Prevention of Overweight/Obesity in Adult Populations: A Systematic Review with Meta-analyses

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Abstract

Background: This report will be used by the Canadian Task Force on Preventive Health Care (CTFPHC) to provide guidelines on the prevention of weight gain in normal weight adults. The last CTFPHC guideline on the prevention of obesity was conducted in 2006 and published in 2007, while obesity screening was last examined in 1994.

Purpose: To synthesize evidence on behavioural interventions for preventing weight gain in normal weight adults.

Data Sources: We searched EMBASE, Medline, Cochrane Central Register of Controlled Trials, and PsychINFO from January 1980 to June 27, 2013. We checked reference lists of included studies and relevant systematic reviews, conducted a grey literature search and considered studies with mixed weight populations from the United States Preventive Services Task Force 2011 review on screening for and management of adult overweight/obesity. We also searched for evidence to answer the contextual questions.

Study Selection: The titles and abstracts of papers considered for the key question and sub-questions were reviewed in duplicate; any article marked for inclusion by either team member went on to full text rating. Full text inclusion was done independently by two people with consensus required for inclusion or exclusion. For intervention benefits we included randomized controlled trials of behavioural interventions for normal weight or mixed weight adults that reported data for at least one weight outcome of interest at a minimum 12 months post baseline assessment. All studies reporting adverse effects of interventions were included, regardless of design, timeframe or outcomes.

Data Abstraction: Review team members extracted data about the population, study design, intervention, analysis and results for outcomes of interest. One team member completed full abstraction, followed by a second team member who verified all extracted data and ratings. We assessed study quality using Cochrane's Risk of Bias tool and the GRADE framework. For the contextual questions, inclusion screening and abstraction were done by one person.

Results: A total of 26 studies were included in this systematic review. Using the GRADE system the bodies of evidence used to answer the key question and sub-questions were mostly rated as low or very low quality. Downgrading occurred primarily as a result of study limitations increasing the risk of bias and indirectness due to inclusion of mixed weight samples, and sometimes due to concerns regarding imprecision or reporting bias.

Pooled effect estimates for all weight loss outcomes showed the programs were successful not only in stabilizing weight but also in producing weight loss by the end of the interventions. Intervention participants had significantly greater weight loss [MD (95% CI) -0.73 kg (-0.93, -0.54); I^2=49%], significantly greater reduction in BMI [MD (95% CI) -0.24 kg/m^2 (-0.34, -0.15); I^2=64%], significantly greater waist circumference reduction [MD (95% CI) -0.95 cm (-1.27, -0.63); I^2=74%] and significantly more reduction of total body fat [MD (95% CI) -1.27% (-1.93, -0.61); I^2=80%], all compared to control participants at the post intervention assessment point. In many

studies, the control group also lost weight; indicating a readiness for weight loss strategies by agreeing to be part of a study. However, several studies found slight increases in weight measures for the intervention participants; in all but one of these studies the control group showed comparatively greater increases in these weight measures. Sensitivity analyses performed on studies providing weight in kg and BMI data found no significant differences between any sub-groups [i.e., type of intervention (diet, exercise, diet plus exercise, lifestyle); duration of intervention (≤12 months; >12 months), gender, baseline CVD risk status (high, low/unknown), baseline mean BMI (<25, ≥25), and study risk of bias rating (low, unclear, high)] that explained the variation across this evidence. Moderate to high statistical heterogeneity was evident in most sub-analyses.

Pooled effect estimates for some secondary health outcomes showed small but statistically significant benefits in favour of the interventions. At the post intervention point, compared to the control group, intervention participants had reduced their total cholesterol level by an additional 0.06 mmol/L (95% CI -0.11, -0.01; I^2=70%) and their LDL-C level by an additional 0.06 mmol/L (95% CI -0.09, -0.03; I^2=0%), and reduced their fasting glucose level by 0.04 mmol/L more (95% CI -0.08, -0.0016; I^2=67%). The effect sizes are not clinically meaningful. No statistically significant results were found for the effect of the interventions on systolic or diastolic blood pressure or on the likelihood of being diagnosed with type 2 diabetes.

Only one study of a nine month exercise intervention was available to address the key question about the long-term benefits of weight gain prevention programs. There was a statistically significant increase in weight in the intervention group as compared to the control group from the point of intervention completion to 15 months later [MD (95% CI) 0.20 kg (0.17, 0.23)]. For the same comparison and the same time period, there was no statistically significant difference in waist circumference, instead both groups increased on this measure by 1.4 cm. None of the benefits in terms of reduced total cholesterol, fasting glucose and systolic blood pressure levels that were observed in intervention participants at the end of the program were maintained over the next 15 months. The intervention group showed significantly greater increases in all three outcomes compared to the control group at the follow-up assessment point.

