304.	Does not meet design requirements in inclusion criteria
Brinkworth GD, Noakes M, Keogh JB, et al. Long-term effects of a high-protein, low-carbohydrate diet on weight control and cardiovascular risk markers in obese hyperinsulinemic subjects. *Int J Obes Relat Metab Disord.* 2004;28:661-70.	Comparative effectiveness
Brinkworth GD, Noakes M, Parker B, et al. Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: one-year follow-up of a randomised trial. *Diabetologia.* 2004;47:1677-86.	Comparative effectiveness
Brownell KD. The LEARN Program for Weight Management. New Haven, CT: American Health Publishing Company; 2000.	Comparative effectiveness
Bryan J, Tiggemann M. The effect of weight-loss dieting on cognitive performance and psychological well-being in overweight women. *Appetite.* 2001;36:147-56.	No harms outcomes
Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA.* 2004;292:1724-37.	Does not meet design requirements in inclusion criteria
Burke V, Beilin LJ, Cutt HE, et al. A lifestyle program for treated hypertensives improved health-related behaviors and cardiovascular risk factors, a randomized controlled trial. *J Clin Epidemiol.* 2007;60:133-41.	No harms outcomes
Burke V, Mansour J, Beilin LJ, Mori TA. Long-term follow-up of participants in a health promotion program for treated hypertensives (ADAPT). *Nutr Metab Cardiovasc Dis.* 2008;18:198-206.	No harms outcomes
Burke V, Mori TA, Giangiulio N, et al. An innovative program for changing health behaviours. *Asia Pac J Clin Nutr.* 2002;11(Suppl 3):S586-97.	No harms outcomes
Caan B, Neuhouser M, Aragaki A, et al. Calcium plus vitamin D supplementation and the risk of postmenopausal weight gain. *Arch Intern Med.* 2007;167:893-902.	Not one of the specified interventions
Calle-Pascual AL, Rodriguez C, Camacho F, et al. Behaviour modification in obese subjects with type 2 diabetes mellitus. *Diabetes Res Clin Pract.* 1992;15:157-62.	Does not meet design requirements in inclusion criteria
Campbell PT, Campbell KL, Wener MH, et al. A yearlong exercise intervention decreases CRP among obese postmenopausal women. *Med Sci Sports Exerc.* 2009;41:1533-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Carr DB, Utzschneider KM, Boyko EJ, et al. A reduced-fat diet and aerobic exercise in Japanese Americans with impaired glucose tolerance decreases intra-abdominal fat and improves insulin sensitivity but not beta-cell function. *Diabetes.* 2005;54:340-7.	Comparative effectiveness
Carr LJ, Bartee RT, Dorozynski CM, et al. Eight-month follow-up of physical activity and central adiposity: results from an Internet-delivered randomized control trial intervention. *J Phys Act Health.* 2009;6:444-55.	Comparative effectiveness
Carter JD, Vasey FB, Valeriano J. The effect of a low-carbohydrate diet on bone turnover. *Osteoporos Int.* 2006;17:1398-403.	Does not include specified harms outcomes
Castaneda C, Layne JE, Munoz-Orians L, et al. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes Care.* 2002;25:2335-41.	No harms outcomes
Chang MW, Nitzke S, Brown R. Design and outcomes of a Mothers In Motion behavioral intervention pilot study. *J Nutr Educ Behav.* 2010;42(Suppl 3):11-21.	No harms outcomes
Charles MA, Morange P, Eschwege E, et al. Effect of weight change and metformin on fibrinolysis and the von Willebrand factor in obese nondiabetic subjects: the BIGPRO1 study. *Diabetes Care.* 1998;21:1967-72.	No harms outcomes
Cheatham RA, Roberts SB, Das SK, et al. Long-term effects of provided low and high glycemic load low energy diets on mood and cognition. *Physiol Behav.* 2009;98:374-9.	Comparative effectiveness
Cheyette C. Weight No More: a randomised controlled trial for people with type 2 diabetes on insulin therapy. *Pract Diabetes Int.* 2007;24:450-6.	Does not include specified harms outcomes
Chiasson JL, Lau DC, Leiter LA, et al. Fluoxetine has potential in obese NIDDM—multicenter Canadian trial. *Diabetes*. 1989;38(Suppl 2):A154.	Not one of the specified interventions

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Reference	Reason for Exclusion
Clark M, Hampson SE, Avery L, Simpson R. Effects of a tailored lifestyle self-management intervention in patients with type 2 diabetes. *Br J Health Psychol.* 2004;9:365-79.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Clarke KK, Freeland-Graves J, Klohe-Lehman DM, et al. Promotion of physical activity in low-income mothers using pedometers. *J Am Diet Assoc.* 2007;107:962-7.	No harms outcomes
Clifford PA, Tan SY, Gorsuch RL. Efficacy of a self-directed behavioral health change program: weight, body composition, cardiovascular fitness, blood pressure, health risk, and psychosocial mediating variables. *J Behav Med.* 1991;14:303-23.	Comparative effectiveness
Cocco G, Pandolfi S, Rousson V. Sufficient weight reduction decreases cardiovascular complications in diabetic patients with the metabolic syndrome: a randomized study of orlistat as an adjunct to lifestyle changes (diet and exercise). *Heart Drug.* 2005;5:68-74.	Does not include specified harms outcomes
Coker RH, Williams RH, Yeo SE, et al. The impact of exercise training compared to caloric restriction on hepatic and peripheral insulin resistance in obesity. *J Clin Endocrinol Metab.* 2009;94:4258-66.	No harms outcomes
Conradt M, Dierk JM, Schlumberger P, et al. A consultation with genetic information about obesity decreases self-blame about eating and leads to realistic weight loss goals in obese individuals. *J Psychosom Res.* 2009;66:287-95.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Corpeleijn E, Feskens EJ, Jansen EH, et al. Improvements in glucose tolerance and insulin sensitivity after lifestyle intervention are related to changes in serum fatty acid profile and desaturase activities: the SLIM study. *Diabetologia.* 2006;49:2392-401.	Not one of the specified interventions
Counterweight Project Team. Evaluation of the Counterweight Programme for obesity management in primary care: a starting point for continuous improvement. *Br J Gen Pract.* 2008;58:548-54.	Does not meet design requirements in inclusion criteria
Counterweight Project Team. Influence of body mass index on prescribing costs and potential cost savings of a weight management programme in primary care. *J Health Serv Res Policy.* 2008;13:158-66.	Does not meet design requirements in inclusion criteria
Cousins JH, Rubovits DS, Dunn JK, et al. Family versus individually oriented intervention for weight loss in Mexican American women. *Public Health Rep.* 1992;107:549-55.	Comparative effectiveness
Cox KL, Burke V, Morton AR, et al. Independent and additive effects of energy restriction and exercise on glucose and insulin concentrations in sedentary overweight men. *Am J Clin Nutr.* 2004;80:308-16.	No harms outcomes
Cuellar GE, Ruiz AM, Monsalve MC, Berber A. Six-month treatment of obesity with sibutramine 15 mg; a double-blind, placebo-controlled monocenter clinical trial in a Hispanic population. *Obes Res.* 2000;8:71-82.	Not on list of countries with HDI > 0.90
Dale KS, Mann JI, McAuley KA, et al. Sustainability of lifestyle changes following an intensive lifestyle intervention in insulin resistant adults: follow-up at 2-years. *Asia Pac J Clin Nutr.* 2009;18:114-20.	Comparative effectiveness
Dale KS, McAuley KA, Taylor RW, et al. Determining optimal approaches for weight maintenance: a randomized controlled trial. *Can Med Assoc J.* 2009;180:E39-46.	Comparative effectiveness
Davies MJ, Heller S, Skinner TC, et al. Effectiveness of the Diabetes Education and Self Management for Ongoing and Newly Diagnosed (DESMOND) Programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. *BMJ.* 2008;336:491-5.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Davis BR, Blaufox MD, Oberman A, et al. Reduction in long-term antihypertensive medication requirements: effects of weight reduction by dietary intervention in overweight persons with mild hypertension. *Arch Intern Med.* 1993;153:1773-82.	No harms outcomes
de Jager J, Kooy A, Lehert P, et al. Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled trial. *BMJ.* 2010;340:c2181.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
de Wit LT, Mathus-Vliegen L, Hey C, et al. Open versus laparoscopic adjustable silicone gastric banding: a prospective randomized trial for treatment of morbid obesity. *Ann Surg.* 1999;230:800-5.	Not one of the specified interventions
Delahanty LM, Nathan DM. Implications of the Diabetes Prevention Program and Look AHEAD clinical trials for lifestyle interventions. *J Am Diet Assoc.* 2008;108(Suppl 1):66-72.	Comparative effectiveness

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Reference	Reason for Exclusion
Delecluse C, Colman V, Roelants M, et al. Exercise programs for older men: mode and intensity to induce the highest possible health-related benefits. *Prev Med.* 2004;39:823-33.	Does not include specified harms outcomes
Dennis KE, Tomoyasu N, McCrone SH, et al. Self-efficacy targeted treatments for weight loss in postmenopausal women. *Sch Inq Nurs Pract.* 2001;15:259-76.	Comparative effectiveness
Derosa G, Cicero AF, Murdolo G, et al. Efficacy and safety comparative evaluation of orlistat and sibutramine treatment in hypertensive obese patients. *Diabetes Obes Metab.* 2005;7:47-55.	Comparative effectiveness
Devine A, Prince RL, Bell R. Nutritional effect of calcium supplementation by skim milk powder or calcium tablets on total nutrient intake in postmenopausal women. *Am J Clin Nutr.* 1996;64:731-7.	Comparative effectiveness
Di Francesco V, Sacco T, Zamboni M, et al. Weight loss and quality of life improvement in obese subjects treated with sibutramine: a double-blind randomized multicenter study. *Ann Nutr Metab.* 2007;51:75-81.	Sibutramine intervention
Di Loreto C, Fanelli C, Lucidi P, et al. Validation of a counseling strategy to promote the adoption and the maintenance of physical activity by type 2 diabetic subjects. *Diabetes Care.* 2003;26:404-8.	Comparative effectiveness
Ditschuneit HH, Flechtner-Mors M, Johnson TD, Adler G. Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *Am J Clin Nutr.* 1999;69:198-204.	Comparative effectiveness
Djuric Z, Lababidi S, Heilbrun LK, et al. Effect of low-fat and/or low-energy diets on anthropometric measures in participants of the Women's Diet Study. *J Am Coll Nutr.* 2002;21:38-46.	No harms outcomes
Donnelly JE, Hill JO, Jacobsen DJ, et al. Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med.* 2003;163:1343-50.	No harms outcomes
Donnelly JE, Jacobsen DJ, Heelan KS, et al. The effects of 18 months of intermittent vs. continuous exercise on aerobic capacity, body weight and composition, and metabolic fitness in previously sedentary, moderately obese females. *Int J Obes Relat Metab Disord.* 2000;24:566-72.	Comparative effectiveness
Donnelly JE, Smith BK, Dunn L, et al. Comparison of a phone vs clinic approach to achieve 10% weight loss. *Int J Obes.* 2007;31:1270-6.	No harms outcomes
Due A, Larsen TM, Mu H, et al. Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease, and diabetes: a 6-mo randomized, controlled trial. *Am J Clin Nutr.* 2008;88:1232-41.	No harms outcomes
Dujovne CA, Zavoral JH, Rowe E, Mendel CM. Effects of sibutramine on body weight and serum lipids: a double-blind, randomized, placebo-controlled study in 322 overweight and obese patients with dyslipidemia. *Am Heart J.* 2001;142:489-97.	Sibutramine intervention
Dunn AL, Marcus BH, Kampert JB, et al. Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. *JAMA.* 1999;281:327-34.	Comparative effectiveness
Dunstan DW, Daly RM, Owen N, et al. Home-based resistance training is not sufficient to maintain improved glycemic control following supervised training in older individuals with type 2 diabetes. *Diabetes Care.* 2005;28:3-9.	Comparative effectiveness
Dutton GR, Davis MP, Welsch MA, Brantley PJ. Promoting physical activity for low-income minority women in primary care. *Am J Health Behav.* 2007;31:622-31.	No harms outcomes
Dymek MP, Le Grange D, Neven K, Alverdy J. Quality of life after gastric bypass surgery: a cross-sectional study. *Obes Res.* 2002;10:1135-42.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dymek MP, Le Grange D, Neven K, Alverdy J. Quality of life and psychosocial adjustment in patients after Roux-en-Y gastric bypass: a brief report. *Obes Surg.* 2001;11:32-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Dyson PA, Hammersley MS, Morris RJ, et al. The Fasting Hyperglycaemia Study, II: randomized controlled trial of reinforced healthy-living advice in subjects with increased but not diabetic fasting plasma glucose. *Metabolism.* 1997;46:50-5.	Not one of the specified interventions
Dzator JA, Hendrie D, Burke V, et al. A randomized trial of interactive group sessions achieved greater improvements in nutrition and physical activity at a tiny increase in cost. *J Clin Epidemiol.* 2004;57:610-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss

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Reference	Reason for Exclusion
Early JL, Apovian CM, Aronne LJ, et al. Sibutramine plus meal replacement therapy for body weight loss and maintenance in obese patients. *Obesity.* 2007;15:1464-72.	Sibutramine intervention
Eddy DM, Schlessinger L, Kahn R. Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. *Ann Intern Med.* 2005;143:251-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Elhayany A, Lustman A, Abel R, et al. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. *Diabetes Obes Metab.* 2010;12:204-9.	Comparative effectiveness
Elmer PJ, Obarzanek E, Vollmer WM, et al. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. *Ann Intern Med.* 2006;144:485-95.	Comparative effectiveness
Ely AC, Banitt A, Befort C, et al. Kansas primary care weighs in: a pilot randomized trial of a chronic care model program for obesity in 3 rural Kansas primary care practices. *J Rural Health.* 2008;24:125-32.	No harms outcomes
Eriksson KM, Westborg CJ, Eliasson MC. A randomized trial of lifestyle intervention in primary healthcare for the modification of cardiovascular risk factors. *Scand J Public Health.* 2006;34:453-61.	Not one of the specified interventions
Esposito K, Giugliano F, Di Palo C, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. *JAMA.* 2004;291:2978-84.	Comparative effectiveness
Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA.* 2004;292:1440-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Esposito K, Pontillo A, Di Palo C, et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. *JAMA.* 2003;289:1799-804.	Comparative effectiveness
Eyjolfson V, Spriet LL, Dyck DJ. Conjugated linoleic acid improves insulin sensitivity in young, sedentary humans. *Med Sci Sports Exerc.* 2004;36:814-20.	Not one of the specified interventions
Fabricatore AN, Wadden TA, Moore RH, et al. Predictors of attrition and weight loss success: results from a randomized controlled trial. *Behav Res Ther.* 2009;47:685-91.	Comparative effectiveness
Fanghanel G, Cortinas L, Sanchez-Reyes L, Berber A. A clinical trial of the use of sibutramine for the treatment of patients suffering essential obesity. *Int J Obes Relat Metab Disord.* 2000;24:144-50.	Does not include specified harms outcomes
Fanghanel G, Cortinas L, Sanchez-Reyes L, et al. Safety and efficacy of sibutramine in overweight Hispanic patients with hypertension. *Adv Ther.* 2003;20:101-13.	No harms outcomes
Faria AN, Ribeiro Filho FF, Kohlmann NE, et al. Effects of sibutramine on abdominal fat mass, insulin resistance and blood pressure in obese hypertensive patients. *Diabetes Obes Metab.* 2005;7:246-53.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Faria AN, Ribeiro Filho FF, Lerario DD, et al. Effects of sibutramine on the treatment of obesity in patients with arterial hypertension. *Arq Bras Cardiol.* 2002;78:172-80.	No harms outcomes
Faulconbridge LF, Wadden TA, Berkowitz RI, et al. Changes in symptoms of depression with weight loss: results of a randomized trial. *Obesity.* 2009;17:1009-16.	No placebo in medication trial
Ferre R, Plana N, Merino J, et al. Effects of therapeutic lifestyle changes on peripheral artery tonometry in patients with abdominal obesity. *Nutr Metab Cardiovasc Dis.* 2010 Aug 11. [Epub ahead of print]	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Field AE, Malspeis S, Willett WC. Weight cycling and mortality among middle-aged or older women. *Arch Intern Med.* 2009;169:881-6.	Other quality issues
Figueroa A, Going SB, Milliken LA, et al. Effects of exercise training and hormone replacement therapy on lean and fat mass in postmenopausal women. *J Gerontol A Biol Sci Med Sci.* 2003;58:266-70.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Finer N, Bloom SR, Frost GS, et al. Sibutramine is effective for weight loss and diabetic control in obesity with type 2 diabetes: a randomised, double-blind, placebo-controlled study. *Diabetes Obes Metab.* 2000;2:105-12.	Sibutramine intervention

