

Evidence-based Practice Center Systematic Review Protocol

Project Title: Comparative Effectiveness of Approaches to Weight Maintenance in Adults

Amendment Date(s) if applicable:

30 November 2011

13 March 2012

(Amendments Details—see Section VII)

Background and Objectives for the Systematic Review

Background

Obesity Is a Major Public Health Concern

One of the Healthy People 2020 national objectives is to reduce the prevalence of obesity among adults to less than 30 percent and increase the prevalence of a healthy weight to 34 percent.¹ During 2005–2008, only 31 percent of adults were a healthy weight.² Body mass index (BMI), expressed as weight in kilograms divided by height in meters squared (kg/m^2), is commonly used to classify underweight (BMI $<18.5 \text{ kg}/\text{m}^2$), healthy or normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2), obesity (BMI $\geq 30.0 \text{ kg}/\text{m}^2$), and extreme obesity (BMI $\geq 40.0 \text{ kg}/\text{m}^2$). The estimated age-adjusted prevalence of overweight and obesity (BMI $\geq 25.0 \text{ kg}/\text{m}^2$) was 68 percent in the United States during 2007–2008. Despite the doubling in the prevalence of obesity between 1976–1980 and 2007–2008 (13 to 34 percent), the prevalence of overweight has remained stable between the same time periods (32 to 34 percent). The largest increase in obesity during these decades was among Americans who live 200 percent or more below the poverty line.³ Those persons living below the poverty line are more likely to live in areas without grocery stores and have fewer places to exercise than individuals who live in more affluent neighborhoods.⁴

Progression to obesity from normal weight can occur gradually over time

Adults tend to progressively gain weight through middle age.⁵ Although the average weight gained per year is 1-2 pounds, the modest accumulation of weight over time can lead to obesity. Twenty-five percent of men and 31 percent of women aged 20–34 years were obese when compared to 40 percent of men and 42 percent of women among adults aged 55–64 years. The prevalence of obesity declines to 26 percent of both men and women aged 75 years and older.

Obesity Differs by Sex and Ethnicity

The sex-specific prevalence of obesity was 32 percent of men and 36 percent of women during 2007–2008. The prevalence of obesity is greater among non-Hispanic blacks and Mexican Americans than non-Hispanic whites.⁶ Access to healthy food and places to exercise, as well as cultural differences, may contribute to the differences in obesity prevalence.^{4 7}

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Obesity Substantially Increases Morbidity and Mortality

Obesity is a risk factor for chronic conditions including cardiovascular disease, type 2 diabetes, arthritis, certain types of cancer and cancer recurrence.⁸⁻¹⁵ Obesity can also be caused by medications to treat chronic disease as is the case for many patients with mental illness.¹⁶ Higher grades of obesity are associated with excess mortality, primarily from cardiovascular disease, type 2 diabetes, and certain types of cancer.¹⁷

Obesity Economically Impacts the United States Health Care System

Obesity was estimated to cost \$79 billion dollars during 1995 in the United States. By 2008, the cost was estimated to have risen to \$147 billion dollars. The United States government is estimated to pay about one-half of the cost of obesity care through Medicaid and Medicare spending.¹⁸

Strategies To Prevent the Progression to Obesity Among Adults Are Needed

Several studies have shown that overweight individuals (BMI 25.0–29.9 kg/m²) may have morbidity and mortality outcomes equal to or sometimes better than normal weight individuals (BMI 18.5–24.9 kg/m²).^{17 19 20} Because the health outcomes for overweight individuals may be more like those of normal weight individuals than those with obesity, factors associated with the maintenance of overweight are also of interest to serve as intervention points to prevent obesity. Maintenance of non-obese weight is considered to be an adult weight between a BMI of 18.5 and 29.9 kg/m² with long-term stability within this range.

Strategies To Prevent the Progression of Further Obesity Among Adults Are Needed.

Adults who have the greatest degree of obesity have worse morbidity and mortality than those whose weight is closer to overweight.¹⁷ For example, adults with a BMI ≥ 40 kg/m² have more comorbidities than those with a BMI of 30–39 kg/m²,¹ and adults with a BMI > 35 kg/m² have more mortality than those with a BMI of 30–34 kg/m².² Maintenance of an obese weight closer to overweight may be advisable compared to progression to more extreme obesity.