No harms of interest to this review were reported. Only six studies mentioned adverse effects, half of which reported no adverse events associated with participation, two showed no significant differences between exercisers and those in the control groups in terms of injuries, falls or serious adverse events, and only one study found significantly more falls and injuries were sustained by those taking part in the exercise program compared to control group participants.

Of the 26 included studies, five (19%) showed a significant effect across all reported weight outcomes of interest; these interventions were designated as efficacious. There were few common elements across these interventions. Four programs included an exercise component and offered individual sessions to some or all participants. Four targeted women only and in all five studies the baseline BMI was in the overweight range. Programs varied in terms of length and number of sessions as well as in setting and country.

Limitations: The findings of this review are based on indirect evidence; only one study included a normal weight sample; all others contained mixed weight groups. Most of the evidence was taken from studies that could not reliably be assessed for risk of bias. Potential reporting bias was also a frequent concern. Using GRADE, the evidence was assessed as low and sometimes very low quality which reduces confidence in the pooled estimates of effect. Results for secondary health outcomes should be interpreted with caution as our review might have missed trials that reported these outcomes but not our primary weight outcomes. Only one study met inclusion criteria to consider maintenance of weight gain prevention and improvements in health outcomes. We searched only for papers in English or French.

Conclusion: There is low quality evidence that behavioural interventions are associated with reductions in weight and improvements in other health outcomes in mixed weight adult populations, but it is uncertain whether the benefits are clinically meaningful and can be maintained over time. In the short term, strategies aimed at weight maintenance appear to have some benefit; if maintained, these could be clinically significant benefits.

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Table of Contents

List of Acronyms

ARR	Absolute Risk Reduction
BMI	Body Mass Index
CCHS	Canadian Community Health Survey
CHMS	Canadian Health Measures Survey
CI	Confidence Interval
cm	Centimeters
CQ	Contextual Question(s)
CTFPHC	Canadian Task Force on Preventive Health Care
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
EOSS	Edmonton Obesity Staging System
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HR	Hazard Ratio
IV	Inverse Variance
kg	Kilograms
KQ	Key Question(s)
LDL-C	Low-Density Lipoprotein Cholesterol
MD	Mean Difference
mg/dL	Milligrams per Decilitre
mmol/L	Millimoles per Litre
NNT	Number Needed to Treat
RCT	Randomized Controlled Trial
RR	Relative Risk / Risk Ratio
SBP	Systolic Blood Pressure
SD	Standard Deviation
SE	Standard Error
SES	Socioeconomic Status
SIGN	Scottish Intercollegiate Guidelines Network
SQ	Supplemental Questions
T2D	Type 2 Diabetes
UK	United Kingdom
US	United States
USPSTF	United States Preventive Services Task Force
WC	Waist Circumference
WHO	World Health Organization

Chapter 1: Introduction

Purpose and Background

This review will be used by the Canadian Task Force on Preventive Health Care (CTFPHC) to provide guidelines on the treatment of overweight and obesity in adults. The last CTFPHC guideline on the management and prevention of obesity was conducted in 2006 and published in 2007,[1] while obesity screening was last examined in 1994.[2] Since this time, other Canadian and international groups have provided guidance on obesity screening, management and prevention, including the Obesity Canada Clinical Guidelines Expert Panel (2006),[3] the Scottish Intercollegiate Guidelines Network (SIGN) (2010),[4] and the United States Preventive Services Task Force (USPSTF) (2011).[5] The lack of updated Canadian guidelines on this topic, the availability of new evidence and the growing burden of obesity were key reasons why this topic was chosen by the CTFPHC.

Definition

Obesity is characterized by an increase in total body fat and is defined by a body mass index (BMI, measured in kg/m^2) $\geq$30, based on the definition used by the World Health Organization (WHO) and adopted by the Canadian Guidelines for Body Weight Classification in Adults.[6] Canadian adults ($\geq$18 years) with BMIs of 25 to 29.9 are currently considered overweight and at risk of becoming obese, whereas those with BMIs of 18.5 to 24.9 are considered normal weight.[7] Studies used to develop the classification system were mainly based on Caucasians and more recently studies world-wide continue to explore the complex associations between body weight and total mortality, with increasing emphasis on determining key characteristics and metabolic profiles associated with excess total and cause-specific mortality.[8-11] More recent studies have also shown that physically fit obese individuals may not be at increased mortality risk, compared to their lower weight peers.[12] Other lines of work have explored the associations among the metabolically healthy versus unhealthy and mortality.[13,14] In the meantime, the current BMI classification system provides one useful indicator of body composition.