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Reference	Reason for Exclusion
Finkelstein EA, Linnan LA, Tate DF, Leese PJ. A longitudinal study on the relationship between weight loss, medical expenditures, and absenteeism among overweight employees in the WAY to Health study. *J Occup Environ Med.* 2009;51:1367-73.	Conducted primarily in a non-relevant setting
Finley CE, Barlow CE, Greenway FL, et al. Retention rates and weight loss in a commercial weight loss program. *Int J Obes (Lond).* 2007;31:292-8.	Does not meet design requirements in inclusion criteria
Fitzgibbon ML, Stolley MR, Ganschow P, et al. Results of a faith-based weight loss intervention for black women. *J Natl Med Assoc.* 2005;97:1393-402.	Comparative effectiveness
Fitzgibbon ML, Stolley MR, Schiffer L, et al. A combined breast health/weight loss intervention for black women. *Prev Med.* 2005;40:373-83.	No harms outcomes
Fitzgibbon ML, Stolley MR, Schiffer L, et al. Obesity Reduction Black Intervention Trial (ORBIT): 18-month results. *Obesity (Silver Spring).* 2010;18:2317-25.	No harms outcomes
Flechtner-Mors M, Ditschuneit HH, Johnson TD, et al. Metabolic and weight loss effects of long-term dietary intervention in obese patients: four-year results. *Obes Res.* 2000;8:399-402.	Comparative effectiveness
Fleming R, Hopkinson ZE, Wallace AM, et al. Ovarian function and metabolic factors in women with oligomenorrhea treated with metformin in a randomized double blind placebo-controlled trial. *J Clin Endocrinol Metab.* 2002;87:569-74.	No harms outcomes
Fleming RM. The effect of high-, moderate-, and low-fat diets on weight loss and cardiovascular disease risk factors. *Prev Cardiol.* 2002;5:110-8.	Comparative effectiveness
Flood A, Mitchell N, Jaeb M, et al. Energy density and weight change in a long-term weight-loss trial. *Int J Behav Nutr Phys Act.* 2009;6:57.	Study of overweight/obesity prevention
Focht BC, Rejeski WJ, Ambrosius WT, et al. Exercise, self-efficacy, and mobility performance in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum.* 2005;53:659-65.	Comparative effectiveness
Fogelholm M, Kukkonen-Harjula K, Nenonen A, Pasanen M. Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. *Arch Intern Med.* 2000;160:2177-84.	Comparative effectiveness
Fogelholm M, Kukkonen-Harjula K, Oja P. Eating control and physical activity as determinants of short-term weight maintenance after a very-low-calorie diet among obese women. *Int J Obes Relat Metab Disord.* 1999;23:203-10.	Comparative effectiveness
Fontana L, Villareal DT, Weiss EP, et al. Calorie restriction or exercise: effects on coronary heart disease risk factors: a randomized, controlled trial. *Am J Physiol Endocrinol Metab.* 2007;293:E197-202.	Comparative effectiveness
Fontbonne A, Diouf I, Baccara-Dinet M, et al. Effects of 1-year treatment with metformin on metabolic and cardiovascular risk factors in non-diabetic upper-body obese subjects with mild glucose anomalies: a post-hoc analysis of the BIGPRO1 trial. *Diabetes Metab.* 2009;35:385-91.	No harms outcomes
Fossati M, Amati F, Painot D, et al. Cognitive-behavioral therapy with simultaneous nutritional and physical activity education in obese patients with binge eating disorder. *Eat Weight Disord.* 2004;9:134-8.	Focus on patients in subgroups other than specified conditions
Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med.* 2009;169:1619-26.	Comparative effectiveness
Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med.* 2003;348:2082-90.	Comparative effectiveness
Foster-Schubert KE, McTiernan A, Frayo RS, et al. Human plasma ghrelin levels increase during a one-year exercise program. *J Clin Endocrinol Metab.* 2005;90:820-5.	No harms outcomes
Fujimoto WY, Jablonski KA, Bray GA, et al. Body size and shape changes and the risk of diabetes in the Diabetes Prevention Program. *Diabetes.* 2007;56:1680-5.	No harms outcomes
Fujioka K, Seaton TB, Rowe E, et al. Weight loss with sibutramine improves glycaemic control and other metabolic parameters in obese patients with type 2 diabetes mellitus. *Diabetes Obes Metab.* 2000;2:175-87.	Sibutramine intervention
Gambineri A, Pelusi C, Genghini S, et al. Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome. *Clin Endocrinol (Oxf).* 2004;60:241-9.	No harms outcomes
Gaullier JM, Halse J, Hoivik HO, et al. Six months supplementation with conjugated linoleic acid induces regional-specific fat mass decreases in overweight and obese. *Br J Nutr.* 2007;97:550-60.	Not one of the specified interventions

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Reference	Reason for Exclusion
Gaullier JM, Halse J, Hoye K, et al. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. *Am J Clin Nutr.* 2004;79:1118-25.	Not one of the specified interventions
Gaullier JM, Halse J, Hoye K, et al. Supplementation with conjugated linoleic acid for 24 months is well tolerated by and reduces body fat mass in healthy, overweight humans. *J Nutr.* 2005;135:778-84.	Not one of the specified interventions
Ghroubi S, Elleuch H, Chikh T, et al. Physical training combined with dietary measures in the treatment of adult obesity; a comparison of two protocols. *Ann Phys Rehab Med.* 2009;52:394-413.	Not on list of countries with HDI > 0.90
Giugliano D, Quatraro A, Consoli G, et al. Metformin for obese, insulin-treated diabetic patients: improvement in glycaemic control and reduction of metabolic risk factors. *Eur J Clin Pharmacol.* 1993;44:107-12.	No harms outcomes
Glasgow RE, La Chance PA, Toobert DJ, et al. Long-term effects and costs of brief behavioural dietary intervention for patients with diabetes delivered from the medical office. *Patient Educ Couns.* 1997;32:175-84.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Glasgow RE, Nelson CC, Kearney KA, et al. Reach, engagement, and retention in an Internet-based weight loss program in a multi-site randomized controlled trial. *J Med Internet Res.* 2007;9:e11.	No harms outcomes
Godoy-Matos A, Carraro L, Vieira A, et al. Treatment of obese adolescents with sibutramine: a randomized, double-blind, controlled study. *J Clin Endocrinol Metab.* 2005;90:1460-5.	Focus on children or adolescents
Gokcel A, Karakose H, Ertorer EM, et al. Effects of sibutramine in obese female subjects with type 2 diabetes and poor blood glucose control. *Diabetes Care.* 2001;24:1957-60.	Not on list of countries with HDI > 0.90
Gold BC, Burke S, Pintauro S, et al. Weight loss on the web: a pilot study comparing a structured behavioral intervention to a commercial program. *Obesity.* 2007;15:155-64.	Comparative effectiveness
Gotfredsen A, Westergren HH, Andersen T. Influence of orlistat on bone turnover and body composition. *Int J Obes Relat Metab Disord.* 2001;25:1154-60.	No harms outcomes
Greaves CJ, Middlebrooke A, O'Loughlin L, et al. Motivational interviewing for modifying diabetes risk: a randomised controlled trial. *Br J Gen Pract.* 2008;58:535-40.	No harms outcomes
Grimm RH Jr, Grandits GA, Cutler JA, et al. Relationships of quality-of-life measures to long-term lifestyle and drug treatment in the Treatment of Mild Hypertension Study. *Arch Intern Med.* 1997;157:638-48.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Guisado JA, Vaz FJ, Alarcon J, et al. Psychopathological status and interpersonal functioning following weight loss in morbidly obese patients undergoing bariatric surgery. *Obes Surg.* 2002;12:835-40.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Gunther CW, Legowski PA, Lyle RM, et al. Dairy products do not lead to alterations in body weight or fat mass in young women in a 1-y intervention. *Am J Clin Nutr.* 2005;81:751-6.	Study of overweight/obesity prevention
Gurka MJ, Wolf AM, Conaway MR, et al. Lifestyle intervention in obese patients with type 2 diabetes: impact of the patient's educational background. *Obesity.* 2006;14:1085-92.	Comparative effectiveness
Gustafson A, Khavjou O, Stearns SC, et al. Cost-effectiveness of a behavioral weight loss intervention for low-income women: the Weight-Wise Program. *Prev Med.* 2009;49:390-5.	No harms outcomes
Guy-Grand B, Drouin P, Eschwege E, et al. Effects of orlistat on obesity-related diseases—a six-month randomized trial. *Diabetes Obes Metab.* 2004;6:375-83.	No harms outcomes
Hainer V, Kunesova M, Bellisle F, et al. Psychobehavioral and nutritional predictors of weight loss in obese women treated with sibutramine. *Int J Obes (Lond).* 2005;29:208-16.	No harms outcomes
Hakala K, Maasilta P, Sovijarvi AR. Upright body position and weight loss improve respiratory mechanics and daytime oxygenation in obese patients with obstructive sleep apnoea. *Clin Physiol.* 2000;20:50-5.	Does not meet design requirements in inclusion criteria
Hall WD, Feng Z, George VA, et al. Low-fat diet: effect on anthropometrics, blood pressure, glucose, and insulin in older women. *Ethn Dis.* 2003;13:337-43.	No harms outcomes
Halpern A, Leite CC, Herszkowicz N, et al. Evaluation of efficacy, reliability, and tolerability of sibutramine in obese patients, with an echocardiographic study. *Rev Hosp Clin Fac Med Sao Paulo.* 2002;57:98-102.	Does not include specified harms outcomes

Appendix D Table 4. Studies Excluded From Review for Key Question 4

Reference	Reason for Exclusion
Hansen D, Astrup A, Toubro S, et al. Predictors of weight loss and maintenance during 2 years of treatment by sibutramine in obesity: results from the European multi-centre STORM trial. *Int J Obes Rel Metab Disord.* 2001;25:496-501.	No harms outcomes
Hansen DL, Toubro S, Stock MJ, et al. The effect of sibutramine on energy expenditure and appetite during chronic treatment without dietary restriction. *Int J Obes Relat Metab Disord.* 1999;23:1016-24.	Sibutramine intervention
Harvey BJ, Gold BC, Lauber R, Starinski A. The impact of calcium and dairy product consumption on weight loss. *Obes Res.* 2005;13:1720-6.	Comparative effectiveness
Harvey-Berino J, Pintauro S, Buzzell P, et al. Does using the Internet facilitate the maintenance of weight loss? *Int J Obes Relat Metab Disord.* 2002;26:1254-60.	Comparative effectiveness
Harvey-Berino J, Pintauro S, Buzzell P, Gold EC. Effect of Internet support on the long-term maintenance of weight loss. *Obes Res.* 2004;12:320-9.	Comparative effectiveness
Harvey-Berino J, Pintauro SJ, Gold EC. The feasibility of using Internet support for the maintenance of weight loss. *Behav Modif.* 2002;26:103-16.	No harms outcomes
Haskell WL, Alderman EL, Fair JM, et al. Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease. *Circulation.* 1994;89:975-90.	Not one of the specified interventions
Haub MD, Simons TR, Cook CM, et al. Calcium-fortified beverage supplementation on body composition in postmenopausal women. *Nutr J.* 2005;4:21.	Not one of the specified interventions
Hauner H, Meier M, Wendland G, et al. Weight reduction by sibutramine in obese subjects in primary care medicine: the SAT Study. *Exp Clin Endocrinol Diabetes.* 2004;112:201-7.	Sibutramine intervention
Hawley G, Horwath C, Gray A, et al. Sustainability of health and lifestyle improvements following a non-dieting randomised trial in overweight women. *Prev Med.* 2008;47:593-9.	Comparative effectiveness
Hays NP, Starling RD, Sullivan DH, et al. Effects of an ad libitum, high carbohydrate diet and aerobic exercise training on insulin action and muscle metabolism in older men and women. *J Gerontol A Biol Sci Med Sci.* 2006;61:299-304.	No harms outcomes
Hazenberg BP. Randomized, double-blind, placebo-controlled, multicenter study of sibutramine in obese hypertensive patients. *Cardiology.* 2000;94:152-8.	Sibutramine intervention
Hensrud DD. Dietary treatment and long-term weight loss and maintenance in type 2 diabetes. *Obes Res.* 2001;9(Suppl 4):S348-53.	Does not meet design requirements in inclusion criteria
Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med.* 2005;142:323-32.	No harms outcomes
Hermann LS, Kalen J, Katzman P, et al. Long-term glycaemic improvement after addition of metformin to insulin in insulin-treated obese type 2 diabetes patients. *Diabetes Obes Metab.* 2001;3:428-34.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Heshka S, Anderson JW, Atkinson RL, et al. Weight loss with self-help compared with a structured commercial program: a randomized trial. *JAMA.* 2003;289:1792-8.	Comparative effectiveness
Heymsfield SB, Segal KR, Hauptman J, et al. Effects of weight loss with orlistat on glucose tolerance and progression to type 2 diabetes in obese adults. *Arch Intern Med.* 2000;160:1321-6.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hivert MF, Langlois MF, Berard P, et al. Prevention of weight gain in young adults through a seminar-based intervention program. *Int J Obes.* 2007;31:1262-9.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Hoeger KM, Kochman L, Wixom N, et al. A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertil Steril.* 2004;82:421-9.	Does not include specified harms outcomes
Hooper L. Primary prevention of CVD: diet and weight loss. *Clin Evid (Online).* 2007.	Does not meet design requirements in inclusion criteria
Hope AA, Kumanyika SK, Shults J, Holmes WC. Changes in health-related quality of life among African-Americans in a lifestyle weight loss program. *Qual Life Res.* 2010;19:1025-33.	Does not meet design requirements in inclusion criteria
Howard BV, Manson JE, Stefanick ML, et al. Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. *JAMA.* 2006;295:39-49.	Not focused on behavioral or pharmacological interventions designed to promote weight loss

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Reference	Reason for Exclusion
Hsieh CJ, Wang PW, Liu RT, et al. Orlistat for obesity: benefits beyond weight loss. *Diabetes Res Clin Pract.* 2005;67:78-83.	Not on list of countries with HDI > 0.90
Hunter GR, Brock DW, Byrne NM, et al. Exercise training prevents regain of visceral fat for 1 year following weight loss. *Obesity.* 2010;18:690-5.	Comparative effectiveness
Jacobs DR, Sluik D, Rokling-Andersen MH, et al. Association of 1-y changes in diet pattern with cardiovascular disease risk factors and adipokines: results from the 1-y randomized Oslo Diet and Exercise Study. *Am J Clin Nutr.* 2009;89:509-17.	No harms outcomes
Jakicic JM, Jaramillo SA, Balasubramanyam A, et al. Effect of a lifestyle intervention on change in cardiorespiratory fitness in adults with type 2 diabetes: results from the Look AHEAD Study. *Int J Obes.* 2009;33:305-16.	Comparative effectiveness
Jakicic JM, Marcus BH, Gallagher KI, et al. Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *JAMA.* 2003;290:1323-30.	Comparative effectiveness
Jakicic JM, Otto AD, Lang W, et al. The effect of physical activity on 18-month weight change in overweight adults. *Obesity (Silver Spring).* 2011;19:100-9.	Comparative effectiveness
Jakicic JM, Winters C, Lang W, Wing RR. Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *JAMA.* 1999;282:1554-60.	Comparative effectiveness
Jakubowicz DJ, Seppala M, Jakubowicz S, et al. Insulin reduction with metformin increases luteal phase serum glycodelin and insulin-like growth factor-binding protein 1 concentrations and enhances uterine vascularity and blood flow in the polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2001;86:1126-33.	No harms outcomes
Jalkanen L. The effect of a weight reduction program on cardiovascular risk factors among overweight hypertensives in primary health care. *Scand J Soc Med.* 1991;19:66-71.	Other quality issues
James WP, Astrup A, Finer N, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. *Lancet.* 2000;356:2119-25.	Sibutramine intervention
Janssen I, Fortier A, Hudson R, Ross R. Effects of an energy-restrictive diet with or without exercise on abdominal fat, intermuscular fat, and metabolic risk factors in obese women. *Diabetes Care.* 2002;25:431-8.	No harms outcomes
Jarjou LM, Prentice A, Sawo Y, et al. Randomized, placebo-controlled, calcium supplementation study in pregnant Gambian women: effects on breast-milk calcium concentrations and infant birth weight, growth, and bone mineral accretion in the first year of life. *Am J Clin Nutr.* 2006;83:657-66.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Jarrett RJ, Keen H, Murrells T. Changes in blood pressure and body weight over ten years in men selected for glucose intolerance. *J Epidemiol Community Health.* 1987;41:145-51.	Comparative effectiveness
Jeffery RW, French SA. Preventing weight gain in adults: design, methods and one year results from the Pound of Prevention study. *Int J Obes Relat Metab Disord.* 1997;21:457-64.	Study of overweight/obesity prevention
Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr.* 2003;78:684-9.	Comparative effectiveness
Jehn ML, Patt MR, Appel LJ, Miller ER III. One year follow-up of overweight and obese hypertensive adults following intensive lifestyle therapy. *J Hum Nutr Diet.* 2006;19:349-54.	Comparative effectiveness
Jensen LB, Kollerup G, Quaade F, Sorensen OH. Bone minerals changes in obese women during a moderate weight loss with and without calcium supplementation. *J Bone Miner Res.* 2001;16:141-7.	Comparative effectiveness
Jirik-Babb P, Geliebter A. Comparison of psychological characteristics of binging and nonbinging obese, adult, female outpatients. *Eat Weight Disord.* 2003;8:173-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Jordan J, Scholze J, Matiba B, et al. Influence of sibutramine on blood pressure: evidence from placebo-controlled trials. *Int J Obes.* 2005;29:509-16.	Does not meet design requirements in inclusion criteria
Kajaste S, Brander PE, Telakivi T, et al. A cognitive-behavioral weight reduction program in the treatment of obstructive sleep apnea syndrome with or without initial nasal CPAP: a randomized study. *Sleep Med.* 2004;5:125-31.	Not one of the specified interventions
Kalter-Leibovici O, Younis-Zeidan N, Atamna A, et al. Lifestyle intervention in obese Arab women: a randomized controlled trial. *Arch Intern Med.* 2010;170:970-6.	Comparative effectiveness