Approaches To Maintain Weight

Multiple approaches have been investigated to identify strategies to effectively maintain weight in adults. These approaches include self-management techniques, diet, physical activity, medications, or combinations of these approaches at the individual or community level. These approaches have been implemented in multiple settings, including clinical care settings, community settings, higher education settings, and workplaces. Some approaches have targeted individuals at high risk of gaining weight because of a family history of obesity or diabetes mellitus or use of medication that contributes to weight gain,²¹ while others have more inclusive enrollment criteria or are directed at the entire population.^{22 23}

Self-management Approaches To Maintain Weight

Participants recruited to weight maintenance studies may have less motivation to change their behavior than those recruited to weight loss studies because of the absence of obesity and/or obesity-related disease.²⁴ Thus, the robust literature on self-management strategies to lose

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weight cannot be applied directly to weight maintenance.²⁴ Components of self-management approaches include goal-setting, self-monitoring, problem-solving, relapse prevention, and stimulus control.²⁵ Other approaches may include regulating time watching television or sleeping, self-care approaches or social support. Studies suggest that frequent contact with interventionists and self-monitoring of weight may be particularly valuable.²⁴ However, to date, the most effective elements of behavioral approaches for weight maintenance are not known. From a public health perspective, less intensive interventions²⁴ and those targeting patients at high risk of complications from weight gain (e.g., those with prediabetes) are of great interest.

Dietary and Physical Activity Approaches To Maintain Weight

Individuals who are maintaining their weight are successfully balancing energy (kilocalories) intake and energy expenditure. There are several approaches that these individuals might be using to remain in energy balance, including consistent intake of adequate (vs. excess) kilocalories²⁶ or use of specific dietary patterns (e.g., low fat or low carbohydrate).²⁷ The approaches that individuals use to obtain adequate physical activity are numerous (e.g., consolidation of exercise and everyday activities or making time for exercise in the daily routine).²⁷ To date, the types of diet and physical activity approaches used for weight maintenance have not been systematically evaluated. Specific dietary approaches of interest include eating patterns, macronutrients (such as fiber) in supplement form and from food sources, micronutrients from food sources, and any physical activity intervention such as walking, biking, or a training program.

Medications To Maintain Weight

In the United States, there are several medications approved for weight control in individuals with a BMI ≥ 27 kg/m². The dietary fat absorption inhibitor, orlistat, has been shown to help maintain weight loss and improve cardiovascular risk factors with continued, long-term use.²⁸ Because the sympathomimetic amines (i.e., phentermine or diethylpropion) are only approved by the U.S. Food and Drug Administration for short-term use under the indication of weight loss, they are not appropriate for this review.²⁹ Because orlistat may be used for weight maintenance independent of weight loss in overweight and obese populations and because orlistat is approved for long-term use, the only medication of interest is orlistat.

Environment-level Approaches To Promote Maintenance of Weight

The built environment encompasses all of the buildings, spaces, and products created or modified by people.³⁰ Built environment approaches are applied at the community level and affect the environment that a community interacts within. A limited number of environment-level approaches have been evaluated to address energy imbalance at the community-level (including both obese and non-obese individuals). These interventions have been implemented in multiple settings such as fast-food outlets and corner food stores. Many approaches have been directed toward individuals at high obesity risk such as low-income minority populations. A previous systematic review that aimed to identify policy studies about weight maintenance, including environment-level approaches, did not report identifying any such studies.³¹ However, the review did not include serial cross-sectional or time-series studies. A national policy research group, PolicyLink, recently published a report on the impact of access to grocery stores on health-related outcomes.³² The authors identified several peer-reviewed reports that

reported weight as a health-related outcome of interest, although it is unclear if weight change was reported.

Current Controversies in the Maintenance of Weight

Previous systematic reviews have concentrated on weight loss or maintenance of weight after weight loss.³³⁻³⁴ Systematic reviews on prevention of weight gain or weight maintenance are lacking. Methods to maintain weight may be different than interventions for weight loss or maintenance after weight loss.