Prevalence and Burden of Obesity

Obesity has become a worldwide issue. According to the WHO report on the global epidemic, an estimated one billion adults are overweight and at least 300 million are clinically obese.[15] Obesity occurs across all ages and ethnic groups, and is associated with socioeconomic status (SES). According to a review by McLaren, the effect of SES differs by the Human Development Index; negative associations (i.e., lower SES associated with larger body size) for women in highly developed countries were most common with education and occupation, while positive associations for women in medium- and low-development countries were most common with income and material possessions.[16] For the first time in history, obesity is more prevalent world-wide than under-nutrition.[17]

In 1980, the prevalence of obesity in Canadian adults was approximately 8%. Since then, the number of obese adults in Canada has tripled.[18] According to results of the 2007-2009 Canadian Health Measures Survey (CHMS), based on measured height and weight the prevalence of obesity in adults was estimated at 24.1%.[19] From 1978/1979 to 2004, the proportion of adults falling into obese Class I (BMI 30 to 34.9 increased from 10.5 to 15.2%, the proportion in Class II (BMI 35.0 to 39.9) doubled from 2.3 to 5.1%, and the proportion in Class III (BMI ≥40) tripled from 0.9 to 2.7%.[16,20] Obesity is more prevalent among men than women; the average BMI was estimated at 27.5 (27 to 28.0) for men and 26.7 (26 to 27.4) for women,[21] however, females are more likely to fall into obese Class II and Class III than males.[21] In Canada, obesity does not appear to be associated with lower SES status, instead it is more prevalent in rural-dwelling adults and among people in Eastern and Northern Canada.[22] Based on the 2008/2009 Canadian Community Health Survey (CCHS) measured data, regional, provincial and territorial variation were observed; obesity varied across provinces and territories, from a low of 12.8% in British Columbia to a high of 25.4% in Labrador. The prevalence of obesity tends to be lower in urban regions and higher in rural areas; obesity ranged from 5.3% in urban/suburban Richmond British Columbia to a high of 35.9% in the Northern Region of Saskatchewan.[16,20] Consistent with these statistics, a recently available report citing data from the CCHS indicated the estimated prevalence of obesity in the Canadian adult population in 2011 was 25.3%.[23]

Etiology, Risk Factors and the Natural History of Obesity

The etiology of weight gain and obesity is multi-faceted, encompassing hereditary, environmental, metabolic, lifestyle, psychological and medical or drug-related conditions (see Table 1). The principal cause of obesity is an imbalance between calories consumed and calories expended; many factors can be responsible for this imbalance. The rapid rise in obesity prevalence since 1980 suggests metabolic, environmental and lifestyle factors are prominent, including an increased intake of energy-dense foods coupled with a decrease in physical activity due to increasing sedentary lifestyles.[21,24,24-27] Metabolic factors include a low baseline metabolic rate, increased carbohydrate oxidation, insulin resistance, and sympathetic activity. However, these factors are not easily measured and are less strongly linked to obesity than are lifestyle factors. Sedentary behaviours, such as prolonged screen time appears to contribute to weight gain.[28] Similarly, among many lifestyle behaviours that predispose people to obesity, sleep deprivation and smoking cessation have also been associated with weight gain.[29,30] Among dietary factors, certain patterns of eating increase the risk for weight gain; these include consuming energy-dense foods, social norms for mealtimes and portion size, fast-food consumption, and frequent snacking, especially during the evening hours.[31] In recent years there has been increasing interest in determining the role of genetic factors in the pathogenesis of obesity. In general, genetic factors are considered to have a role in determining inter-individual variability in body weight. However, in adults with more severe obesity, less than 5% will have recognized obesity-associated mutations such as those that cause leptin (a hormone that affects energy intake and expenditure) deficiency or leptin receptor dysfunction.[25] Obesity can develop at any age but

prevalence is highest in middle age and typically declines in the elderly, partly due to increased mortality and a multi-factorial age-related decline in BMI, with loss of both lean and fat mass.[32]

Health Consequences of Obesity

Some obese adults, especially those who are sedentary and with an adverse metabolic profile or other risk factors are at increased risk for developing major diseases that include type 2 diabetes, coronary artery disease, stroke, depression, and certain cancers (see Table 2)[33-35] and weight loss can reduce the severity or incidence of some conditions, especially diabetes.[36] Obesity can also exacerbate the severity of gastrointestinal, muscular and skeletal conditions or make medical management more difficult. Weight loss with exercise and pain management can improve mobility and functional ability in some cases, but evidence is still limited.[37] It is also estimated that one in 10 premature deaths in adults, aged 20 to 64 years, is directly attributable to overweight and obesity.[38,39] Declines in total mortality after lifestyle interventions for diabetes prevention have not yet been demonstrated.