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Reference	Reason for Exclusion
Kamioka H, Nakamura Y, Okada S, et al. Effectiveness of comprehensive health education combining lifestyle education and hot spa bathing for male white-collar employees: a randomized controlled trial with 1-year follow-up. *J Epidemiol.* 2009;19:219-30.	Conducted primarily in a non-relevant setting
Kansanen M, Vanninen E, Tuunainen A, et al. The effect of a very low-calorie diet-induced weight loss on the severity of obstructive sleep apnoea and autonomic nervous function in obese patients with obstructive sleep apnoea syndrome. *Clin Physiol.* 1998;18:377-85.	Does not meet design requirements in inclusion criteria
Karhunen L, Franssila-Kallunki A, Rissanen P, et al. Effect of orlistat treatment on body composition and resting energy expenditure during a two-year weight-reduction programme in obese Finns. *Int J Obes Relat Metab Disord.* 2000;24:1567-72.	No harms outcomes
Katzer L, Bradshaw AJ, Horwath CC, et al. Evaluation of a "nondieting" stress reduction program for overweight women: a randomized trial. *Am J Health Promot.* 2008;22:264-74.	Comparative effectiveness
Kaukua JK, Pekkarinen TA, Rissanen AM. Health-related quality of life in a randomised placebo-controlled trial of sibutramine in obese patients with type II diabetes. *Int J Obes Relat Metab Disord.* 2004;28:600-5.	Sibutramine intervention
Kawano M, Shono N, Yoshimura T, et al. Improved cardio-respiratory fitness correlates with changes in the number and size of small dense LDL: randomized controlled trial with exercise training and dietary instruction. *Intern Med.* 2009;48:25-32.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Keating GM, Jarvis B. Orlistat: in the prevention and treatment of type 2 diabetes mellitus. *Drugs.* 2120;61:2107-19.	Does not meet design requirements in inclusion criteria
Keller C, Trevino RP. Effects of two frequencies of walking on cardiovascular risk factor reduction in Mexican American women. *Res Nurs Health.* 2001;24:390-401.	No harms outcomes
Keogh JB, Luscombe-Marsh ND, Noakes M, et al. Long-term weight maintenance and cardiovascular risk factors are not different following weight loss on carbohydrate-restricted diets high in either monounsaturated fat or protein in obese hyperinsulinaemic men and women. *Br J Nutr.* 2007;97:405-10.	Comparative effectiveness
Keranen AM, Savolainen MJ, Reponen AH, et al. The effect of eating behavior on weight loss and maintenance during a lifestyle intervention. *Prev Med.* 2009;49:32-8.	Comparative effectiveness
Kerr J, Patrick K, Norman G, et al. Randomized control trial of a behavioral intervention for overweight women: impact on depressive symptoms. *Depress Anxiety.* 2008;25:555-8.	No harms outcomes
Ketola E, Makela M, Klockars M. Individualised multifactorial lifestyle intervention trial for high-risk cardiovascular patients in primary care. *Br J Gen Pract.* 2001;51:291-4.	Not one of the specified interventions
Kilicdag EB, Bagis T, Zeyneloglu HB, et al. Homocysteine levels in women with polycystic ovary syndrome treated with metformin versus rosiglitazone: a randomized study. *Hum Reprod.* 2005;20:894-9.	Does not meet design requirements in inclusion criteria
Kim SH, Lee YM, Jee SH, Nam CM. Effect of sibutramine on weight loss and blood pressure: a meta-analysis of controlled trials. *Obes Res.* 2003;11:1116-23.	Does not meet design requirements in inclusion criteria
Kim SI, Kim HS. Effectiveness of mobile and Internet intervention in patients with obese type 2 diabetes. *Int J Med Inf.* 2008;77:399-404.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kim Y, Pike J, Adams H, et al. Telephone intervention promoting weight-related health behaviors. *Prev Med.* 2010;50:112-7.	Comparative effectiveness
Kirk SF, Harvey EL, McConnon A, et al. A randomised trial of an Internet weight control resource: the UK Weight Control Trial. *BMC Health Serv Res.* 2003;3:19.	No harms outcomes
Kjotrod SB, von During V, Carlsen SM. Metformin treatment before IVF/ICSI in women with polycystic ovary syndrome; a prospective, randomized, double blind study. *Hum Reprod.* 2004;19:1315-22.	No harms outcomes
Knopp RH, Paramsothy P, Retzlaff BM, et al. Undesirable effects of extreme dietary carbohydrate and saturated fat intakes: the search for the middle ground. *Curr Atheroscler Rep.* 2005;7:409-11.	Comparative effectiveness
Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet.* 2009;274:1677-86.	No harms outcomes

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Reference	Reason for Exclusion
Kocak M, Caliskan E, Simsir C, Haberal A. Metformin therapy improves ovulatory rates, cervical scores, and pregnancy rates in clomiphene citrate-resistant women with polycystic ovary syndrome. *Fertil Steril.* 2002;77:101-6.	No harms outcomes
Kolotkin RL, Norquist JM, Crosby RD, et al. One-year health-related quality of life outcomes in weight loss trial participants: comparison of three measures. *Health Qual Life Outcomes.* 2009;7:53.	Not one of the specified interventions
Kostis JB, Wilson AC, Hooper WC, et al. Association of angiotensin-converting enzyme DD genotype with blood pressure sensitivity to weight loss. *Am Heart J.* 2002;144:625-9.	No harms outcomes
Kostis JB, Wilson AC, Shindler DM, et al. Persistence of normotension after discontinuation of lifestyle intervention in the trial of TONE. *Am J Hypertens.* 2002;15:732-4.	No harms outcomes
Krakoff J, Clark JM, Crandall JP, et al. Effects of metformin and weight loss on serum alanine aminotransferase activity in the Diabetes Prevention Program. *Obesity (Silver Spring).* 2010;18:1762-7.	No harms outcomes
Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med.* 2002;347:1483-92.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kreider RB, Ferreira MP, Greenwood M, et al. Effects of conjugated linoleic acid supplementation during resistance training on body composition, bone density, strength, and selected hematological markers. *J Strength Cond Res.* 2002;16:325-34.	Not one of the specified interventions
Kukkonen-Harjula KT, Borg PT, Nenonen AM, Fogelholm MG. Effects of a weight maintenance program with or without exercise on the metabolic syndrome: a randomized trial in obese men. *Prev Med.* 2005;41:784-90.	Comparative effectiveness
Kuller LH, Kinzel LS, Pettee KK, et al. Lifestyle intervention and coronary heart disease risk factor changes over 18 months in postmenopausal women: the Women On the Move through Activity and Nutrition (WOMAN study) clinical trial. *J Womens Health.* 2006;15:962-74.	Comparative effectiveness
Kuller LH, Kriska AM, Kinzel LS, et al. The clinical trial of Women On the Move through Activity and Nutrition (WOMAN) study. *Contemp Clin Trials.* 2006;28:370-81.	Comparative effectiveness
Kumanyika SK, Cook NR, Cutler JA, et al. Sodium reduction for hypertension prevention in overweight adults: further results from the Trials of Hypertension Prevention phase II. *J Hum Hypertens.* 2005;19:33-45.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Kumanyika SK, Shults J, Fassbender J, et al. Outpatient weight management in African-Americans: the Healthy Eating and Lifestyle Program (HELP) study. *Prev Med.* 2005;41:488-502.	Comparative effectiveness
Kumanyika SK, Wadden TA, Shults J, et al. Trial of family and friend support for weight loss in African American adults. *Arch Intern Med.* 2009;169:1795-804.	Comparative effectiveness
Laaksonen DE, Laitinen T, Schonberg J, et al. Weight loss and weight maintenance, ambulatory blood pressure and cardiac autonomic tone in obese persons with the metabolic syndrome. *J Hypertens.* 2003;21:371-8.	No harms outcomes
Laaksonen DE, Lindstrom J, Lakka TA, et al. Physical activity in the prevention of type 2 diabetes: the Finnish Diabetes Prevention Study. *Diabetes.* 2005;54:158-65.	No harms outcomes
Lally P, Chipperfield A, Wardle J. Healthy habits: efficacy of simple advice on weight control based on a habit-formation model. *Int J Obes (Lond).* 2008;32:700-7.	No harms outcomes
Lambert EV, Goedecke JH, Bluett K, et al. Conjugated linoleic acid versus high-oleic acid sunflower oil: effects on energy metabolism, glucose tolerance, blood lipids, appetite and body composition in regularly exercising individuals. *Br J Nutr.* 2007;97:1001-11.	Not one of the specified interventions
Larsen TM, Dalskov S, van Baak M, et al. The Diet, Obesity and Genes (Diogenes) dietary study in eight European countries—a comprehensive design for long-term intervention. *Obes Rev.* 2009;76-91.	Comparative effectiveness
Lasser VI, Raczynski JM, Stevens VJ, et al. Trials of Hypertension Prevention, phase II: structure and content of the weight loss and dietary sodium reduction interventions. *Ann Epidemiol.* 1995;5:156-64.	No harms outcomes
Laws R; Counterweight Project Team. A new evidence-based model for weight management in primary care: the Counterweight Programme. *J Hum Nutr Diet.* 2004;17:191-208.	Does not meet design requirements in inclusion criteria

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Reference	Reason for Exclusion
Layman DK, Evans EM, Erickson D, et al. A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *J Nutr.* 2009;139:514-21.	Comparative effectiveness
Lee JS, Visser M, Tylavsky FA, et al. Weight loss and regain and effects on body composition: the Health, Aging, and Body Composition Study. *J Gerontol A Biol Sci Med Sci.* 2010;65:78-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Leermakers EA, Perri MG, Shigaki CL, Fuller PR. Effects of exercise-focused versus weight-focused maintenance programs on the management of obesity. *Addict Behav.* 1999;24:219-27.	Comparative effectiveness
Lehtovirta M, Forsen B, Gullstrom M, et al. Metabolic effects of metformin in patients with impaired glucose tolerance. *Diabet Med.* 2001;18:578-83.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Leibbrand R, Fichter MM. Maintenance of weight loss after obesity treatment: is continuous support necessary? *Behav Res Ther.* 2002;40:1275-89.	Focus on patients in subgroups other than specified conditions
Leinum CJ, Dopp JM, Morgan BJ. Sleep-disordered breathing and obesity: pathophysiology, complications, and treatment. *Nutr Clin Pract.* 2009;24:675-87.	Does not meet design requirements in inclusion criteria
Lejeune MP, Kovacs EM, Westerterp-Plantenga MS. Additional protein intake limits weight regain after weight loss in humans. *Br J Nutr.* 2005;93:281-9.	Not one of the specified interventions
Liao D, Asberry PJ, Shofer JB, et al. Improvement of BMI, body composition, and body fat distribution with lifestyle modification in Japanese Americans with impaired glucose tolerance. *Diabetes Care.* 2002;25:1504-10.	Comparative effectiveness
Lien LF, Brown AJ, Ard JD, et al. Effects of PREMIER lifestyle modifications on participants with and without the metabolic syndrome. *Hypertension.* 2007;50:609-16.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Ligibel JA, Giobbie-Hurder A, Olenczuk D, et al. Impact of a mixed strength and endurance exercise intervention on levels of adiponectin, high molecular weight adiponectin and leptin in breast cancer survivors. *Cancer Causes Control.* 2009;20:1523-8.	No harms outcomes
Linde JA, Jeffery RW, Finch EA, et al. Are unrealistic weight loss goals associated with outcomes for overweight women? *Obes Res.* 2004;12:569-76.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Lindegarde F. Orlistat with diet was effective and safe for weight loss and coronary risk reduction in obesity. *Evid Based Med.* 2001;6:54.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Lindholm A, Bixo M, Bjorn I, et al. Effect of sibutramine on weight reduction in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Fertil Steril.* 2008;89:1221-8.	No harms outcomes
Lindholm LH, Ekbom T, Dash C, et al. The impact of health care advice given in primary care on cardiovascular risk. *BMJ.* 1995;310:1105-9.	Comparative effectiveness
Lindstrom J, Eriksson JG, Valle TT, et al. Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish Diabetes Prevention Study: results from a randomized clinical trial. *J Am Soc Nephrol.* 2003;14:S108-13.	No harms outcomes
Lindstrom J, Ilanne PP, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet.* 2006;368:1673-9.	No harms outcomes
Lindstrom J, Peltonen M, Eriksson JG, et al. High-fibre, low-fat diet predicts long-term weight loss and decreased type 2 diabetes risk: the Finnish Diabetes Prevention Study. *Diabetologia.* 2006;49:912-20.	No harms outcomes
Littman AJ, Vitiello MV, Foster-Schubert K, et al. Sleep, ghrelin, leptin and changes in body weight during a 1-year moderate-intensity physical activity intervention. *Int J Obes.* 2007;31:466-75.	No harms outcomes
Logue E, Sutton K, Jarjoura D, et al. Transtheoretical model-chronic disease care for obesity in primary care: a randomized trial. *Obes Res.* 2005;13:917-27.	Comparative effectiveness
Logue EE, Jarjoura DG, Sutton KS, et al. Longitudinal relationship between elapsed time in the action stages of change and weight loss. *Obes Res.* 2004;12:1499-508.	Does not meet design requirements in inclusion criteria
Lojander J, Mustajoki P, Ronka S, et al. A nurse-managed weight reduction programme for obstructive sleep apnoea syndrome. *J Intern Med.* 1998;244:251-5.	Does not meet design requirements in inclusion criteria

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Reference	Reason for Exclusion
Lombard CB, Deeks AA, Ball K, et al. Weight, physical activity and dietary behavior change in young mothers: short term results of the HeLP-HER cluster randomized controlled trial. *Nutr J.* 2009;8:17.	No harms outcomes
Bray G, Gregg E, et al; Look AHEAD Research Group. Baseline characteristics of the randomised cohort from the Look AHEAD (Action for Health in Diabetes) study. *Diabetes Vasc Dis Res.* 2006;3:202-15.	Comparative effectiveness
Wadden TA, West DS, et al; Look AHEAD Research Group. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity.* 2006;14:737-52.	Comparative effectiveness
Lucas CP, Boldrin MN, Reaven GM. Effect of orlistat added to diet (30% of calories from fat) on plasma lipids, glucose, and insulin in obese patients with hypercholesterolemia. *Am J Cardiol.* 2003;91:961-4.	Comparative effectiveness
Lucas KH, Kaplan-Machlis B. Orlistat—a novel weight loss therapy. *Ann Pharmacother.* 2001;35:314-28.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Major GC, Alarie F, Dore J, et al. Supplementation with calcium + vitamin D enhances the beneficial effect of weight loss on plasma lipid and lipoprotein concentrations. *Am J Clin Nutr.* 2007;85:54-9.	Not one of the specified interventions
Malone DC, Raebel MA, Porter JA, et al. Cost-effectiveness of sibutramine in the LOSE Weight Study: evaluating the role of pharmacologic weight-loss therapy within a weight management program. *J Manag Care Pharm.* 2005;11:458-68.	Comparative effectiveness
Malone M, Alger-Mayer S. Binge status and quality of life after gastric bypass surgery: a one-year study. *Obes Res.* 2004;12:473-81.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Malpuech-Brugere C, Verboeket-van de Venne WP, Mensink RP, et al. Effects of two conjugated linoleic acid isomers on body fat mass in overweight humans. *Obes Res.* 2004;12:591-8.	Not one of the specified interventions
Manini TM, Newman AB, Fielding R, et al. Effects of exercise on mobility in obese and nonobese older adults. *Obesity (Silver Spring).* 2010;18:1168-75.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Manning RM, Jung RT, Leese GP, Newton RW. The comparison of four weight reduction strategies aimed at overweight patients with diabetes mellitus: four-year follow-up. *Diabet Med.* 1998;15:497-502.	Comparative effectiveness
Marinilli PA, Gorin AA, Raynor HA, et al. Successful weight-loss maintenance in relation to method of weight loss. *Obesity.* 2008;16:2456-61.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Marshall NS, Grunstein RR. Losing weight in moderate to severe obstructive sleep apnoea. *BMJ.* 2009;339:b4363.	Conducted primarily in a non-relevant setting
Maruthur NM, Wang NY, Appel LJ. Lifestyle interventions reduce coronary heart disease risk: results from the PREMIER trial. *Circulation.* 2009;119:2026-31.	Not one of the specified interventions
Mata J, Silva MN, Vieira PN, et al. Motivational "spill-over" during weight control: increased self-determination and exercise intrinsic motivation predict eating self-regulation. *Health Psychol.* 2009;28:709-16.	No harms outcomes
Mathus-Vliegen EM; Balance Study Group. Long-term maintenance of weight loss with sibutramine in a GP setting following a specialist guided very-low-calorie diet: a double-blind, placebo-controlled, parallel group study. *Eur J Clin Nutr.* 2005;59(Suppl 1):31-8.	Sibutramine intervention
Matvienko OA, Hoehns JD. A lifestyle intervention study in patients with diabetes or impaired glucose tolerance: translation of a research intervention into practice. *J Am Board Fam Med.* 2009;22:535-43.	Does not meet design requirements in inclusion criteria
McConnon A, Kirk SF, Cockroft JE, et al. The Internet for weight control in an obese sample: results of a randomised controlled trial. *BMC Health Serv Res.* 2007;7:206.	No harms outcomes
McConnon A, Kirk SF, Ransley JK. Process evaluation of an Internet-based resource for weight control: use and views of an obese sample. *J Nutr Educ Behav.* 2009;41:261-7.	No harms outcomes
McLaughlin T, Carter S, Lamendola C, et al. Clinical efficacy of two hypocaloric diets that vary in overweight patients with type 2 diabetes: comparison of moderate fat versus carbohydrate reductions. *Diabetes Care.* 2007;30:1877-9.	Comparative effectiveness