Treatment Guidelines and Meta-analyses on Maintenance of Weight

No treatment guidelines for maintenance of weight were identified, although several guidelines and systematic reviews exist for weight loss or maintenance of weight after weight loss.³³⁻³⁸ Only one previous review with a meta-analysis aimed to study obesity prevention as an outcome. The review was conducted as background for a study on the impact of cancer prevention interventions on obesity prevention.³¹ The primary outcome of interest for the meta-analysis was the difference in change in BMI or body weight between the intervention and control groups among studies published in 1998–2008.

A recent Cochrane review examined workplace-based diet and physical activity interventions and change in BMI from baseline among nonobese and obese employees. The investigators found that the interventions decreased weight by 2.8 pounds, on average, at 6–12 months of follow-up and that BMI decreased by 0.5 kg/m². The findings are reported as recommendations to implement workplace interventions for controlling overweight and obesity in the Task Force on Community Preventive Services.³⁸

Expected Use of the Comparative Effectiveness Review

The results of the proposed report will be of use to individuals aiming to maintain their weight, those involved in clinical care, and policymakers. The results will help provide an evidence base for future practice guidelines to influence individual decision making, patient management, and policy decisions. The safety issues to be addressed will also help individuals and clinicians to take into consideration the implications of weight maintenance strategies and their impacts on daily life.

Objectives

We aim to compare the effectiveness, safety and impact on quality of life of individual and combined approaches to prevent weight gain in adults.

II. The Key Questions

Summary of Revisions to Key Questions

There were no changes to the Key Questions as a result of TEP input.

Based on TEP input, the EPC is adding more information to the protocol on definitions of self-management, clarification of types of dietary management approaches that will be evaluated, clarification of the definition of physical activity and exercise, examples of built-environment level interventions.

KQ 1:	What is the comparative effectiveness of self-management approaches for the prevention of weight gain in adults?
KQ 2:	What is the comparative effectiveness of dietary approaches for the prevention of weight gain in adults?
KQ 3:	What is the comparative effectiveness of physical activity approaches for the prevention of weight gain in adults?
KQ 4:	What is the comparative effectiveness of medications for the prevention of weight gain in adults?
KQ 5:	What is the comparative effectiveness of a combination of self-management, dietary, physical activity and medication approaches for the prevention of weight gain in adults?
KQ 6:	What is the comparative effectiveness of environment-level approaches for the prevention of weight gain in adults?

Population:	<ul style="list-style-type: none"> Adults (18 years and older) We will perform additional sub-group analyses on populations at greatest risk for weight gain including by baseline weight (normal/overweight); age groups; life events (college, menopause, retirement); race, ethnicity or cultural group; gender; income, socioeconomic status or educational attainment; family history of obesity; persons with mental illness; cancer survivors not at risk of weight loss; and persons with diabetes or cardiovascular disease or those at high-risk of these conditions.
Interventions:	<ul style="list-style-type: none"> For KQ1-6: Self-management, dietary, physical activity, medication or a combination of these approaches. Approaches that <i>educate</i> the participants about an intervention will be reported in the section about that intervention. Behavior change about an intervention will be reported with the intervention and not with the self-management interventions.
Comparisons:	<ul style="list-style-type: none"> For KQ1-6: No approach, usual care, or comparison to other self-management, dietary, physical activity, medication or combination of approaches.

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Outcomes:

- The potential comparisons of interest are outlined in the intervention matrix for single approaches (Table N1) and combinations of approaches (Table N2).

- Intermediate outcomes of interest include adherence to the approach; knowledge, attitudes or behaviors relating to the approaches for KQ1-6 and use of environmental modifications for KQ6.
- Prevention of obesity-related clinical outcomes including sleep apnea, degenerative joint disease, diabetes, cardiovascular disease, cancer, liver disease, or death.
- Health-related quality of life as measured by absenteeism, presenteeism, the SF-36 or other scales.
- Adverse effects of approaches including burden of approach, nutritional deficiencies or eating disorders, activity related injuries including fracture, and adverse events of medications (e.g., diarrhea or leakage).
- Percent or mean change from baseline weight.
- Maintenance of weight within same BMI category as the baseline measure. The CDC recommended categories of BMI by race/ethnicity will be used. If change in weight by BMI categories is not reported, we will report the percent or mean change from baseline BMI. Clinically meaningful weight maintenance as measured by BMI will be defined as within $\pm 3\%$ of the baseline measure.³⁹
- Among those with $18.5 \leq \text{BMI} < 30.0$ at the first measure, maintenance of weight as non-obese.
- Alternative measures of weight other than weight in pounds or kilograms or BMI (e.g., waist-to-hip circumference, percent body fat).
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Timing:

- The approach of interest must occur after age 18.
- The study must report the change in weight over at least 1 year during adulthood.
- Follow-up duration will be considered in the analysis. In addition to 1 year, specific timepoints of interest include 2, 5 and 10 years of follow-up when available.
- For intermediate outcomes, adverse effects and quality of life, additional time points of interest include 3 and 6 months after the commencement of the intervention.