Once excess weight has been added, it is very difficult for many people to lose body weight, recognizing that there is substantial interplay and variation in individuals' neurological, physiological and behavioural systems. Thus, weight loss as a therapy for increased health risk in the overweight and obese has been controversial. Modest weight loss and increased physical fitness both appear to have modest beneficial effects on health. Weight loss in the range of 5% has often been quoted as being clinically relevant and is a more easily measured clinical indicator than physical fitness in most primary care settings.[40]

Rationale for Screening for Overweight and Obesity

Screening directly for overweight and obesity may help guide clinical practice to improve patients' health.

Potential Benefits of Screening

Screening for overweight and obesity can improve patients' health in three ways:

- In adults found to be obese and who have obesity-related diseases, modest weight loss (5% to 10% of total body weight) has been shown to improve control of such diseases and related symptoms and can reduce drug therapy requirements.[3,41]
- In adults found to be obese but who do not have obesity-related diseases, lifestyle interventions such as starting a regular exercise program can reduce the risk of developing such diseases or can curtail their progression, (e.g., prevention of diabetes in adults with impaired glucose tolerance).[3,41]
- In adults found to be overweight but who are otherwise healthy, promoting healthy lifestyle practices may prevent the development of obesity.[3,41]

Screening to Guide Clinical Practice

In clinical practice, an intervention relating to obesity could have two main goals:[3]

- *Prevention of obesity*. Prevention can be considered in individual adults who are overweight and at risk for developing obesity, through interventions aimed at attaining a healthy weight or preventing weight gain.
- *Treatment of obesity*. Treatment interventions can be aimed to achieve weight loss in people who are already obese, thus reducing associated symptoms or burden of comorbidities. An example of this is a weight loss intervention for an obese adult with diabetes that aims to reduce hyperglycemia-related symptoms and reduce the need for glucose-lowering drugs.

Detection of Overweight and Obesity

There are several screening methods for assessing obesity and overweight. Methods include waist to hip and waist to height ratios; however the two main measures used in everyday practice are BMI and waist circumference (WC).

- BMI is strongly correlated with direct measures of body fat, such as magnetic resonance imaging, and is a reliable determinant of adiposity-related health risks in adult men and women.[42]
- WC measures abdominal (or central) body fat, which is strongly correlated with an increased risk for type 2 diabetes (T2D), hypertension, dyslipidemia, and the metabolic syndrome, the latter combining all three former conditions.[42]

Practical Considerations when Using BMI and WC in Clinical Practice

Combining BMI and WC to assess health risk. Although BMI and WC are correlated, WC provides an additional independent estimate of health risk beyond that provided by BMI.[43,44] Considering both BMI and WC may be especially useful in adults with normal BMI as this can identify adults with an abdominal fat distribution who are at increased health risk despite normal BMI.[42]

BMI and WC as part of an overall health risk assessment. The classification schemes for BMI and WC were originally derived based on health risk assessments from large, heterogeneous population studies. Consequently, the value of using BMI and WC only to assess health risk in individual adults is limited. BMI and WC are useful however, as part of an overall risk assessment:

- BMI and WC should be combined with other determinants of individual health risk, which include smoking, concomitant disease, diet, physical activity, and personal and family weight history. However, what may be under-appreciated is the importance of BMI and WC on health risk compared to other, more traditional, risk factors. For example, until recently obesity was considered to increase the risk of coronary artery disease through its association with hypertension, dyslipidemia, and diabetes. However, BMIs ≥30 appear to independently confer an increased risk for coronary artery disease which is comparable to the effect of hypertension.[35] A similar effect also occurs with WC, as adults with increased WC were more likely to develop hypertension, T2D, and dyslipidemia.
- The Edmonton Obesity Staging System (EOSS)[45] contributes to our ability to assess obesity-related comorbidity. Applied to those with a BMI ≥25, data from interview, exam or laboratory testing are used to assign a rating of 0 (no apparent comorbidity) to 4 (severe

obesity-related comorbidities or functional disability).[45] Using data from the National Health and Nutrition Examination Survey 1999-2004, the scale independently predicts increased mortality.[46]

- Because BMI and WC reflect an individual's risk at a single time point, longitudinal changes in BMI and WC may provide additional information on health risk. For example, an upward trend in BMI and WC in adults with impaired glucose tolerance places such individuals at increased risk for clinically overt T2D.[47] Conversely, a downward trend in BMI and WC with unintentional weight loss may indicate increased health risk due to the development of underlying disease.