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Reference	Reason for Exclusion
McMahon FG, Fujioka K, Singh BN, et al. Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. *Arch Intern Med.* 2000;160:2185-91.	Sibutramine intervention
McMahon FG, Weinstein SP, Rowe E, et al. Sibutramine is safe and effective for weight loss in obese patients whose hypertension is well controlled with angiotensin-converting enzyme inhibitors. *J Hum Hypertens.* 2002;16:5-11.	Sibutramine intervention
McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low fat, low-energy diet for weight loss in overweight adults. *Int J Obes Relat Metab Disord.* 2001;25:1503-11.	Comparative effectiveness
McNulty SJ, Ur E, Williams G. A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. *Diabetes Care.* 2003;26:125-31.	Sibutramine intervention
McTiernan A, Sorensen B, Irwin ML, et al. Exercise effect on weight and body fat in men and women. *Obesity.* 2007;15:1496-512.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Meenan RT, Vogt TM, Williams AE, et al. Economic evaluation of a worksite obesity prevention and intervention trial among hotel workers in Hawaii. *J Occup Environ Med.* 2010;52(Suppl 1):8-13.	Conducted primarily in a non-relevant setting
Mengham LH, Morris BF, Palmer CR, White AJ. Is intensive dietetic intervention effective for overweight patients with diabetes mellitus? A randomised controlled trial in a general practice. *Pract Diab Int.* 1999;16:8.	Comparative effectiveness
Menon T, Quaddus S, Cohen L. Revision of failed vertical banded gastroplasty to non-resectional Scopinaro biliopancreatic diversion: early experience. *Obes Surg.* 2006;16:1420-4.	Comparative effectiveness
Messerli-Burgy N, Znoj H, Laederach K. Eating behavior, emotional regulation, and coping strategies in obese patients following a comprehensive weight reduction program. *Verhaltenstherapie.* 2007;17:56.	Does not meet design requirements in inclusion criteria
Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum.* 2004;50:1501-10.	Comparative effectiveness
Meyer HE, Sogaard AJ, Falch JA, et al. Weight change over three decades and the risk of osteoporosis in men: the Norwegian Epidemiological Osteoporosis Studies (NOREPOS). *Am J Epidemiol.* 2008;168:454-60.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Micic D, Ivkovic-Lazar T, Dragojevic R, et al. Orlistat, a gastrointestinal lipase inhibitor, in therapy of obesity with concomitant hyperlipidemia. *Med Pregl.* 1999;52:323-33.	No harms outcomes
Mitkov M, Pehlivanov B, Terzieva D. Metformin versus rosiglitazone in the treatment of polycystic ovary syndrome. *Eur J Obstet Gynecol Reprod Biol.* 2006;126:93-8.	Does not meet design requirements in inclusion criteria
Miyatake N, Nishikawa H, Morishita A, et al. Daily walking reduces visceral adipose tissue areas and improves insulin resistance in Japanese obese subjects. *Diabetes Res Clin Pract.* 2002;58:101-7.	Does not meet design requirements in inclusion criteria
Molenaar EA, van Ameijden EJ, Vergouwe Y, et al. Effect of nutritional counselling and nutritional plus exercise counselling in overweight adults: a randomized trial in multidisciplinary primary care practice. *Fam Pract.* 2010;27:143-50.	High or differential attrition.
Molitch ME, Fujimoto W, Hamman RF, et al. The Diabetes Prevention Program and its global implications. *J Am Soc Nephrol.* 2003;14(Suppl 2):103-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Morgan PJ, Lubans DR, Collins CE, et al. 12-Month outcomes and process evaluation of the SHED-IT RCT: an Internet-based weight loss program targeting men. *Obesity (Silver Spring).* 2011;19:142-51.	Conducted primarily in a non-relevant setting
Mougios V, Matsakas A, Petridou A, et al. Effect of supplementation with conjugated linoleic acid on human serum lipids and body fat. *J Nutr Biochem.* 2001;12:585-94.	Not one of the specified interventions
Multiple Risk Factor Intervention Trial Research Group. Risk factor changes and mortality results: Multiple Risk Factor Intervention Trial. *JAMA.* 1982;248:1465-77.	Not one of the specified interventions
Munsch S, Biedert E, Keller U. Evaluation of a lifestyle change programme for the treatment of obesity in general practice. *Swiss Med Wkly.* 2003;133:148-54.	No harms outcomes
Murawski ME. Problem solving and the management of obesity in women from underserved rural settings. *Dissert Abstr Int B Sci Eng*. 2008;69:690.	Comparative effectiveness

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Reference	Reason for Exclusion
Nahmias J, Kirschner M, Karetzky MS. Weight loss and OSA and pulmonary function in obesity. *N J Med.* 1993;90:48-53.	Does not meet design requirements in inclusion criteria
Nakata Y, Ohkawara K, Lee DJ, et al. Effects of additional resistance training during diet-induced weight loss on bone mineral density in overweight premenopausal women. *J Bone Miner Metab.* 2008;26:172-7.	Comparative effectiveness
Nanchahal K, Townsend J, Letley L, et al. Weight-management interventions in primary care: a pilot randomised controlled trial. *Br J Gen Pract.* 2009;59:e157-66.	No harms outcomes
Nauta H, Hospers H, Jansen A. One-year follow-up effects of two obesity treatments on psychological well-being and weight. *Br J Health Psychol.* 2001;6:271-84.	Comparative effectiveness
Neaton JD, Grimm RH Jr, Cutler JA. Recruitment of participants for the Multiple Risk Factor Intervention Trial (MRFIT). *Control Clin Trials.* 1987;8:S41-53.	Not one of the specified interventions
Nelson MS, Robbins AS, Thornton JA. An intervention to reduce excess body weight in adults with or at risk for type 2 diabetes. *Mil Med.* 2006;171:409-14.	No harms outcomes
Nicklas BJ, Ambrosius W, Messier SP, et al. Diet-induced weight loss, exercise, and chronic inflammation in older, obese adults: a randomized controlled clinical trial. *Am J Clin Nutr.* 2004;79:544-51.	Comparative effectiveness
Nowson CA, Worsley A, Margerison C, et al. Blood pressure change with weight loss is affected by diet type in men. *Am J Clin Nutr.* 2005;81:983-9.	Comparative effectiveness
Ockene IS, Hebert JR, Ockene JK, et al. Effect of physician-delivered nutrition counseling training and an office-support program on saturated fat intake, weight, and serum lipid measurements in a hyperlipidemic population: Worcester Area Trial for Counseling in Hyperlipidemia (WATCH). *Arch Intern Med.* 1999;159:725-31.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Olson TP, Dengel DR, Leon AS, Schmitz KH. Changes in inflammatory biomarkers following one-year of moderate resistance training in overweight women. *Int J Obes (Lond).* 2007;31:996-1003.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Olson TP, Dengel DR, Leon AS, Schmitz KH. Moderate resistance training and vascular health in overweight women. *Med Sci Sports Exerc.* 2006;38:1558-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Omsland TK, Schei B, Gronskag AB, et al. Weight loss and distal forearm fractures in postmenopausal women: the Nord-Trondelag health study, Norway. *Osteoporos Int.* 2009;20:2009-16.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Ortega-Gonzalez C, Luna S, Hernandez L, et al. Responses of serum androgen and insulin resistance to metformin and pioglitazone in obese, insulin-resistant women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2005;90:1360-5.	No harms outcomes
Osei-Assibey G, Kyrou I, Adi Y, et al. Dietary and lifestyle interventions for weight management in adults from minority ethnic/non-white groups: a systematic review. *Obes Rev.* 2010;11:769-76.	Does not meet design requirements in inclusion criteria
Ostbye T, Krause KM, Lovelady CA, et al. Active Mothers Postpartum: a randomized controlled weight-loss intervention trial. *Am J Prev Med.* 2009;37:173-80.	No harms outcomes
O'Toole ML, Sawicki MA, Artal R. Structured diet and physical activity prevent postpartum weight retention. *J Womens Health (Larchmt).* 2003;12:991-8.	Comparative effectiveness
Page RC, Harnden KE, Cook JT, Turner RC. Can life-styles of subjects with impaired glucose tolerance be changed? A feasibility study. *Diabet Med.* 1992;9:562-6.	Not one of the specified interventions
Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care.* 1997;20:537-44.	Not on list of countries with HDI > 0.90
Papalazarou A, Yannakoulia M, Kavouras SA, et al. Lifestyle intervention favorably affects weight loss and maintenance following obesity surgery. *Obesity (Silver Spring).* 2010;18:1348-53.	Comparative effectiveness
Parikh P, Simon EP, Fei K, et al. Results of a pilot diabetes prevention intervention in East Harlem, New York City: Project HEED. *Am J Public Health.* 2010;100(Suppl 1):S232-9.	No harms outcomes
Park SK, Park JH, Kwon YC, et al. The effect of combined aerobic and resistance exercise training on abdominal fat in obese middle-aged women. *J Physiol Anthropol Appl Human Sci.* 2003;22:129-35.	No harms outcomes

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Reference	Reason for Exclusion
Pasquali R, Colella P, Cirignotta F, et al. Treatment of obese patients with obstructive sleep apnea syndrome (OSAS): effect of weight loss and interference of otorhinolaryngoiatric pathology. *Int J Obes.* 1990;14:207-17.	Does not meet design requirements in inclusion criteria
Paul-Ebhohimhen V, Avenell A. A systematic review of the effectiveness of group versus individual treatments for adult obesity. *Obesity Facts.* 2009;2:17-24.	No harms outcomes
Perreault L, Kahn SE, Christophi CA, et al. Regression from pre-diabetes to normal glucose regulation in the Diabetes Prevention Program. *Diabetes Care.* 2009;32:1583-8.	No harms outcomes
Perreault L, Ma Y, Dagogo-Jack S, et al. Sex differences in diabetes risk and the effect of intensive lifestyle modification in the Diabetes Prevention Program. *Diabetes Care.* 2008;31:1416-21.	No harms outcomes
Perri MG, Limacher MC, Durning PE, et al. Extended-care programs for weight management in rural communities: the Treatment of Obesity in Underserved Rural Settings (TOURS) randomized trial. *Arch Intern Med.* 2008;168:2347-54.	Comparative effectiveness
Petridou A, Mougios V, Sagredos A. Supplementation with CLA: isomer incorporation into serum lipids and effect on body fat of women. *Lipids.* 2003;38:805-11.	Not one of the specified interventions
Petrofsky J, Batt J, Berk L, et al. The effect of an aerobic dance and diet program on cardiovascular fitness, body composition, and weight loss in women. *J Appl Res.* 2008;8:179-88.	No harms outcomes
Phelan S, Wadden TA, Berkowitz RI, et al. Impact of weight loss on the metabolic syndrome. *Int J Obes.* 2007;31:1442-8.	Does not meet design requirements in inclusion criteria
Philippou E, Neary NM, Chaudhri O, et al. The effect of dietary glycemic index on weight maintenance in overweight subjects: a pilot study. *Obesity.* 2009;17:396-401.	Comparative effectiveness
Pinkston MM, Poston WS, Reeves RS, et al. Does metabolic syndrome mitigate weight loss in overweight Mexican American women treated for 1-year with orlistat and lifestyle modification? *Eat Weight Disord.* 2006;11:e35-41.	No placebo in medication trial
Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the Look AHEAD trial. *Diabetes Care.* 2007;30:1374-83.	Comparative effectiveness
Porter JA, Raebel MA, Conner DA, et al. The Long-term Outcomes of Sibutramine Effectiveness on Weight (LOSE Weight) study: evaluating the role of drug therapy within a weight management program in a group-model health maintenance organization. *Am J Manag Care.* 2004;10:369-76.	No placebo in medication trial
Poston WS, Haddock CK, Olvera NE, et al. Evaluation of a culturally appropriate intervention to increase physical activity. *Am J Health Behav.* 2001;25:396-406.	Not one of the specified interventions
Poston WS, Haddock CK, Pinkston MM, et al. Evaluation of a primary care-oriented brief counselling intervention for obesity with and without orlistat. *J Intern Med.* 2006;260:388-98.	Does not meet design requirements in inclusion criteria
Poston WS, Reeves RS, Haddock CK, et al. Weight loss in obese Mexican Americans treated for 1-year with orlistat and lifestyle modification. *Int J Obes Relat Metab Disord.* 2003;27:1486-93.	No placebo in medication trial
Potteiger JA, Jacobsen DJ, Donnelly JE, Hill JO. Glucose and insulin responses following 16 months of exercise training in overweight adults: the Midwest Exercise Trial. *Metabolism.* 2003;52:1175-81.	No harms outcomes
Potteiger JA, Kirk EP, Jacobsen DJ, Donnelly JE. Changes in resting metabolic rate and substrate oxidation after 16 months of exercise training in overweight adults. *Int J Sport Nutr Exerc Metab.* 2008;18:79-95.	No harms outcomes
Pritchard JE, Nowson CA, Wark JD. A worksite program for overweight middle-aged men achieves lesser weight loss with exercise than with dietary change. *J Am Diet Assoc.* 1997;97:37-42.	Conducted primarily in a non-relevant setting
Promrat K, Kleiner DE, Niemeier HM, et al. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. *Hepatology.* 2010;51:121-9.	Focus on patients in subgroups other than specified conditions
Proper KI, Hildebrandt VH, Van der Beek AJ, et al. Effect of individual counseling on physical activity fitness and health: a randomized controlled trial in a workplace setting. *Am J Prev Med.* 2003;24:218-26.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Provencher V, Begin C, Tremblay A, et al. Health-at-every-size and eating behaviors: 1-year follow-up results of a size acceptance intervention. *J Am Diet Assoc.* 2009;109:1854-61.	Not one of the specified interventions

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Reference	Reason for Exclusion
Racette SB, Deusinger SS, Inman CL, et al. Worksite Opportunities for Wellness (WOW): effects on cardiovascular disease risk factors after 1 year. *Prev Med.* 2009;49:108-14.	Conducted primarily in a non-relevant setting
Racette SB, Weiss EP, Obert KA, et al. Modest lifestyle intervention and glucose tolerance in obese African Americans. *Obes Res.* 2001;9:348-55.	Comparative effectiveness
Racette SB, Weiss EP, Villareal DT, et al. One year of caloric restriction in humans: feasibility and effects on body composition and abdominal adipose tissue. *J Gerontol A Biol Sci Med Sci.* 2006;61:943-50.	Comparative effectiveness
Ramachandran A, Snehalatha C, Mary S, et al. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia.* 2006;49:289-97.	Not on list of countries with HDI > 0.90
Ramirez EM, Rosen JC. A comparison of weight control and weight control plus body image therapy for obese men and women. *J Consult Clin Psychol.* 2001;69:440-6.	Comparative effectiveness
Randomised trial of jejunoileal bypass versus medical treatment in morbid obesity. *Lancet.* 1979;2:1255-8.	Not one of the specified interventions
Rapoport L, Clark M, Wardle J. Evaluation of a modified cognitive-behavioural programme for weight management. *Int J Obes Relat Metab Disord.* 2000;24:1726-37.	Comparative effectiveness
Ratner RE; Diabetes Prevention Program. An update on the Diabetes Prevention Program. *Endocr Pract.* 2006;12(Suppl 1):20-4.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Razquin C, Martinez JA, Martinez-Gonzalez MA, et al. A 3 years follow-up of a Mediterranean diet rich in virgin olive oil is associated with high plasma antioxidant capacity and reduced body weight gain. *Eur J Clin Nutr.* 2009;63:1387-93.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Reaven G, Segal K, Hauptman J, et al. Effect of orlistat-assisted weight loss in decreasing coronary heart disease risk in patients with syndrome X. *Am J Cardiol.* 2001;87:827-31.	Other quality issues
Redman LM, Rood J, Anton SD, et al. Calorie restriction and bone health in young, overweight individuals. *Arch Intern Med.* 2008;168:1859-66.	No harms outcomes
Redmon JB, Bertoni AG, Connelly S, et al. Effect of the Look AHEAD study intervention on medication use and related cost to treat cardiovascular disease risk factors in individuals with type 2 diabetes. *Diabetes Care.* 2010;33:1153-8.	Comparative effectiveness
Reid IR, Horne A, Mason B, et al. Effects of calcium supplementation on body weight and blood pressure in normal older women: a randomized controlled trial. *J Clin Endocrinol Metab.* 2005;90:3824-9.	Not one of the specified interventions
Rejeski WJ, Focht BC, Messier SP, et al. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol.* 2002;21:419-26.	Comparative effectiveness
Renzaho AM, Mellor D, Boulton K, Swinburn B. Effectiveness of prevention programmes for obesity and chronic diseases among immigrants to developed countries—a systematic review. *Public Health Nutr.* 2010;13:438-50.	Does not meet design requirements in inclusion criteria
Ricci TA, Chowdhury HA, Heymsfield SB, et al. Calcium supplementation suppresses bone turnover during weight reduction in postmenopausal women. *J Bone Miner Res.* 1998;13:1045-50.	No harms outcomes
Riedt CS, Schlussel Y, von Thun N, et al. Premenopausal overweight women do not lose bone during moderate weight loss with adequate or higher calcium intake. *Am J Clin Nutr.* 2007;85:972-80.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Rimmer JH, Rauworth A, Wang E, et al. A randomized controlled trial to increase physical activity and reduce obesity in a predominantly African American group of women with mobility disabilities and severe obesity. *Prev Med.* 2009;48:473-9.	No harms outcomes
Riserus U, Arner P, Brismar K, Vessby B. Treatment with dietary trans10cis12 conjugated linoleic acid causes isomer-specific insulin resistance in obese men with the metabolic syndrome. *Diabetes Care.* 2002;25:1516-21.	Not one of the specified interventions
Rissanen P, Vahtera E, Krusius T, et al. Weight change and blood coagulability and fibrinolysis in healthy obese women. *Int J Obes Relat Metab Disord.* 2001;25:212-8.	No harms outcomes