Setting:

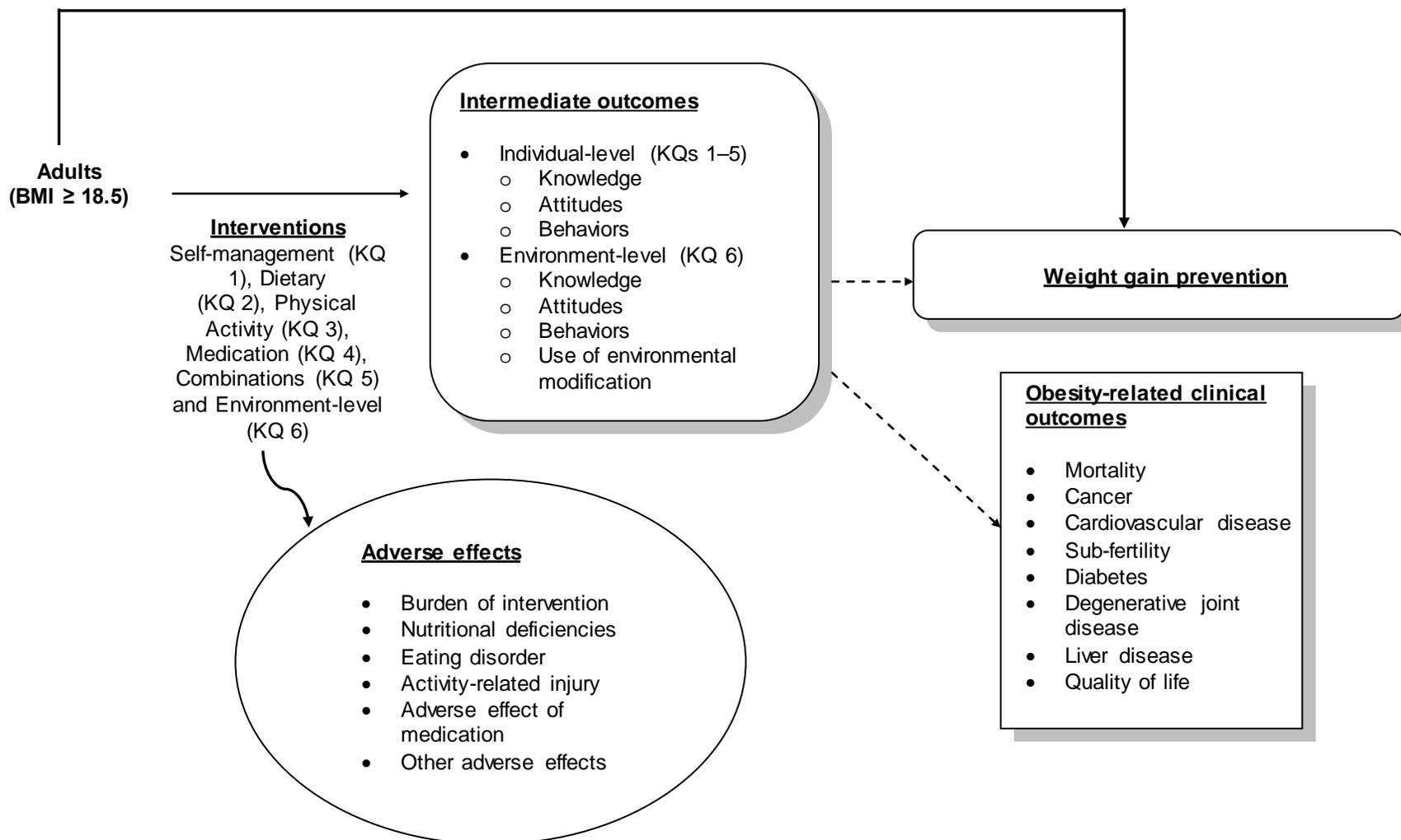
- Any setting
- Studies conducted in educational settings or workplaces will be reported with other studies conducted in the same setting regardless



of the approach.

III. Analytic Framework (see alternative text in separate document)

Figure 1. Analytic framework for Comparative Effectiveness of Approaches to Weight Maintenance in Adults.



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IV. Methods

We will conduct a systematic review of the comparative effectiveness and safety of individual and combined approaches to prevent weight gain in adults.

A. Criteria for Inclusion/Exclusion of Studies in the Review.

Inclusion and exclusion criteria are provided in Table 1. All studies of weight gain prevention in adults that measure weight change over at least one year comparing an approach of interest are eligible.

Table 1. Inclusion and exclusion criteria

<p>Population and condition of interest</p>	<ul style="list-style-type: none"> <input type="checkbox"/> All studies will include human subjects exclusively. <input type="checkbox"/> We will include studies of adults for KQ1-5. If a study includes a portion of participants under age 18 and results are not reported separately for adults, the study will be included as long as 90% of the total population is 18 years and older. <input type="checkbox"/> All ages are included for KQ6; approaches are implemented at the community-level. <input type="checkbox"/> We will <i>exclude</i> studies if they included only pregnant women. <input type="checkbox"/> Studies that include only patients at risk of weight loss (e.g., wasting disease, eating disorders) will be <i>excluded</i>.
<p>Interventions and approaches</p>	<ul style="list-style-type: none"> <input type="checkbox"/> All studies must have evaluated an approach of interest as defined by KQ1-5 to be included. <input type="checkbox"/> Orlistat, the Food and Drug Administration (FDA)-approved medication for long-term (>1 year) weight control, is described in Table 2. Orlistat is the only medication that will be included. Lifestyle interventions will be included under KQ5. <input type="checkbox"/> KQ6 will evaluate approaches on the community, instead of the individual level to be included. <input type="checkbox"/> If a goal of a study is weight loss, a combination of weight loss and weight gain prevention (without a separate reporting of results), or weight maintenance after weight loss, the study will be <i>excluded</i>. <input type="checkbox"/> Studies of biological determinants (such as genes) will be <i>excluded</i>. In the event a study examines an approach of interest, and a biological determinant, we will only abstract information about the approach of interest. <input type="checkbox"/> We will include studies of caloric substitutes, such as olestra or artificial sweeteners. <input type="checkbox"/> We will exclude studies of herbal supplements, vitamins, and minerals. <input type="checkbox"/> We will exclude studies that included a smoking cessation intervention or approach.
<p>Comparisons of interest</p>	<ul style="list-style-type: none"> <input type="checkbox"/> No approach, usual care, or comparison to other self-management, dietary, physical activity, device, pharmaceutical or combination of approaches will be included. <input type="checkbox"/> If a study compares different intensities of the same approach (e.g.,

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	<p>low fat versus high fat diet), the study will be included.</p> <ul style="list-style-type: none"> <input type="checkbox"/> If a study compares an approach of interest to an approach not of interest, the study will be <i>excluded</i>. <input type="checkbox"/> If a study compares an approach of interest to another approach of interest and an approach not of interest, only information on the approaches of interest will be included. <input type="checkbox"/> If there is no comparison, the study will be <i>excluded</i>. <ul style="list-style-type: none"> <input type="checkbox"/> We will <i>exclude</i> studies that do not apply to the key questions.
Outcomes and Timing	<ul style="list-style-type: none"> <input type="checkbox"/> All studies must measure and report weight change over at least 1 year during adulthood to be included. Weight change must be reported in relation to an approach of interest to be included. <ul style="list-style-type: none"> • Obesity-related clinical outcomes, intermediate outcomes, adverse effects and quality of life will be considered only if the study also reports a qualifying measure of weight.
Type of study	<ul style="list-style-type: none"> <input type="checkbox"/> We will <i>exclude</i> studies with no original data (reviews, editorials, comments, letters, modeling only studies). <input type="checkbox"/> We will <i>exclude</i> studies published only as abstracts. <input type="checkbox"/> We will <i>exclude</i> qualitative studies that do not provide quantitative information on an approach of interest and weight or adiposity, such as focus groups or directed interviews. <input type="checkbox"/> We will include studies with any sample size from any year that meet all other criteria. <input type="checkbox"/> We will only include studies with a comparison group or that reports multiple levels of the same approach (e.g., low fat versus high fat diet). These study designs include prospective (randomized and non-randomized), retrospective, crossover, and case-control studies. Serial cross-sectional studies of the same population are also eligible for KQ6. <input type="checkbox"/> Crossover studies must report at least 1 year of weight change in each phase of the crossover to be included. <input type="checkbox"/> For KQ1-5 inclusion, the participants measured at the first timepoint must be the same participants measure at least 1 year later. <input type="checkbox"/> For KQ6 inclusion, the participants measured at the first timepoint are not required to be the same participants as those measured at least 1 year later.