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Reference	Reason for Exclusion
Rock CL, Flatt SW, Sherwood NE, et al. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *JAMA*. 2010;304:1803-10.	Comparative effectiveness
Rock CL, Pakiz B, Flatt SW, Quintana EL. Randomized trial of a multifaceted commercial weight loss program. *Obesity.* 2007;15:939-49.	Comparative effectiveness
Rosenfalck AM, Hendel H, Rasmussen MH, et al. Minor long-term changes in weight have beneficial effects on insulin sensitivity and beta-cell function in obese subjects. *Diabetes Obes Metab.* 2002;4:19-28.	No harms outcomes
Ross R, Blair SN, Godwin M, et al. Prevention and Reduction of Obesity through Active Living (PROACTIVE): rationale, design and methods. *Br J Sports Med.* 2009;43:57-63.	No harms outcomes
Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obes Res.* 2004;12:789-98.	No harms outcomes
Rothacker DQ, Staniszewski BA, Ellis PK. Liquid meal replacement vs traditional food: a potential model for women who cannot maintain eating habit change. *J Am Diet Assoc.* 2001;101:345-7.	Comparative effectiveness
Rothert K, Strecher VJ, Doyle LA, et al. Web-based weight management programs in an integrated health care setting: a randomized, controlled trial. *Obesity.* 2006;14:266-72.	No harms outcomes
Ryan DH, Johnson WD, Myers VH, et al. Nonsurgical weight loss for extreme obesity in primary care settings: results of the Louisiana Obese Subjects Study. *Arch Intern Med.* 2010;170:146-54.	No placebo in medication trial
Sabbioni ME, Dickson MH, Eychmuller S, et al. Intermediate results of health related quality of life after vertical banded gastroplasty. *Int J Obes Relat Metab Disord.* 2002;26:277-80.	Not one of the specified interventions
Saccone A, Israel A. Effects of experimenter versus significant other-controlled reinforcement and choice of target behavior on weight loss. *Behav Ther*. 1978;9:271-8.	Precedes search period
Salas SJ, Fernández BJ, Ros E, et al. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. *Arch Intern Med.* 2008;168:2449-58.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Samaras K, Ashwell S, Mackintosh AM, et al. Will older sedentary people with non-insulin-dependent diabetes mellitus start exercising? A health promotion model. *Diabetes Res Clin Pract.* 1997;37:121-8.	Not one of the specified interventions
Sampol G, Munoz X, Sagales MT, et al. Long-term efficacy of dietary weight loss in sleep apnoea/hypopnoea syndrome. *Eur Respir J.* 1998;12:1156-9.	Does not meet design requirements in inclusion criteria
Samsa GP, Kolotkin RL, Williams GR, et al. Effect of moderate weight loss on health-related quality of life: an analysis of combined data from 4 randomized trials of sibutramine vs placebo. *Am J Manag Care.* 2001;7:875-83.	Does not meet design requirements in inclusion criteria
Sanchez-Reyes L, Fanghanel G, Yamamoto J, et al. Use of sibutramine in overweight adult Hispanic patients with type 2 diabetes mellitus: a 12-month, randomized, double-blind, placebo-controlled clinical trial. *Clin Ther.* 2004;26:1427-35.	Not on list of countries with HDI > 0.90
Sarac S, Sarac F. Cardiac valve evaluation and adipokine levels in obese women treated with sibutramine. *Anadolu Kardiyoloji Dergisi.* 2010;10:226-32.	Sibutramine intervention
Sari R, Eray E, Ozdem S, et al. Comparison of the effects of sibutramine versus sibutramine plus metformin in obese women. *Clin Exp Med.* 2010;10:179-84.	Sibutramine intervention
Sarwer DB, von Sydow GA, Vetter ML, Wadden TA. Behavior therapy for obesity: where are we now? *Curr Opin Endocrinol Diabetes Obes.* 2009;16:347-52.	Does not meet design requirements in inclusion criteria
Sbrocco T, Nedegaard RC, Stone JM, Lewis EL. Behavioral choice treatment promotes continuing weight loss: preliminary results of a cognitive-behavioral decision-based treatment for obesity. *J Consult Clin Psychol.* 1999;67:260-6.	Comparative effectiveness
Schmitz KH, Hannan PJ, Stovitz SD, et al. Strength training and adiposity in premenopausal women: Strong, Healthy, and Empowered Study. *Am J Clin Nutr.* 2007;86:566-72.	No harms outcomes
Schneider PL, Bassett DR Jr, Thompson DL, et al. Effects of a 10,000 steps per day goal in overweight adults. *Am J Health Promot.* 2006;21:85-9.	No harms outcomes

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Reference	Reason for Exclusion
Scholze J, Grimm E, Herrmann D, et al. Optimal treatment of obesity-related hypertension: the Hypertension-Obesity-Sibutramine (HOS) study. *Circulation.* 2007;115:1991-8.	Sibutramine intervention
Schuler G, Hambrecht R, Schlierf G, et al. Regular physical exercise and low-fat diet: effects on progression of coronary artery disease. *Circulation.* 1992;86:1-11.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Schuster RJ, Tasosa J, Terwoord NA. Translational research—implementation of NHLBI Obesity Guidelines in a primary care community setting: the Physician Obesity Awareness Project. *J Nutr Health Aging.* 2008;12:S764-9.	Comparative effectiveness
Serrano-Rios M, Melchionda N, Moreno-Carretero E. Role of sibutramine in the treatment of obese type 2 diabetic patients receiving sulphonylurea therapy. *Diabet Med.* 2002;19:119-24.	Sibutramine intervention
Shapses SA, Heshka S, Heymsfield SB. Effect of calcium supplementation on weight and fat loss in women. *J Clin Endocrinol Metab.* 2004;89:632-7.	Not one of the specified interventions
Shea MK, Houston DK, Nicklas BJ, et al. The effect of randomization to weight loss on total mortality in older overweight and obese adults: the ADAPT study. *J Gerontol A Biol Sci Med Sci.* 2010;65:519-25.	Comparative effectiveness
Sherwood NE, Jeffery RW, Pronk NP, et al. Mail and phone interventions for weight loss in a managed-care setting: Weigh-To-Be 2-year outcomes. *Int J Obes.* 2006;30:1565-73.	No harms outcomes
Short KR, Vittone JL, Bigelow ML, et al. Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. *Diabetes.* 2003;52:1888-96.	No harms outcomes
Siegel JM, Prelip ML, Erausquin JT, Kim SA. A worksite obesity intervention: results from a group-randomized trial. *Am J Public Health.* 2010;100:327-33.	Conducted primarily in a non-relevant setting
Silva MN, Markland D, Carraca EV, et al. Exercise autonomous motivation predicts three-year weight loss in women. *Med Sci Sports Exerc.* 2011;43:728-37.	Study of overweight/obesity prevention
Simmons D, Rush E, Crook N; Te Wai o Rona Diabetes Prevention Strategy Team. Development and piloting of a community health worker-based intervention for the prevention of diabetes among New Zealand Maori in Te Wai o Rona: Diabetes Prevention Strategy. *Public Health Nutr.* 2008;11:1318-25.	Focus on patients in subgroups other than specified conditions
Sircar AR, Kumar A, Lal M. Clinical evaluation of sibutramine in obese type 2 diabetic patients refractory to dietary management. *J Assoc Physicians India.* 2001;49:885-8.	Other quality issues
Sjostrom L. Analysis of the XENDOS study (Xenical in the Prevention of Diabetes in Obese Subjects). *Endocr Pract.* 2006;12(Suppl 1):31-3.	No harms outcomes
Skender ML, Goodrick GK, Del Junco DJ, et al. Comparison of 2-year weight loss trends in behavioral treatments of obesity: diet, exercise, and combination interventions. *J Am Diet Assoc.* 1996;96:342-6.	Comparative effectiveness
Skinner TC, Carey ME, Cradock S, et al. Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND): process modelling of pilot study. *Patient Educ Couns.* 2006;64:369-77.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Slentz CA, Aiken LB, Houmard JA, et al. Inactivity, exercise, and visceral fat—STRRIDE: a randomized, controlled study of exercise intensity and amount. *J Appl Physiol.* 2005;99:1613-8.	No harms outcomes
Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE—a randomized controlled study. *Arch Intern Med.* 2004;164:31-9.	No harms outcomes
Smedman A, Vessby B. Conjugated linoleic acid supplementation in humans—metabolic effects. *Lipids.* 2001;36:773-81.	Not one of the specified interventions
Smith IG, Goulder MA. Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. *J Fam Pract.* 2001;50:505-12.	Sibutramine intervention
Smith PL, Gold AR, Meyers DA, et al. Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med.* 1985;103:850-5.	No harms outcomes
Southard BH, Southard DR, Nuckolls J. Clinical trial of an Internet-based case management system for secondary prevention of heart disease. *J Cardiopulm Rehabil.* 2003;23:341-8.	No harms outcomes

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Reference	Reason for Exclusion
Sramek JJ, Leibowitz MT, Weinstein SP, et al. Efficacy and safety of sibutramine for weight loss in obese patients with hypertension well controlled by beta-adrenergic blocking agents: a placebo-controlled, double-blind, randomised trial. *J Hum Hypertens.* 2002;16:13-9.	No harms outcomes
Stahre L, Hallstrom T. A short-term cognitive group treatment program gives substantial weight reduction up to 18 months from the end of treatment: a randomized controlled trial. *Eat Weight Disord.* 2005;10:51-8.	No harms outcomes
Stefanick ML, Mackey S, Sheehan M, et al. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. *N Engl J Med.* 1998;339:12-20.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Stenius-Aarniala B, Poussa T, Kvarnstrom J, et al. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ.* 2000;320:827-32.	Comparative effectiveness
Stensel DJ, Brooke-Wavell K, Hardman AE, et al. The influence of a 1-year programme of brisk walking on endurance fitness and body composition in previously sedentary men aged 42-59 years. *Eur J Appl Physiol Occup Physiol.* 1994;68:531-7.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Stern L, Iqbal N, Seshadri P, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med.* 2004;140:778-85.	Comparative effectiveness
Stuart RB. A three-dimensional program for the treatment of obesity. *Behav Res Ther.* 1971;9:177-86.	Precedes search period
Sun Q, Townsend MK, Okereke OI, et al. Adiposity and weight change in mid-life in relation to healthy survival after age 70 in women: prospective cohort study. *BMJ.* 2009;339:b3796.	Does not meet design requirements in inclusion criteria
Suratt PM, McTier RF, Findley LJ, et al. Effect of very-low-calorie diets with weight loss on obstructive sleep apnea. *Am J Clin Nutr.* 1992;56:S182-4.	Does not meet design requirements in inclusion criteria
Svendsen M, Helgeland M, Tonstad S. The long-term influence of orlistat on dietary intake in obese subjects with components of metabolic syndrome. *J Human Nutr Diet.* 2009;22:55-63.	No harms outcomes
Svetkey LP, Pollak KI, Yancy WS Jr, et al. Hypertension Improvement Project: randomized trial of quality improvement for physicians and lifestyle modification for patients. *Hypertension.* 2009;54:1226-33.	Not one of the specified interventions
Swartz AM, Strath SJ, Bassett DR, et al. Increasing daily walking improves glucose tolerance in overweight women. *Prev Med.* 2003;37:356-62.	No harms outcomes
Swinburn BA, Metcalf PA, Ley SJ. Long-term (5-year) effects of a reduced-fat diet intervention in individuals with glucose intolerance. *Diabetes Care.* 2001;24:619-24.	Conducted primarily in a non-relevant setting
Swinburn BA, Woollard GA, Chang EC, Wilson MR. Effects of reduced-fat diets consumed ad libitum on intake of nutrients, particularly antioxidant vitamins. *J Am Diet Assoc.* 1999;99:1400-5.	Conducted primarily in a non-relevant setting
Tanco S, Linden W, Earle T. Well-being and morbid obesity in women: a controlled therapy evaluation. *Int J Eat Disord.* 1998;23:325-39.	No harms outcomes
Taner ED, Yavuz B, Okhan AK, et al. An obesity drug sibutramine reduces brain natriuretic peptide (BNP) levels in severely obese patients. *Int J Clin Pract.* 2010;64:518-22.	Does not include specified harms outcomes
Tang T, Glanville J, Hayden CJ, et al. Combined lifestyle modification and metformin in obese patients with polycystic ovary syndrome: a randomized, placebo-controlled, double-blind multicentre study. *Hum Reprod.* 2006;21:80-9.	No harms outcomes
Tanumihardjo SA, Valentine AR, Zhang Z, et al. Strategies to increase vegetable or reduce energy and fat intake induce weight loss in adults. *Exp Biol Med.* 2009;234:542-52.	Comparative effectiveness
Tate DF, Jackvony EH, Wing RR. A randomized trial comparing human e-mail counseling, computer-automated tailored counseling, and no counseling in an Internet weight loss program. *Arch Intern Med.* 2006;166:1620-5.	No harms outcomes
Tate DF, Jackvony EH, Wing RR. Effects of Internet behavioral counseling on weight loss in adults at risk for type 2 diabetes: a randomized trial. *JAMA.* 2003;289:1833-6.	Comparative effectiveness
Tate DF, Jeffery RW, Sherwood NE, Wing RR. Long-term weight losses associated with prescription of higher physical activity goals: are higher levels of physical activity protective against weight regain? *Am J Clin Nutr.* 2007;85:954-9.	Comparative effectiveness

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Reference	Reason for Exclusion
Tate DF, Wing RR, Winett RA. Using Internet technology to deliver a behavioral weight loss program. *JAMA.* 2001;285:1172-7.	No harms outcomes
Taylor JS, Williams SR, Rhys R, et al. Conjugated linoleic acid impairs endothelial function. *Arterioscler Thromb Vasc Biol.* 2006;26:307-12.	Not one of the specified interventions
Teixeira PJ, Going SB, Houtkooper LB, et al. Resistance training in postmenopausal women with and without hormone therapy. *Med Sci Sports Exerc.* 2003;35:555-62.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
ODES Investigators. The Oslo Diet and Exercise Study (ODES): design and objectives. *Control Clin Trials.* 1993;14:229-43.	No harms outcomes
Thomas TR, Warner SO, Dellsperger KC, et al. Exercise and the metabolic syndrome with weight regain. *J Appl Physiol.* 2010;109:3-10.	Comparative effectiveness
Thompson WG, Rostad HN, Janzow DJ, et al. Effect of energy-reduced diets high in dairy products and fiber on weight loss in obese adults. *Obes Res.* 2005;13:1344-53.	Comparative effectiveness
Thorpe MP, Jacobson EH, Layman DK, et al. A diet high in protein, dairy, and calcium attenuates bone loss over twelve months of weight loss and maintenance relative to a conventional high-carbohydrate diet in adults. *J Nutr.* 2008;138:1096-100.	Comparative effectiveness
Tiikkainen M, Bergholm R, Rissanen A, et al. Effects of equal weight loss with orlistat and placebo on body fat and serum fatty acid composition and insulin resistance in obese women. *Am J Clin Nutr.* 2004;79:22-30.	Does not include specified harms outcomes
Tinker LF, Bonds DE, Margolis KL, et al. Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: the Women's Health Initiative randomized controlled dietary modification trial. *Arch Intern Med.* 2008;168:1500-11.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Toft U, Kristoffersen L, Ladelund S, et al. The effect of adding group-based counselling to individual lifestyle counselling on changes in dietary intake: the Inter99 Study—a randomized controlled trial. *Int J Behav Nutr Phys Act.* 2008;5:59.	No harms outcomes
Toobert DJ, Glasgow RE, Radcliffe JL. Physiologic and related behavioral outcomes from the Women's Lifestyle Heart Trial. *Ann Behav Med.* 2000;22:1-9.	Focus on patients in subgroups other than specified conditions
What is TOPS (Take Off Pounds Sensibly). Milwaukee, WI: TOPS Club, Inc; 2011. http://www.tops.org/TOPSInformation/AboutTOPS.aspx	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Trento M, Passera P, Tomalino M, et al. Group visits improve metabolic control in type 2 diabetes: a 2-year follow-up. *Diabetes Care.* 2001;24:995-1000.	Comparative effectiveness
Tsai AG, Wadden TA, Rogers MA, et al. A primary care intervention for weight loss: results of a randomized controlled pilot study. *Obesity (Silver Spring).* 2010;18:1614-8.	Comparative effectiveness
Tsai AG, Wadden TA. Treatment of obesity in primary care practice in the United States: a systematic review. *J Gen Intern Med.* 2009;24:1073-9.	Does not meet design requirements in inclusion criteria
Tseng MC, Lee MB, Chen SY, et al. Response of Taiwanese obese binge eaters to a hospital-based weight reduction program. *J Psychosom Res.* 2004;57:279-85.	Focus on patients in subgroups other than specified conditions
Turnin MC, Bourgeois O, Cathelineau G, et al. Multicenter randomized evaluation of a nutritional education software in obese patients. *Diabetes Metab.* 2001;27:139-47.	Comparative effectiveness
Tuthill A, Quinn A, McColgan D, et al. A prospective randomized controlled trial of lifestyle intervention on quality of life and cardiovascular risk score in patients with obesity and type 2 diabetes. *Diabetes Obes Metab.* 2007;9:917-9.	No harms outcomes
Van Aggel-Leijssen DP, Saris WH, Hul GB, van Baak MA. Long-term effects of low-intensity exercise training on fat metabolism in weight-reduced obese men. *Metabolism.* 2002;51:1003-10.	Comparative effectiveness
Van Aggel-Leijssen DP, Saris WH, Hul GB, van Baak MA. Short-term effects of weight loss with or without low-intensity exercise training on fat metabolism in obese men. *Am J Clin Nutr.* 2001;73:523-31.	No harms outcomes
Van Aggel-Leijssen DP, Saris WH, Wagenmakers AJ, et al. The effect of low-intensity exercise training on fat metabolism of obese women. *Obes Res.* 2001;9:86-96.	No harms outcomes
Van Aggel-Leijssen DP, Saris WH, Wagenmakers AJ, et al. Effect of exercise training at different intensities on fat metabolism of obese men. *J Appl Physiol.* 2002;92:1300-9.	No harms outcomes