RCT = randomized controlled trial



Table 2. List of FDA-approved weight management devices or pharmaceutical agents approved for long-term use

Generic name	US Trade Name	Route	Half-Life	Mechanism of Action	FDA approved for Weight Maintenance	Recommended duration of use
Orlistat	Alli, Xenical	Oral	1-2 hours	Lipase inhibitor	BMI \geq 27	Safety and effectiveness beyond 4 years have not been determined (FDA label 12/17/2010)

B. Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies to Answer the Key Questions

We will search the following databases for primary studies: MEDLINE[®], EMBASE[®], PsychInfo, CINAHL, and the Cochrane Library. We will develop a search strategy for MEDLINE, accessed via PubMed, based on an analysis of the medical subject headings (MeSH) terms and text words of key articles identified a priori. The search strategy for MEDLINE can be found in Appendix A. We will also review the reference lists of each included article, relevant review articles and related systematic reviews to identify articles that may have been missed by the database searches.

To identify gray literature, we will search the World Health Organization International Trials Registry (<http://apps.who.int/trialsearch/>); Scopus (<http://www.scopus.com/home.url>); PsycEXTRA and will use the information provided in the Scientific Information Package (SIP) provided by the Scientific Resource Center on the one drug included in this study.

C. Data Abstraction and Data Management

The EPC will use DistillerSR (Evidence Partners, 2010), to manage the screening and review process. DistillerSR is a web-based database management program that manages all levels of the review process. All applicable citations identified by the search strategies are uploaded to the system and reviewed in the following manner:

- i. Title screening: Each title will be screened by 2 independent reviewers for potential relevance to this project. This level of screening is liberal requiring only one reviewer indicating that a title is potentially relevant for the title to progress to the next stage of review. In order for a title to be eliminated at this level, both reviewers must indicate that it is not relevant to this project. Liberal review is used at this level to capture any title that



might apply to the key questions. Reasons for exclusion will include: studies that did not include humans, studies clearly listed as a review or editorial not related to weight, and weight loss only studies.

- ii. Abstract screening: Each abstract will be reviewed by 2 independent reviewers. Both reviewers must agree on whether or not an abstract is applicable to any of the key questions. If there is disagreement between the 2 reviewers they are asked to review their answers and come to an agreement. Conflicts that cannot be resolved by the two original reviewers are resolved by a third-party. Reasons for exclusion at the abstract level will include: no original data, followup clearly stated as less than 1 year, study of children only, goal of study was clearly stated as weight loss or weight maintenance after weight loss, study did not report weight or adiposity or weight-related outcomes in the abstract, the study population was at risk for malnourishment or underweight (e.g., dialysis patients; anorexia), no intervention or approach of interest was studied, no comparison group included (*i.e.*, all patients received intervention or a case series of obese patients), no human data reported, abstract only (no full publication available), or a qualitative study (focus group, directed interviews). Studies that did not address a key question or interest and did not fit into the previous list can be excluded if the reviewer writes in why the study did not apply to the key question. Relevant reviews, including systematic reviews and meta-analyses, will be tagged for a references list search.
- iii. Full-text article screening: The review protocol for this level is the same as for the abstract inclusion/exclusion level. Conflicts at this level are resolved by a third-party senior reviewer. Reasons for exclusion will be the same as those for the abstract review with the addition of: study did not report weight change over 1 year and study did not report weight gain by an approach of interest.
- iv. Data abstraction: Eligible articles will be sent to data abstraction with a focus on items related to the population, approaches and interventions, comparisons, outcomes, timing and setting to answer the key questions. Each article will be serially abstracted first by a junior reviewer then by a senior reviewer. Articles referring to the same study will be abstracted on a single review form if reporting the same data or on separate forms if necessary with clear information that the results should be interpreted as from the same study. Data abstraction will be randomly quality checked by a third-party senior reviewer (investigator) to ensure that data is being abstracted accurately and thoroughly.

D. Assessment of Methodological Quality of Individual Studies



Article quality will be assessed using the Downs and Black methodologic quality assessment checklist.⁴⁰ This checklist was developed to assess the quality of reporting, internal validity and external validity for individual RCTs and observational studies. We will add a question on funding source (industry, government, foundational, other, not reported). For both the RCTs and the non-randomized studies, the overall study quality will be assessed as:

- **Good** (low risk of bias). These studies had the least bias, and the results were considered valid. These studies adhered to the commonly held concepts of high quality, including the following: a clear description of the population, setting, approaches, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytic methods and reporting; no reporting errors; a low dropout rate; and clear reporting of dropouts.
- **Fair**. These studies were susceptible to some bias, but not enough to invalidate the results. They did not meet all the criteria required for a rating of good quality because they had some deficiencies, but no flaw was likely to cause major bias. The study may have been missing information, making it difficult to assess limitations and potential problems.
- **Poor** (high risk of bias). These studies had significant flaws that might have invalidated the results. They had serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

E. Data Synthesis

For each Key Question, we will create a set of detailed evidence tables containing all information abstracted from eligible studies. We will conduct meta-analyses when there is sufficient data (at least 3 studies of the same design) and studies are sufficiently homogenous with respect to the population characteristics, intervention, comparison, outcome, and timing. The timepoints of interest for weight maintenance are: 1 year, 2 years, 5 years and later than 5 years if available in multiple studies. For the intermediate outcomes, safety and quality of life outcomes the timepoints of interest are: 3 months, 6 months, 1 year, 3 years, 5 years and later than 5 years if available.

- For studies amenable to pooling with meta-analyses, we will calculate pooled mean differences, risk differences or relative risks using a DerSimonian and Laird random effects model. Clinically meaningful weight maintenance as measured by BMI will be defined as within $\pm 3\%$ of the baseline measure.³⁹ We will identify statistical heterogeneity between the trials in all the meta-analyses using: (1) a chi-squared test with a significance level of alpha less than or equal to 0.10, and (2) an I-squared statistic with a value greater than 50% indicating substantial heterogeneity. We will not report the pooled result if substantial heterogeneity is found. We will conduct sensitivity analyses by omitting one study



at a time to assess the influence of any single study on the pooled estimate. For all meta-analyses, we will conduct formal tests for publication bias using Begg's and Eggers tests including evaluation of the asymmetry of funnel plots for each comparison of interest. All meta-analyses will be conducted using STATA (Intercooled, version 11, StataCorp, College Station, TX).

When we are unable to pool studies, we will calculate and display the individual mean differences, risk differences or relative risks with 95% confidence intervals (CI) for the individual studies. For infrequent adverse effects, we will calculate the Peto odds ratios when the combined number of events in each arm is greater than 5.

We will report on subgroups of interest including baseline weight (normal/overweight); age groups; life events (college, menopause, retirement); race, ethnicity or cultural group; gender; income, socioeconomic status or educational attainment; family history of obesity; persons with mental illness; cancer survivors not at risk of weight loss; and persons with diabetes or cardiovascular disease or those at high-risk of these conditions.

F. Grading the Evidence for Each Key Question

At the completion of our review, we will grade the quantity, quality and consistency of the best available evidence addressing Key Questions 1 – 6 by adapting an evidence grading scheme recommended by the Guide for Conducting Comparative Effectiveness Reviews.⁴¹ We will apply evidence grades to the bodies of evidence about each approach comparison for each outcome. We will assess the strength of the study designs according to those which best control confounding, selection and information bias. We will assess the quality and consistency of the best available evidence, including assessment of limitations to individual study quality (using individual quality scores), consistency, directness, precision, and the magnitude of the effect.