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Reference	Reason for Exclusion
van Sluijs EM, van Poppel MN, Twisk JW, et al. Effect of a tailored physical activity intervention delivered in general practice settings: results of a randomized controlled trial. *Am J Public Health.* 2005;95:1825-31.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
van Wier MF, Ariens GA, Dekkers JC, et al. ALIFE@Work: a randomised controlled trial of a distance counselling lifestyle programme for weight control among an overweight working population. *BMC Public Health.* 2006;6:140.	No harms outcomes
van Wier MF, Ariens GA, Dekkers JC, et al. Phone and e-mail counselling are effective for weight management in an overweight working population: a randomized controlled trial. *BMC Public Health.* 2009;9:6.	No harms outcomes
VanWormer JJ, Martinez AM, Benson GA, et al. Telephone counseling and home telemonitoring: the Weigh by Day Trial. *Am J Health Behav.* 2009;33:445-54.	Comparative effectiveness
Velthuis MJ, Schuit AJ, Peeters PH, Monninkhof EM. Exercise program affects body composition but not weight in postmenopausal women. *Menopause.* 2009;16:777-84.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Venditti EM, Bray GA, Carrion-Petersen ML, et al. First versus repeat treatment with a lifestyle intervention program: attendance and weight loss outcomes. *Int J Obes.* 2008;32:1537-44.	No harms outcomes
Veverka DV, Anderson J, Auld GW, et al. Use of the stages of change model in improving nutrition and exercise habits in enlisted Air Force men. *Mil Med.* 2003;168:373-9.	No harms outcomes
Vidgren HM, Agren JJ, Valve RS, et al. The effect of orlistat on the fatty acid composition of serum lipid fractions in obese subjects. *Clin Pharmacol Ther.* 1999;66:315-22.	No harms outcomes
Villareal DT, Banks MR, Patterson BW, et al. Weight loss therapy improves pancreatic endocrine function in obese older adults. *Obesity.* 2008;16:1349-54.	No harms outcomes
Villareal DT, Fontana L, Weiss EP, et al. Bone mineral density response to caloric restriction-induced weight loss or exercise-induced weight loss: a randomized controlled trial. *Arch Intern Med.* 2006;166:2502-10.	Comparative effectiveness
Vissers D, Verrijken A, Mertens I, et al. Effect of long-term whole body vibration training on visceral adipose tissue: a preliminary report. *Obesity Facts.* 2010;3:93-100.	No harms outcomes
Volpe SL, Kobusingye H, Bailur S, Stanek E. Effect of diet and exercise on body composition, energy intake and leptin levels in overweight women and men. *J Am Coll Nutr.* 2008;27:195-208.	Comparative effectiveness
von Huth SL, Ladelund S, Borch-Johnsen K, Jorgensen T. A randomized multifactorial intervention study for prevention of ischaemic heart disease (Inter99): the long-term effect on physical activity. *Scand J Public Health.* 2008;36:380-8.	No harms outcomes
Wadden TA, Berkowitz RI, Sarwer DB, et al. Benefits of lifestyle modification in the pharmacologic treatment of obesity: a randomized trial. *Arch Intern Med.* 2001;161:218-27.	Comparative effectiveness
Wadden TA, Berkowitz RI, Womble LG, et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity. *N Engl J Med.* 2005;353:2111-20.	No placebo in medication trial
Wadden TA, Foster GD, Sarwer DB, et al. Dieting and the development of eating disorders in obese women: results of a randomized controlled trial. *Am J Clin Nutr.* 2004;80:560-8.	Comparative effectiveness
Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity.* 2009;17:713-22.	Comparative effectiveness
Wardle J, Rogers P, Judd P, et al. Randomized trial of the effects of cholesterol-lowering dietary treatment on psychological function. *Am J Med.* 2000;108:547-53.	No harms outcomes
Waring ME, Roberts MB, Parker DR, Eaton CB. Documentation and management of overweight and obesity in primary care. *J Am Board Fam Med.* 2009;22:544-52.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Warziski MT, Sereika SM, Styn MA, et al. Changes in self-efficacy and dietary adherence: the impact on weight loss in the PREFER study. *J Behav Med.* 2008;31:81-92.	Comparative effectiveness
Wassertheil-Smoller S, Oberman A, Blaufox MD, et al. The Trial of Antihypertensive Interventions and Management (TAIM) study: final results with regard to blood pressure, cardiovascular risk, and quality of life. *Am J Hypertens.* 1992;5:37-44.	No harms outcomes

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Reference	Reason for Exclusion
Wee CC, Davis RB, Phillips RS. Stage of readiness to control weight and adopt weight control behaviors in primary care. *J Gen Intern Med.* 2005;20:410-5.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Weiner R, Bockhorn H, Rosenthal R, Wagner D. A prospective randomized trial of different laparoscopic gastric banding techniques for morbid obesity. *Surg Endosc.* 2001;15:63-8.	Not one of the specified interventions
Weiss EP, Racette SB, Villareal DT, et al. Improvements in glucose tolerance and insulin action induced by increasing energy expenditure or decreasing energy intake: a randomized controlled trial. *Am J Clin Nutr.* 2006;84:1033-42.	Comparative effectiveness
Whittemore R, Melkus G, Wagner J, et al. Translating the Diabetes Prevention Program to primary care: a pilot study. *Nurs Res.* 2009;58:2-12.	No harms outcomes
Williamson DA, Rejeski J, Lang W, et al. Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. *Arch Intern Med.* 2009;169:163-71.	Comparative effectiveness
Williamson DF. Re: randomized trial of weight loss and total mortality. *J Gerontol A Biol Sci Med Sci.* 2010;65:904.	Does not meet design requirements in inclusion criteria
Wing RR, Anglin K. Effectiveness of a behavioral weight control program for blacks and whites with NIDDM. *Diabetes Care.* 1996;19:409-13.	Comparative effectiveness
Wing RR, Creasman JM, West DS, et al. Improving urinary incontinence in overweight and obese women through modest weight loss. *Obstetrics Gynecol.* 2010;116:284-92.	Comparative effectiveness
Wing RR, Epstein LH, Paternostro-Bayles M, et al. Exercise in a behavioural weight control programme for obese patients with type 2 (non-insulin-dependent) diabetes. *Diabetologia.* 1988;31:902-9.	Comparative effectiveness
Wing RR, Tate DF, Gorin AA, et al. STOP regain: are there negative effects of daily weighing? *J Consult Clin Psychol.* 2007;75:652-6.	No harms outcomes
Wing RR, Tate DF, Gorin AA, et al. A self-regulation program for maintenance of weight loss. *New Engl J Med.* 2006;355:1563-71.	Comparative effectiveness
Wing RR, West DS, Grady D, et al. Effect of weight loss on urinary incontinence in overweight and obese women: results at 12 and 18 months. *J Urol.* 2010;184:1005-10.	Comparative effectiveness
Wing RR. Behavioral approaches to the treatment of obesity. In: Bray G, Bouchard C, James WP, eds. *Handbook of Obesity*. New York: Marcel Dekker; 1998:855-73.	Does not meet design requirements in inclusion criteria
Wing RR. Behavioral weight control. In: Wadden TA, Stunkard AJ, eds. *Handbook of Obesity Treatment*. New York: Guilford Press; 2002:301-16.	Does not meet design requirements in inclusion criteria
Wirth A, Krause J. Long-term weight loss with sibutramine: a randomized controlled trial. *JAMA.* 2001;286:1331-9.	Sibutramine intervention
Wister A, Loewen N, Kennedy-Symonds H, et al. One-year follow-up of a therapeutic lifestyle intervention targeting cardiovascular disease risk. *Can Med Assoc J.* 2007;177:859-65.	Not one of the specified interventions
Wolf AM, Conaway MR, Crowther JQ, et al. Translating lifestyle intervention to practice in obese patients with type 2 diabetes: Improving Control with Activity and Nutrition (ICAN) study. *Diabetes Care.* 2004;27:1570-6.	Comparative effectiveness
Wolf AM, Siadaty MS, Crowther JQ, et al. Impact of lifestyle intervention on lost productivity and disability: improving control with activity and nutrition. *J Occup Environ Med.* 2009;51:139-45.	Comparative effectiveness
Womble LG, Wadden TA, McGuckin BG, et al. A randomized controlled trial of a commercial Internet weight loss program. *Obes Res.* 2004;12:1011-8.	Comparative effectiveness
Wong SY, Lau EM, Lau WW, Lynn HS. Is dietary counselling effective in increasing dietary calcium, protein and energy intake in patients with osteoporotic fractures? A randomized controlled clinical trial. *J Hum Nutr Diet.* 2004;17:359-64.	Not focused on behavioral or pharmacological interventions designed to promote weight loss
Woo J, Sea MM, Tong P, et al. Effectiveness of a lifestyle modification programme in weight maintenance in obese subjects after cessation of treatment with orlistat. *J Eval Clin Pract.* 2007;13:853-9.	Does not include specified harms outcomes
Wosje KS, Kalkwarf HJ. Lactation, weaning, and calcium supplementation: effects on body composition in postpartum women. *Am J Clin Nutr.* 2004;80:423-9.	Not one of the specified interventions
Wright AD, Cull CA, MacLeod KM, et al. Hypoglycemia in type 2 diabetic patients randomized to and maintained on monotherapy with diet, sulfonylurea, metformin, or insulin for 6 years from diagnosis: UKPDS73. *J Diabetes Complications.* 2006;20:395-401.	Comparative effectiveness

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Reference	Reason for Exclusion
Wylie-Rosett J, Swencionis C, Ginsberg M, et al. Computerized weight loss intervention optimizes staff time: the clinical and cost results of a controlled clinical trial conducted in a managed care setting. *J Am Diet Assoc.* 2001;101:1155-62.	Comparative effectiveness
Yalcin AA, Yavuz B, Ertugrul DT, et al. Elevation of QT dispersion after obesity drug sibutramine. *J Cardiovasc Med (Hagerstown).* 2010;11:832-5.	Sibutramine intervention
Yancey AK, McCarthy WJ, Harrison GG, et al. Challenges in improving fitness: results of a community-based, randomized, controlled lifestyle change intervention. *J Womens Health.* 2006;15:412-29.	Not one of the specified interventions
Yarali H, Yildiz BO, Demirol A, et al. Co-administration of metformin during rFSH treatment in patients with clomiphene citrate-resistant polycystic ovarian syndrome: a prospective randomized trial. *Hum Reprod.* 2002;17:289-94.	No harms outcomes
Yassine HN, Marchetti CM, Krishnan RK, et al. Effects of exercise and caloric restriction on insulin resistance and cardiometabolic risk factors in older obese adults—a randomized clinical trial. *J Gerontol A Biol Sci Med Sci.* 2009;64:90-5.	Comparative effectiveness
Yates T, Davies M, Gorely T, et al. Effectiveness of a pragmatic education program designed to promote walking activity in individuals with impaired glucose tolerance: a randomized controlled trial. *Diabetes Care.* 2009;32:1404-10.	Not one of the specified interventions
Yeh MC, Rodriguez E, Nawaz H, et al. Technical skills for weight loss: 2-y follow-up results of a randomized trial. *Int J Obes Relat Metab Disord.* 2003;27:1500-6.	Comparative effectiveness
Zannad F, Gille B, Grentzinger A, et al. Effects of sibutramine on ventricular dimensions and heart valves in obese patients during weight reduction. *Am Heart J.* 2002;144:508-15.	Sibutramine intervention
Zavoral JH. Treatment with orlistat reduces cardiovascular risk in obese patients. *J Hypertens.* 1998;16:2013-7.	Other quality issues
Zemel MB, Richards J, Mathis S, et al. Dairy augmentation of total and central fat loss in obese subjects. *Int J Obes.* 2005;29:391-7.	Not one of the specified interventions
Zemel MB, Richards J, Milstead A, Campbell P. Effects of calcium and dairy on body composition and weight loss in African-American adults. *Obes Res.* 2005;13:1218-25.	No harms outcomes
Zemel MB, Thompson W, Milstead A, et al. Calcium and dairy acceleration of weight and fat loss during energy restriction in obese adults. *Obes Res.* 2004;12:582-90.	Comparative effectiveness
The Hypertension Prevention Trial: three-year effects of dietary changes on blood pressure. *Arch Intern Med.* 1990;150:153-62.	No harms outcomes
Anderssen S, Holme I, Urdal P, Hjermann I. Diet and exercise intervention have favourable effects on blood pressure in mild hypertensives: the Oslo Diet and Exercise Study (ODES). *Blood Press.* 1995;4:343-9.	No harms outcomes
Burke V, Beilin LJ, Cutt HE, et al. Effects of a lifestyle programme on ambulatory blood pressure and drug dosage in treated hypertensive patients: a randomized controlled trial. *J Hypertens.* 2005;23:1241-9.	No harms outcomes
Christian JG, Bessesen DH, Byers TE, et al. Clinic-based support to help overweight patients with type 2 diabetes increase physical activity and lose weight. *Arch Intern Med.* 2008;168:141-6.	No harms outcomes
Cohen MD, D'Amico FJ, Merenstein JH. Weight reduction in obese hypertensive patients. *Fam Med.* 1991;23:25-8.	No harms outcomes
Cussler EC, Teixeira PJ, Going SB, et al. Maintenance of weight loss in overweight middle-aged women through the Internet. *Obesity.* 2008;16:1052-60.	No harms outcomes
Davis BR, Oberman A, Blaufox MD, et al. Effect of antihypertensive therapy on weight loss. *Hypertension.* 1992;19:393-9.	No harms outcomes
Davis BR, Blaufox MD, Hawkins CM, et al. Trial of antihypertensive interventions and management: design, methods, and selected baseline results. *Control Clin Trials.* 1989;10:11-30.	No harms outcomes
Eriksson J, Lindstrom J, Valle T, et al. Prevention of type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland—study design and 1-year interim report on the feasibility of the lifestyle intervention programme. *Diabetologia.* 1999;42:793-801.	No harms outcomes
Frey-Hewitt B, Vranizan KM, Dreon DM, Wood PD. The effect of weight loss by dieting or exercise on resting metabolic rate in overweight men. *Int J Obes.* 1990;14:327-34.	No harms outcomes

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Reference	Reason for Exclusion
Haapala I, Barengo NC, Biggs S, et al. Weight loss by mobile phone: a 1-year effectiveness study. *Public Health Nutr.* 2009;12:2382-91.	No harms outcomes
Hansson L, Zanchetti A. The Hypertension Optimal Treatment (HOT) study—patient characteristics: randomization, risk profiles, and early blood pressure results. *Blood Press.* 1994;3:322-7.	No harms outcomes
Hollis JF, Satterfield S, Smith F, et al. Recruitment for phase II of the Trials of Hypertension Prevention: effective strategies and predictors of randomization. *Ann Epidemiol.* 1995;5:140-8.	No harms outcomes
Jeffery RW, Wing RR. Long-term effects of interventions for weight loss using food provision and monetary incentives. *J Consult Clin Psychol.* 1995;63:793-6.	No harms outcomes
Jeffery RW, Wing RR, Thorson C, et al. Strengthening behavioral interventions for weight loss: a randomized trial of food provision and monetary incentives. *J Consult Clin Psychol.* 1993;61:1038-45.	No harms outcomes
Jones DW, Miller ME, Wofford MR, et al. The effect of weight loss intervention on antihypertensive medication requirements in the Hypertension Optimal Treatment (HOT) study. *Am J Hypertens.* 1999;12:1175-80.	No harms outcomes
Kastarinen MJ, Puska PM, Korhonen MH, et al. Non-pharmacological treatment of hypertension in primary health care: a 2-year open randomized controlled trial of lifestyle intervention against hypertension in eastern Finland. *J Hypertens.* 2002;20:2505-12.	No harms outcomes
Kiernan M, King AC, Stefanick ML, Killen JD. Men gain additional psychological benefits by adding exercise to a weight-loss program. *Obes Res.* 2001;9:770-7.	No harms outcomes
Kulzer B, Hermanns N, Gorges D, et al. Prevention of Diabetes Self-Management Program (PREDIAS): effects on weight, metabolic risk factors, and behavioral outcomes. *Diabetes Care.* 2009;32:1143-6.	No harms outcomes
Langford HG, Blaufox MD, Oberman A, et al. Dietary therapy slows the return of hypertension after stopping prolonged medication. *JAMA.* 1985;253:657-64.	No harms outcomes
Langford HG, Davis BR, Blaufox D, et al. Effect of drug and diet treatment of mild hypertension on diastolic blood pressure. *Hypertension.* 1991;17:210-7.	No harms outcomes
Lindstrom J, Louheranta A, Mannelin M, et al. The Finnish Diabetes Prevention Study (DPS): lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care.* 2003;26:3230-6.	No harms outcomes
Martin DP, Rhode PC, Dutton GR, et al. A primary care weight management intervention for low-income African-American women. *Obesity.* 2006;14:1412-20.	No harms outcomes
Martin PD, Dutton GR, Rhode PC, et al. Weight loss maintenance following a primary care intervention for low-income minority women. *Obesity.* 2008;16:2462-7.	No harms outcomes
Mayer-Davis EJ, D'Antonio AM, Smith SM, et al. Pounds Off With Empowerment (POWER): a clinical trial of weight management strategies for black and white adults with diabetes who live in medically underserved rural communities. *Am J Public Health.* 2004;94:1736-42.	No harms outcomes
Mitsui T, Shimaoka K, Tsuzuku S, et al. Gentle exercise of 40 minutes with dietary counseling is effective in treating metabolic syndrome. *Tohoku J Exp Med.* 2008;215:355-61.	No harms outcomes
Moore H, Summerbell CD, Greenwood DC, et al. Improving management of obesity in primary care: cluster randomised trial. *BMJ.* 2003;327:1085.	No harms outcomes
Narayan KM, Hoskin M, Kozak D, et al. Randomized clinical trial of lifestyle interventions in Pima Indians: a pilot study. *Diabet Med.* 1998;15:66-72.	No harms outcomes
Perri MG, McAllister DA, Gange JJ, et al. Effects of four maintenance programs on the long-term management of obesity. *J Consult Clin Psychol.* 1988;56:529-34.	No harms outcomes
Pritchard DA, Hyndman J, Taba F. Nutritional counselling in general practice: a cost effective analysis. *J Epidemiol Community Health.* 1999;53:311-6.	No harms outcomes
Silva MN, Markland D, Minderico CS, et al. A randomized controlled trial to evaluate self-determination theory for exercise adherence and weight control: rationale and intervention description. *BMC Public Health.* 2008;8:234.	No harms outcomes
Silva MN, Vieira PN, Coutinho SR, et al. Using self-determination theory to promote physical activity and weight control: a randomized controlled trial in women. *J Behav Med.* 2010;33:110-22.	No harms outcomes
Stevens VJ, Obarzanek E, Cook NR, et al. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Ann Intern Med.* 2001;134:1-11.	No harms outcomes