We will classify evidence pertaining to Key Questions 1 – 6 into four basic categories: (1) “high” grade (indicating high confidence that the evidence reflects the true effect and further research is very unlikely to change our confidence in the estimate of the effect); (2) “moderate” grade (indicating moderate confidence that the evidence reflects the true effect and further research may change our confidence in the estimate of the effect and may change the estimate); (3) “low” grade (indicating low confidence that the evidence reflects the true effect and further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate); and (4) “insufficient” grade (evidence is unavailable). The grade of evidence for each key question will be based on consensus.

G. Assessing Applicability – Throughout the report, we will discuss the applicability of studies in terms of the degree to which the study population, interventions, outcomes, and settings are relevant to individuals at risk of weight gain and features that may affect the effectiveness of the intervention.

V. References

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VI. Definition of Terms

Not applicable.

VII. Summary of Protocol Amendments

In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

Date	Section	Change From	Proposed change to*	Rationale
30-Nov-11	PICOTS (outcomes)	Alternative measures of weight other than weight in pounds or kilograms or BMI (e.g., waist-to-hip circumference, percent body fat).	Remove this section	The main outcome measure will be Percent or mean change from baseline weight, percent or mean change in BMI, or percent or mean change in waist circumference. The additional alternative measures of weight have variable reporting consistency, and not including this outcome does not exclude additional studies.
30-Nov-11	PICOTS (outcomes)	Percent or mean change from baseline weight.	Revise this section to make it clear that the following measures are the primary measures of interest: "Percent or mean change from baseline weight, percent or mean change in BMI, or percent or mean change in waist circumference"	We wish to be more explicit about the main outcome measures of interest of this report.
30-Nov-11	PICOTS (outcomes)	Intermediate outcomes of interest include adherence to the approach; knowledge, attitudes or behaviors relating to the approaches for KQ1-6 and use of environmental modifications for KQ6.	Intermediate outcomes of interest include adherence to the approach/intervention and KQ1-6 and use of environmental modifications for KQ6.	We are abstracting intermediate outcomes from studies that are reporting the clinical outcomes. Adherence to the intervention is the intermediate outcome of most interest. Adherence to the intervention can help explain heterogeneity of intervention effects.

Date	Section	Change From	Proposed change to*	Rationale
13-Mar-12	Criteria for inclusion/exclusion of studies in the review. Table 1: "Type of Study"	We will only include studies with a comparison group or that reports multiple levels of the same approach (e.g., low fat versus high fat diet). These study designs include prospective (randomized and non-randomized), retrospective, crossover, and case-control studies. Serial cross-sectional studies of the same population are also eligible for KQ6.	ADD: Observational studies must be of at least moderate quality according to the risk of bias criteria established by Downs and Black with particular attention to confounding and loss to followup. Observational studies will be assessed as moderate quality if they adequately adjust for the following confounders in their analysis: age, sex, race or SES, diet (for physical activity studies), physical activity (for energy intake studies). Observational studies must account for losses to follow-up in the analysis or state that the loss to followup was less than 20%. If the study meets both of these criteria and most or all of the other Downs and Black internal validity criteria are met, the study will be considered moderate quality (the highest quality possible for non-randomized studies).	The added value of including observational studies with a high risk of bias is minimal. Therefore, we will only include observational studies that have a moderate or low risk of bias.

VIII. Review of Key Questions

For all EPC reviews, key questions were reviewed and refined as needed by the EPC with input from Key Informants and the Technical Expert Panel (TEP) to assure that the questions are specific and explicit about what information is being reviewed. In addition, the key questions were posted for public comment and finalized by the EPC after review of the comments.

IX. Key Informants

Key Informants are the end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the Key Questions for research that will inform healthcare decisions. The EPC solicits input from Key Informants when developing questions for systematic review or when identifying high priority research gaps and needed new research. Key Informants are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism

Key Informants must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts

Technical Experts comprise a multi-disciplinary group of clinical, content, and methodologic experts who provide input in defining populations, approaches, comparisons, or outcomes as well as identifying particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicted opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore study questions, design and/or methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor contribute to the writing of the report and have not reviewed the report, except as given the opportunity to do so through the public review mechanism

Technical Experts must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodologic expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments are documented and will, for CERs and Technical briefs, be published three months after the publication of the Evidence report.

Potential Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.