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Reference	Reason for Exclusion
Stevens VJ, Corrigan SA, Obarzanek E, et al. Weight loss intervention in phase 1 of the Trials of Hypertension Prevention. *Arch Intern Med.* 1993;153:849-58.	No harms outcomes
Svetkey LP, Stevens VJ, Brantley PJ, et al. Comparison of strategies for sustaining weight loss: the weight loss maintenance randomized controlled trial. *JAMA.* 2008;299:1139-48.	No harms outcomes
Teixeira PJ, Silva MN, Coutinho SR, et al. Mediators of weight loss and weight loss maintenance in middle-aged women. *Obesity (Silver Spring).* 2010;18:725-35.	No harms outcomes
ter Bogt NC, Bemelmans WJ, Beltman FW, et al. Preventing weight gain: one-year results of a randomized lifestyle intervention. *Am J Prev Med.* 2009;37:270-7.	No harms outcomes
HOT Study Group. The Hypertension Optimal Treatment Study (the HOT Study). *Blood Press.* 1993;2:62-8.	No harms outcomes
Trials of Hypertention Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. *Arch Intern Med*. 1997;157:657-67.	No harms outcomes
Trials of Hypertension Prevention Collaborative Research Group. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels: results of the Trials of Hypertension Prevention, phase I. *JAMA.* 1992;267:1213-20.	No harms outcomes
Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med.* 2001;344:1343-50.	No harms outcomes
Uusitupa M, Peltonen M, Lindstrom J, et al. Ten-year mortality and cardiovascular morbidity in the Finnish Diabetes Prevention Study—secondary analysis of the randomized trial. *PLoS One.* 2009;4:e5656.	No harms outcomes
Wassertheil-Smoller S, Langford HG, Blaufox MD, et al. Effective dietary intervention in hypertensives: sodium restriction and weight reduction. *J Am Diet Assoc.* 1985;85:423-30.	No harms outcomes
Weight Loss Maintenance Trial: Protocol. Portland, OR: Kaiser Permanente Center for Health Research; 2008. http://www.kpchr.org/wlmpublic/public/common/getdoc.aspx?docid=02E06ADF-1194-456A-904F-8AD81DB8EB8B	No harms outcomes
Werkman A, Hulshof PJ, Stafleu A, et al. Effect of an individually tailored one-year energy balance programme on body weight, body composition and lifestyle in recent retirees: a cluster randomised controlled trial. *BMC Public Health.* 2010;10:110.	No harms outcomes
Whelton PK, Hebert PR, Cutler J, et al. Baseline characteristics of participants in phase I of the Trials of Hypertension Prevention. *Ann Epidemiol.* 1992;2:295-310.	No harms outcomes
Wood PD, Stefanick ML, Dreon DM, et al. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N Engl J Med.* 1988;319:1173-9.	No harms outcomes
Wood PD, Stefanick ML, Williams PT, Haskell WL. The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. *N Engl J Med.* 1991;325:461-6.	No harms outcomes
Woollard J, Burke V, Beilin LJ, et al. Effects of a general practice-based intervention on diet, body mass index and blood lipids in patients at cardiovascular risk. *J Cardiovasc Risk.* 2003;10:31-40.	No harms outcomes
Riserus U, Vessby B, Arnlov J, Basu S. Effects of cis-9,trans-11 conjugated linoleic acid supplementation on insulin sensitivity, lipid peroxidation, and proinflammatory markers in obese men. *Am J Clin Nutr.* 2004;80:279-83.	Not one of the specified interventions
Lakerveld J, Bot SD, Chinapaw MJ, et al. Primary prevention of diabetes mellitus type 2 and cardiovascular diseases using a cognitive behavior program aimed at lifestyle changes in people at risk: design of a randomized controlled trial. *BMC Endocr Disord.* 2008;8:6.	No harms outcomes
Davey SG, Bracha Y, Svendsen KH, et al. Incidence of type 2 diabetes in the randomized Multiple Risk Factor Intervention Trial. *Ann Intern Med.* 2005;142:313-22.	Not one of the specified interventions
Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract.* 2005;67:152-62.	Comparative effectiveness

Appendix D Table 4. Studies Excluded From Review for Key Question 4

Reference	Reason for Exclusion
Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. *Arch Intern Med.* 1559;168:1550-9.	Comparative effectiveness
Jacob S, Rabbia M, Meier MK, Hauptman J. Orlistat 120 mg improves glycaemic control in type 2 diabetic patients with or without concurrent weight loss. *Diabetes Obes Metab.* 2009;11:361-71.	No harms outcomes
Gaciong Z, Placha G. Efficacy and safety of sibutramine in 2225 subjects with cardiovascular risk factors: short-term, open-label, observational study. *J Hum Hypertens.* 2005;19:737-43.	Sibutramine intervention

Appendix E. Trials Pending Assessment

Investigator, Study Name	Location	Number of Participants	Intervention	Outcomes	2010 Status
Dr. R. Ross PROACTIVE	Ontario, Canada	491	Behaviorally based physical activity and diet composition program	Primary: waist circumference and prevalence of metabolic syndrome Secondary: body composition, serum cholesterol, physical activity, barriers to physical activity and other psychosocial barriers	Last data collection planned for January 2010
Dr. M. Silva	Lisbon, Portugal	259	Behavioral group sessions covering physical activity, eating/nutrition, body image, and other cognitive-behavioral contents	Weight, physical activity and exercise levels, dietary intake, psychosocial measures	Completed July 2009, results not yet published
Dr. Marieke F van Wier	The Netherlands	1386	Phone-based and internet-based behavioral intervention addressing diet and physical activity	Body weight, BMI, diet, physical activity, perceived health, empowerment, stage of change and self-efficacy concerning weight control, physical activity and eating and eating habits, work performance/productivity, waist circumference, sum of skin folds, blood pressure, total blood cholesterol level, and aerobic fitness	Results at 6 months published. 12, 18, and 24 months not yet published
Dr. Neree Claes PreCardio	Belgium	350	Prevention consultations using a cardiovascular risk calculator with personalized feedback on behavioral risk factors, followup with intensive support of health behavior change	Cardiovascular risk factors, cardiovascular events, quality of life, costs, and incremental cost effectiveness ratios	Protocol published in 2007, 3-year followup planned
Dr. Karen Hosper Exercise on Prescription	The Netherlands	360	Weekly exercise sessions for 20 weeks	Minutes of self-reported physical activity per week, mediating motivational factors regarding physical activity, wellbeing, perceived health, fitness, body size, and use of health care	Protocol published in December 2008, 12 months of followup planned
Dr. Jacqueline Kerr Illinois WISEWOMAN	Chicago, Illinois	1021	CVD risk factor screening, educational materials, and a 12-week lifestyle intervention	Dietary intake, physical activity, blood pressure, cholesterol, blood glucose, BMI	Baseline results published in 2009
Dr. Philip Merriam LLDPP	Lawrence, Massachusetts	312	13 group sessions and 3 individual home visits intended to increase awareness of diabetes prevention strategies, foster positive diabetes prevention attitudes, and promote healthy lifestyle behaviors.	Stern equation components, weight, glycosylated hemoglobin, diet, physical activity, depression, social support, and quality of life	Baseline results published in 2009, 12 months of followup planned
Dr. Truls Ostbye AMP	Durham, North Carolina	450	10 physical activity group sessions, 8 healthy eating classes, 6 telephone counseling sessions promoting a reduction in BMI up to 2 years postpartum	Teachable moment factors, intervention participation, Nutrition Data System, brief food frequency questions, 7-Day Physical Activity Recall, weight, and height	Baseline results published in 2008, 10.5 month results published in 2009, 24 months of followup planned

Appendix E. Trials Pending Assessment

Investigator, Study Name	Location	Number of Participants	Intervention	Outcomes	2010 Status
Dr. Kristin Schneider	Massachusetts	174	Behavioral Activation condition: 10 weekly individual visits of behavior therapy for treatment of depression followed by 16 group behavioral weight loss visits Standard Weight Loss condition: 10 individual visits of health education (attention control) followed by 16 group behavioral weight loss visits	Weight, depression, physical activity and dietary intake, emotional eating, quality of life, blood pressure, serum lipids, C-reactive protein	Protocol published 2008, 24 months of followup planned
Dr. Mark Vander Weg The Treatment and Prevention Study	Iowa City, Iowa Memphis, Tennessee Rochester, Minnesota	1267	3-4 individual smoking-cessation sessions; 5 individual and 12 weekly group sessions for modifying diet and physical activity; weight loss and sodium restriction modeled after the TONE study	Blood pressure, height, weight, body composition, waist circumference, smoking status, dietary intake, urinary chloride excretion, physical activity, and assessment of predictor, mediator, and moderator variables	Protocol published 2008, 5 years of followup planned
Dr. Deborah Parra-Medina HHER	Columbia and Orangeburg, SC	266	Stage-based behavioral counseling from primary-care provider, nurse-assisted goal setting, community resource guide of free or low-cost programs and facilities, and ethnically tailored educational materials. 12 newsletters, 14 brief telephone counseling calls over 12 months.	Physical activity, food consumption, BMI, waist circumference, total cholesterol, barriers-based self-efficacy for exercise, self-efficacy for low-fat diet, social support for physical activity and low-fat diet, decisional balance for physical activity and low-fat diet	Protocol and baseline measures published 2010, 12 months of followup planned
Dr. Juan Jose Rodriguez Cristobal	Spain	1200	32 group sessions. 4 sessions to provide information about the benefits of change and recommended diets. 8 sessions to have patients feel motivated to make a change and be committed to continuing the program. 20 sessions to work with changed and maintenance.	Age, ethnicity, sex, medical history, medications, quality of life, dietary survey, height, weight, BP, pulse, fasting serum glucose, fasting lipid panel	Protocol published in 2010, 26 moths of followup planned
Dr. Jun Ma BE WELL	California	324	Goal-based approach with the same weight loss and physical activity goals for each participant. Physical activity time gradually increased and a moderate reduction of calories. 12 weekly small group sessions, 2 individual counseling sessions, optional contact with interventionist.	QOL, 3-day food record, pedometer, angina and peripheral vascular disease, depression, adverse events, height, weight, waist circumference, waist-to-hip ratio, blood pressure, current medical problems	Protocol published in 2010, 12 moths of followup planned
Dr. Gianluca Castelnuovo TECNOB	Italy	154	In hospital treatment for 1 month for diet, physical activity, psychological and dietitian counseling. Extensive outpatient telecare through a web platform and mobile phones for 12 months.	Weight, height, binge eating, eating disorder inventory, psychological problems, QOL	Protocol published in 2010, 13 months of followup planned.

Appendix E. Trials Pending Assessment

Investigator, Study Name	Location	Number of Participants	Intervention	Outcomes	2010 Status
Dr. Giovanni Cizza	Maryland	150	During first 12 months strive to increase sleep duration. During subsequent 36 months, individual counseling on sleep, nutrition, and physical activity offered to all participants; individualized sleep plans, long-term lifestyle changes to daily routine encouraged.	Body composition, psychological assessment, insulin resistance, endocrine assessment, metabolic assessment, QOL	Protocol published in 2010, 48 months of followup planned.
Dr. Elizabeth Eakin Living Well with Diabetes	Australia	300	Repeated assessment of study outcomes and participant self-monitoring; feedback provided for weight, dietary intake, and physical activity using motivational interviewing techniques; collaborative goals for weight, physical activity, and dietary change with telephone counselor; behaviorally-specific action plan; barriers and supports identified; confidence is assessed and problem-solving discussed as necessary (up to 27 calls).	Weight, physical activity, HbA1c, dietary and energy intake, waist circumference, percent body fat, fasting plasma glucose, blood lipids, liver function enzymes, blood pressure, health-related QOL.	Protocol published in 2010, 24 months of followup planned
Dr. Kate Jolly Lighten Up	UK	740	Weight Watchers: Food points system, beating hunger, taking more physical activity, keeping motivated Slimming World: Encouraged to eat low energy dense foods plus some extras rich in calcium and fiber with controlled amounts of high energy dense foods. Rosemary Conley: Weight loss and improved diet, fitness, and improvement of physical condition, motivation and self esteem, use of group support. NHS Size Down: Managing behavior around food and relapse prevention, eatwell plate, nutrition information. General practice/pharmacy: Client-led sessions, weight and dieting history, goals and expectations, eatwell plate, goals to reduce calorie intake and increase physical activity.	Weight, physical activity.	Protocol published in 2010, 12 months of followup planned.

Appendix E. Trials Pending Assessment

Investigator, Study Name	Location	Number of Participants	Intervention	Outcomes	2010 Status
Dr. Hsin-Chieh Yeh POWER Trials Collaborative Group	Maryland, Pennsylvania, Massachusetts	~1100	Be Fit, Be Well: Behavior change prescription and skills training via internet or a combination of tailored print materials and an interactive voice response system. POWER Hopkins: Phone calls with Healthways coach, interactive website, PCP reinforcement (IG1). Individual and group meetings and phone calls with Hopkins interventionist, interactive website, PCP reinforcement (IG2). POWER-UP: Usual medical care plus 26 brief counseling sessions with auxiliary health care provider (IG1). Usual medical care plus 26 brief counseling sessions plus the choice of adjunctive meal replacements or pharmacotherapy (IG2).	Be Fit, Be Well: Blood pressure, dietary change, physical activity, medication adherence POWER Hopkins: Weight, BMI, blood pressure, hypertension control, lipid levels, HOMA-IR, Framingham risk score POWER-UP: Weight, BMI, metabolic syndrome, eating and activity habit changes, quality of life, cardiovascular disease risk factors, HOMA-IR	Protocol for all 3 published in 2010. Be Fit, Be Well: Followup at 24 months POWER Hopkins: Followup at 24 months POWER-UP: Followup at 12 and 24 months

Key Questions 4 and 4a. What Are the Adverse Effects of Primary Care–Relevant Interventions in Obese or Overweight Adults? Are There Differences in Adverse Effects Between Patient Subgroups?

In addition to evaluating all 61 studies from KQs 2 and 3 for harms, we abstracted an additional 27 weight loss studies for harms data (see methods for inclusion and quality criteria for additional studies).

Orlistat

General characteristics of studies. We included a total of 23 studies on the harms of orlistat (120 mg tid) (Table 16). Seventeen were RCTs from KQs 2 and 3,[180-184,187,189-191,193,194,197-202] five were additional published RCTs,[126,127,129,130,132] and one was an event monitoring study from the United Kingdom.[133] The event monitoring study relied on doctors' retrospective reports of adverse events and had low response rates. We chose to include the study because we wanted to capture rare adverse events that might not be picked up in relatively small RCTs. Of the RCTs, eight recruited unselected populations[129,182,184,189,190,193,199,200] and 14 recruited participants with at least one clinical or subclinical cardiovascular risk factor.[126,127,130,132,180,181,183,187,191,194,197,198,201,202]

Seven of the 22 trials (32 percent) were conducted in the United States.[126,127,182,189-191,197] All trials included both men and women (overall weighted average percent of female participants, 66 percent). The overall weighted average age of the entire group was 46.9 years (range, 41 to 59 years). Only nine of 23 trials reported ethnicity of the participants, and in these trials the weighted average percent of nonwhite participants was 15.6 percent (range, 0 to 28 percent). The median trial duration was 52 weeks (range, 24 to 208 weeks), but five provided data beyond 52 weeks.

Withdrawals due to adverse effects. More participants who were randomized to orlistat were withdrawn from the study due to adverse effects compared with those who were randomized to placebo. Twenty-two trials included data on withdrawals due to harms and were combined by meta-analysis.[126,127,129,130,132,180-184,187,189-191,193,194,197-202] Particpants taking orlistat were 1.6 times more likely to withdraw from the study due to adverse effects (RR, 1.63 [95% CI, 1.28-2.09]; I^2=51.1%; k=22; n=11,920) (Figure 14). In absolute terms, the weighted mean withdrawal rates in the orlistat and placebo groups were 8 (range, 2 to 15 percent) and 4 percent (range, 2 to 14 percent), respectively. Many studies did not list specific adverse effects that led to withdrawal. In three of the four studies that listed reasons for withdrawal, gastrointestinal-related symptoms were the main cause of withdrawal.[126,129,133] The fourth study reported that syncope, bradycardia, vomiting, and vomiting/trauma led to withdrawal.[295]

Total number reporting adverse effects. More participants reported adverse effects in the orlistat group compared with the placebo group. Data on the total proportion of participants with adverse effects from eight of 22 orlistat trials were combined by meta-analysis. Participants given orlistat were 1.1 times more likely to have an adverse effect than participants in the

placebo group (RR, 1.10 [95% CI, 1.03-2.17]; I^2=70.8%; k=8; n=11,920) (Figure 13). In absolute terms, the weighted mean rate of adverse effects was 78 percent (range, 32 to 95 percent) in the orlistat group and 70 percent (range, 26 to 93 percent) in the placebo group. Gastrointestinal events were the leading etiology of excess adverse effects.[126,129,130,200]

Number with serious adverse effects. Serious adverse effects were those labeled by the authors as "serious" or "severe" adverse effects. A similar number of participants reported serious adverse effects in the orlistat group compared with the placebo groups. Data on serious adverse effects from 12 of 22 studies were combined in a meta-analysis. Those taking orlistat were not more likely to suffer serious adverse effects compared with those in the placebo group (RR, 1.21 [95% CI, 0.88-21.68]; I^2=62.3%; k=12; N=7724) (Figure 15). In absolute terms, the weighted mean average serious rate of adverse effects was 10 percent (range, 0 to 15 percent) in the orlistat group and 9 percent (range, 0 to 18 percent) in the placebo group. Three trials reported an elevated risk of serious adverse effects in the orlistat group compared with the control group (RR, 3.11-6.15).[129,199,209] The rate of serious adverse effects in these three orlistat trials ranged from less than 1 percent[199] to 10 percent.[194] The serious adverse effects in these studies included fecal incontinence, diverticulitis, and abdominal pain.

Number with gastrointestinal-related adverse effects. Orlistat was associated with more gastrointestinal-related adverse effects than the placebo group. Data on gastrointestinal adverse effects from 18 studies were combined in a meta-analysis. Participants given orlistat had a 1.4 greater risk of suffering from a gastrointestinal-related adverse effect than those given placebo (RR, 1.42 [95% CI, 1.33-1.52]; I^2=81.5%; k=18; N=10,401) (Figure 16). In absolute terms, the weighted mean average rate of gastrointestinal side effects in the orlistat group was 83 percent (range, 63 to 95 percent) and 59 percent (range, 39 to 82 percent) in the placebo group. Gastrointestinal side effects included loose stools, increased defecation, uncontrolled oily discharge/oily evacuation, oily spotting, fatty/oily stool, fecal urgency, discolored feces, flatus with discharge, fecal incontinence, and abdominal pain. Most gastrointestinal adverse effects were mild to moderate in intensity, occurred early in treatment, and resolved spontaneously. In an orlistat event monitoring study from the United Kingdom, gastrointestinal symptoms were the main adverse effect that general practitioners reported as the cause of patients stopping orlistat treatment.[133]

Hypoglycemia. Data were limited and contradictory regarding whether orlistat led to hypoglycemia in drug-treated patients with type 2 diabetes. Two studies found an increased incidence of hypoglycemia in participants treated with orlistat compared with placebo (16.9 vs. 9.7 percent; 10 percent in intervention group vs. 4 percent in control group),[127,197] although the difference was not statistically significant in one study.[127] A third study found no difference in the number of hypoglycemic episodes between treatment arms.[187]

Bone density. Data were insufficient to determine whether orlistat had detrimental effects on bone density. In a small subsample (N=30) of participants from a larger study,[200] bone density did not differ between orlistat and placebo groups.[216]

Vitamins. Orlistat treatment appeared to be associated with a decrease in some fat-soluble vitamin levels compared with placebo. Data were strongest for vitamins E and beta-carotene, but there were also several reports for vitamin D. Evidence was sparser and/or conflicting for

vitamins A and K. Five trials examined the effects of orlistat on changes in vitamin E levels, and all found that orlistat resulted in a greater decrease in vitamin E compared with placebo.[129,190,191,199,202] All four trials examining beta-carotene[129,190,191,199] and all three examining vitamin D[129,199,202] noted a greater decrease in vitamin levels in the orlistat group compared with placebo. One trial noted a decrease in vitamins A and K in the orlistat group compared with placebo;[202] however, another study did not find that 120 mg of orlistat resulted in a lower vitamin A level compared with placebo.[129]

Two trials compared the number of participants in the orlistat and placebo groups with low vitamin levels at multiple measurement time points throughout the trial.[200,202] More orlistat participants compared with placebo participants experienced at least two low vitamin E levels (3.2 to 4.6 percent in orlistat groups vs. 0.5 to 0.9 percent in placebo groups).[200,202] Neither trial found that more orlistat participants had two or more low vitamin A levels.[200,202] Data on orlistat's effects on the development of low vitamin D and beta-carotene levels were mixed.[200,202]

More orlistat participants than placebo participants required vitamin supplementation during the study.[129,182,191,199,200] In the one study that listed the type of vitamin supplementation required, vitamins D and beta-carotene, but not vitamin E, were required more in the orlistat group compared with placebo.[191]

Liver injury. Data to evaluate orlistat's effects on the liver were insufficient. No trial reported specifically screening for liver disease. No trial recorded liver injury as an adverse effect. In an orlistat event monitoring study in the United Kingdom, no cases of serious hepatic adverse reactions were reported.[133,134] There were reports of elevated liver tests with two cases felt to be causally related to orlistat treatment.[133]

Dosage effect. In terms of dosing, all 22 trials prescribed orlistat 120 mg tid.[126,127,129,130,132,180-184,187,189-191,193,194,197-202] Four trials included more than just a 120 mg tid dosage group (30 to 240 mg tid).[129,189,190,199] Although none of the studies presented statistical comparisons between dosing groups, their data do not suggest that dosage was associated with different adverse effect rates, although the results were somewhat mixed. Three of the four trials reported similar adverse effect rates with increasing dose. For example, in one study,[129] withdrawal rates due to adverse effect were 6, 5, 2, and 3 percent in the 30, 60, 120, and 240 mg tid treatment groups, respectively. In another study, severe gastrointestinal event rates were 6.6 percent in the 60 mg tid group and 10.3 percent in the 120 mg tid group; however, withdrawals for gastrointestinal events were 5 percent in the 60 mg tid group and 3.7 percent in the 120 mg tid group.[199] In contrast, in the fourth trial, a weight maintenance trial, overweight and obese unselected/low risk participants who took 30, 60, and 120 mg tid of orlistat had 5.4, 7.0, and 11.7 percent, respectively, withdrawal from adverse effects (however, no statistical testing was reported to determine if these were statistically different).[190]

Subgroup analysis. Withdrawals from adverse effects were more likely in trials of unselected participants taking orlistat than in participants with cardiovascular risk factors, regardless of age. In eight studies of unselected populations,[129,182,184,189,190,193,199,200] those who were randomized to orlistat were 2.2 times more likely to withdraw due to adverse effects than those taking placebo (RR, 2.18 [95% CI, 1.57-3.01]; I^2=21.2%; k=8; N=4029). In contrast, in the 12 studies of participants with type 2 diabetes, hypertension, or dyslipidemia,[126,127,130,132,180,181,183,187,191,194,197,

[198,201,202] the orlistat group had no greater risk of withdrawing due to adverse effects (RR, 1.34 [95% CI, 0.93-1.94]; I^2=50.5%; k=12; N=4277). Similarly, in the four trials of participants with a mean age of at least 55 years who had type 2 diabetes, hypertension, or dyslipidemia,[127,180,187,191] the orlistat group did not withdraw more than the placebo group (RR, 0.8 [95% CI, 0.43-1.49]; I^2=46.9%; k=4; N=1475).

Similarly, serious adverse effects from orlistat may also be less likely in those with cardiovascular risk factors than unselected participants. In eight studies of participants with type 2 diabetes, hypertension, or dyslipidemia,[126,132,181,183,194,198,201,202] serious adverse effects were not increased in the orlistat group compared with placebo (RR, 1.08 [95% CI, 0.59-1.97]; I^2=63.3%; k=6; N=1992). In the four studies of unselected populations,[129,193,199,200] however, there was a nonsignificant increase in the risk of serious adverse effects in those who were randomized to orlistat (RR, 2.01 [95% CI, 0.91-4.47]; I^2=65.9%; k=4; N=2118). This elevated risk ratio was primarily the result of two studies.[129,199] The serious adverse effects in these two studies included fecal incontinence, diverticulitis, and abdominal pain.

Metformin

General characteristics of studies. We included a total of four studies on the harms of metformin (850 mg twice daily) (Table 16). Three trials were RCTs from KQs 2 and 3[142,185,186] and one was an additional published RCT.[131] Recruitment criteria included impaired fasting glucose or impaired glucose tolerance,[142] high waist-to-hip ratios,[185] or PCOS.[131,186] Only one trial was conducted in the United States.[142] The overall weighted average percent of female participants in all trials was 83.6 percent (range, 66 to 100 percent; two trials included only women). The overall weighted average age of participants was 39.8 years (range, 27 to 50 years), and 45.3 percent of the participants in the largest trial of metformin were nonwhite.[142] The other trials did not describe ethnicity. The average trial duration was 84 weeks (range, 26 to 208 weeks).

Withdrawals due to adverse effects. More participants who were randomized to metformin withdrew from the study due to adverse effects compared with those who were randomized to placebo. Two of the four trials included data on withdrawals due to harms and were combined by meta-analysis. Participants taking metformin were almost four times more likely to withdraw from the study due to adverse events (RR, 3.92 [95% CI, 1.23-12.57]; k=2; I^2=0%; N=4118) (Figure 14). In absolute terms, the weighted mean average rate of withdrawal due to adverse effects was 5 percent (range, 0 to 7 percent) in the metformin group and 1 percent (range, 0 to 1 percent) in the placebo group. Studies did not list what adverse effects led to withdrawal. The largest trial and only study rated as good quality, DPP, did not list withdrawals due to adverse effects.[142]

Total number with adverse effects. More participants experienced adverse effects in the metformin group compared with the placebo group. Two of the four metformin trials listed the total proportion of participants with adverse effects and were combined by meta-analysis. Participants given metformin were almost five times more likely to suffer an adverse effect compared with those in the placebo group (RR, 4.83 [95% CI, 0.84-27.63]; I^2=87.6%; k=2; N=517) (Figure 13). In absolute terms, the weighted mean average rate of adverse effects was 46 percent (range, 4 to 100 percent) in the metformin group and 16 percent (range, 6 to 17 percent)

in the placebo group. Excess adverse effects were mostly due to gastrointestinal events in these two trials. DPP was not combined in the meta-analysis because it did not record the total number of adverse effects; it only reported gastrointestinal and musculoskeletal adverse effects.[206]

Number with serious adverse effects. No studies reported the number of participants with serious adverse effects in the two treatment groups.

Number with gastrointestinal-related adverse effects. Gastrointestinal adverse effects were more likely to occur in participants who were randomized to metformin compared with placebo. One small study of 40 women with PCOS found that two women had transient abdominal gastrointestinal events (abdominal swelling, mild diarrhea, and flatulence) during the first two weeks of treatment (RR, 5.0 [95% CI, 0.26-98.00]; N=40).[185] In DPP, participants taking metformin had an increased risk of gastrointestinal symptoms (diarrhea, flatulence, nausea, vomiting) compared with the placebo group (77.8 vs. 30.7 events/100 person-years; $p<0.05$).[206] This pattern was consistent across age groups.[210] In another study of 457 people with high waist-to-hip ratio, diarrhea and nausea/vomiting were more common in the metformin group compared with placebo (diarrhea: 45/457 [9.8 percent] vs. 10/457 [2.2 percent]; nausea/vomiting: 14/457 [3.1 percent] vs. 6/457 [1.3 percent]).[185] However, the incidence of abdominal pain and cramps was not different between treatment groups.[185]

Bone density. There were no data about the effects of metformin on bone density.

Hypoglycemia. No metformin study reported rates of hypoglycemia in treatment groups.

Dosage effects. We were unable to examine the relationship between metformin dose and adverse effects, as all four studies prescribed the same dose of metformin (850 mg twice daily).

Subgroup analysis. In DPP, the relative increase in gastrointestinal adverse events in the metformin group did not appear to differ by age.[210] No other subgroup analyses were reported in DPP or could be done with meta-analysis.

Comparison of the Two Drugs

One study randomized 150 obese women to 6 months of one of three weight loss drugs: sibutramine, orlistat, and metformin.[136] Abdominal discomfort occurred in the orlistat (22/50) and metformin groups (14/50). Both metformin and orlistat resulted in decreases in blood pressure and heart rate.[136]

Heterogeneity of Medication Studies (Meta-Regression Analysis)

We performed meta-regression to examine whether certain study characteristics influenced the association between the medication and the proportion of participants withdrawing due to adverse effects, reporting any adverse effects, reporting any serious adverse effects, and reporting gastrointestinal-related adverse effects in all cases controlling for risk status of participants and medication type. We examined multiple trial factors, including how many participants returned for followup, whether the study was conducted in the United States, and duration of the study. None of these trial factors influenced the harms effect size of the

medications. Sex and age did not predict effect size for any adverse effect associated with medications. We were unable to examine ethnicity because of the paucity of reporting (nine studies) and low percentage of nonwhite participants in all of the medication studies combined (13 percent).

We had limited ability to detect differences in harms between medications, since we did not include trials that did not have placebo comparison groups. Only one trial of medication harms included head-to-head comparisons of orlistat and metformin in 150 obese women (50 in each medication group and 50 in a sibutramine group) after 6 months of treatment.[136] The trial reported only two participants withdrawing from the orlistat group due to side effects, none of which were reported as serious, and there were no differences in blood pressure or heart rate. The type of medication did not influence withdrawal due to adverse effects, total adverse effects, or serious adverse effects in any of the meta-regression models.

Surgical Interventions to Treat Obesity

The use of bariatric surgery to treat obesity in adults is increasing in the United States. This increase is likely due to advancing surgical expertise and a recognition of bariatric surgery's effectiveness for weight loss and reducing obesity-related health problems. Current practice is to refer patients to specialized multidisciplinary centers in order to reduce risks of surgery, while providing support before and after bariatric surgery.[296] Bariatric surgery results in significant short- and intermediate-term weight loss for patients who meet current criteria for surgery.[239,244,296] Criteria for bariatric surgery are usually defined as class III obesity (BMI of >40 kg/m^2) or class II obesity (BMI of 35 to 40 kg/m^2) with comorbidity such as diabetes.[297]

Health Outcomes

A recent Health Technology Assessment (HTA) summarized evidence on the clinical and cost effectiveness of bariatric surgery for obesity.[239] This HTA identified 26 studies with a followup of at least 12 months that included outcomes on weight change, quality of life, perioperative and postoperative morbidity and mortality, and change in obesity-related comorbidity.[239]

Weight reduction. Although the degree of weight reduction varied, all surgical methods resulted in significant weight loss. The Swedish Obese Subjects (SOS) study was the largest and longest study included in the HTA. The SOS study is an ongoing prospective cohort study of 2010 subjects who underwent bariatric surgery and 2037 matched controls.[244] After 15 years of followup, the vertical banded gastroplasty (VBG) group had a weight reduction of 16 percent, the gastric bypass (GBP) group had a reduction of 25 percent, and the banding group had a reduction of 14 percent. This translates to an average sustained weight loss of 19.7 kg from the presurgical weight and BMI reduction from 42 to 35.3 kg/m^2.

The remaining included studies generally reported followup of 1 to 3 years and a range of weight reduction from baseline of 16 to 29 percent. BMI losses were as much as 8 to 11 kg/m^2 below baseline, and average weight lost ranged from around 21 kg to over 50 kg. Weight loss differed significantly depending on procedure, sex, and baseline weight and/or BMI.

Harms of surgery. Deaths rarely occurred due to surgical complications. In the SOS study, postoperative mortality was 0.25 percent (5 of 2010 at 90 days).[244] Long- and short-term complications, however, can be quite significant. Common complications included infections, bleeding, deep vein thrombosis and pulmonary embolism, leakage, symptomatic ulcer and gastroesophageal reflux disease, diarrhea, gallstones, and vitamin deficiency. Complications requiring reoperation in the postoperative period occurred in 2 to 13 percent of patients. Surgical reoperations or conversions during 10 years of followup in the SOS study were high at 17 percent for GBP, 21 percent for VBG), and 31 percent for banding (excluding early postoperative complications requiring surgery).[239,243,244] However, reporting of adverse events has not been standardized, and they were generally not reported well.

Other health outcomes. The SOS study provides the only longer-term data on bariatric surgery's mortality benefit. At 10 years, unadjusted overall mortality was reduced by 23.7 percent in the surgery group (p=0.0419). Sex-, age-, and risk factor-adjusted mortality reduction

was 30.7 percent (p=0.0102). The most common cause of death were myocardial infarction and cancer.[244]

Physiologic measures also improved with weight loss. The most significant reduction was apparent in the development of metabolic syndrome and remission of type 2 diabetes. For diabetes resolution, data at 2 years reported that 72 percent of those with type 2 diabetes had reversed, and 36 percent were still in remission at 10 years. Other studies reported higher rates, but did not have as long of followup. In one small study included in the HTA, for example, diabetes resolution was reported as high as 100 percent at 3 years, but it referred to only five of 59 patients after laparoscopic Roux-en-Y gastric bypass.[239] Even using the most conservative estimates available, the treatment effect is quite marked for surgery and diabetes reversal. In modeling of cost effectiveness over 20 years, the delay in developing or redeveloping diabetes still results in a quality-adjusted life year improvement.

Comorbidity improved after surgery in all groups, but the quality of this data was poor in general. At 10 years, the SOS study found a statistically significant reduction in the incidence of diabetes, hypertriglyceridemia, and hyperuricemia compared with conventional therapy. Other reported improved (although not necessarily significant) comorbidities include sleep apnea, pulmonary problems, joint problems, reflux disease, and psychological problems. Although the SOS study found that cancer rates were statistically significantly lower for women treated with surgery, men did not show the same results. More data on cancer and obesity is needed to further characterize this effect. In surgical patients, triglycerides and low HDL cholesterol did improve even after 10 years, but there was no statistically significant recovery from hypercholesterolemia; hypertension also improved at 2 years, but not to statistical significance at 10 years. Pooled comparisons of comorbidity across different surgical procedure groups showed no significant difference between procedures.

Generalizability

Data included in the referenced review was strongest for women, whites, patients with diabetes, and those meeting current surgical criteria. This is probably because these groups were the most likely to have been recommended for surgery, and thus the most studied. The positive effects of surgery on health over time were significant for these populations. Unfortunately, there is a paucity of data related to race and ethnicity, as the vast majority of patients studied thus far have been of European origin/ethnicity. More studies targeting specific populations are needed, especially because many nonwhite populations have higher rates of diabetes and other obesity-related diseases.[298] We cannot generalize the current recommendations for surgery without specific data. For example, morbidity and mortality do not follow the same BMI data curves in some groups—most notably blacks. More information is also needed on whether other methods of classification of obesity should be used, such as waist-to-hip ratio or waist circumference instead of (or in addition to) BMI, and/or different cutoff values.[86,98,99,299]

There are likely other factors that may influence obesity's complex relationship with health outcomes that differ based on genetic susceptibility and other societal and cultural factors that have not yet been identified. For example, one of the few studies that examined differences in obesity and surgical weight loss between black and white females found that the former had greater adiposity and lost significantly less body fat after surgery.[300] The clinical significance of

this is not clear, but is suggestive of the need for more and larger studies to examine these questions.

The complexity of evaluating bariatric surgery, with multiple surgeons and surgical techniques, staffing-related factors, and range of outcomes, makes it very difficult to eliminate bias and standardize results. Improved study techniques are needed for more accurate conclusions based on effects of surgical interventions.[301] This is particularly true for the evolution of management and study of surgical weight loss, where techniques and effects are still being studied and additional innovations tried, at the same time as recommendations and payer coverage are changing.