Current Clinical Practice: Prevention and Treatment of Obesity

Prevention of Obesity

A variety of individually-focused preventive interventions exist, mostly focusing on healthy living guidelines (e.g., Canada's Food Guide and Physical Activities Guidelines) with recommendations to maintain a healthy weight. There is some information on the use of such interventions in primary care.[48] See recommendation according to 2006 Canadian clinical practice guideline below.[3]

Treatment of Obesity

Many therapeutic interventions aimed at weight loss to treat obesity and obesity-related complications exist and can be broadly categorized by main focus as: dietary, physical exercise, behaviour, psychological, pharmacologic therapy, and bariatric surgery. Non-pharmacologic, non-surgical approaches can result in modest three to five kilograms (kg) weight loss.[49] Such losses may have health benefits, but rarely achieve individuals' weight loss goals. The addition of pharmacologic agents adds modestly to such weight loss (e.g., a further reduction of approximately 2.8 to 4.5 kg).[50]

Bariatric surgery, typically with Roux-en-Y gastric bypass, can result in considerable weight loss of 50 to 70 kg but is reserved for adults with severe obesity (BMI >40) or those with less severe obesity (BMI >35) that is associated with significant obesity-related comorbidities.[51] Although bariatric surgery has been shown to be effective in severely obese patients, it is excluded from this review because the CTFPHC Working Group considered populations with extreme BMIs for whom surgery would be indicated to be out of scope; the same exclusion was applied in the 2011 USPSTF review.[5] Pharmacological and behavioural therapies, on the other hand, may be considered in primary care of overweight and obese patients (i.e., not limited to those who are very obese) and as such remain within our scope.

Previous Review and Recommendations

The 2006 CTFPHC guidelines for the management and prevention of obesity made the following recommendations:[1]

- There is insufficient evidence to recommend for or against community-wide cardiovascular disease preventive programs to prevent obesity (I recommendation).
- There is fair evidence to recommend intensive individual and small group counselling for a reduced calorie or low fat diet to prevent obesity (B recommendation).
- There is fair evidence to recommend an intensive individual or structured group program of endurance exercise to prevent obesity (B recommendation).
- There is insufficient evidence to recommend a program of strength training exercise to prevent obesity (I recommendation).
- There is fair evidence to recommend an intensive individual or small group program of a combined low fat/reduced calorie diet and endurance exercise intervention to prevent obesity (B recommendation).
- There is fair evidence to recommend against low intensity interventions employing telephone or mail support, or financial incentives to promote a low fat/reduced calorie diet and endurance exercise as a means to prevent obesity (D recommendation).

The 2011 the CTFPHC Adult Obesity Working Group reviewed other relevant guidelines. The Australian[52] and New Zealand[53] guidelines only considered evidence from treatment of overweight and obesity. Neither the Obesity Canada Clinical Guidelines Expert Panel[3] or the National Institute for Health and Care Excellence[54] considered mortality or morbidity outcomes of screening, but both made recommendations about treatment. The review for the SIGN[4] guidelines searched for studies on the effectiveness of screening but found none. The SIGN group also made recommendations for obesity management. The USPSTF conducted a review[5] and released guideline recommending that clinicians screen adults for obesity and offer or refer patients with a BMI $\geq$30 to intensive, multicomponent behavioural interventions (B recommendation).[55]

Chapter 2: Methods

Review Approach

At the outset of the review process the CTFPHC Working Group conceptualized an "ideal approach," considering the analytic framework and key questions for both screening and prevention of obesity in adults that they believed were most important for clinicians. An evidence based analysis on screening and prevention of obesity was planned to address key questions about the effectiveness of screening and preventive efforts for normal weight, overweight or obese adults in primary care on mortality, morbidity, various anthropometric measures of weight reduction or stabilization, costs, and harms. However, our preliminary search revealed recent reviews by the USPSTF[5] and SIGN[4] that asked similar questions and identified no evidence on screening. To avoid duplication of effort, we removed the key question related to screening and instead added a series of supplemental questions. These questions were examined through a condensed review process that searched for evidence on screening for obesity published since the 2011 USPSTF review. The USPSTF[5] also examined interventions for preventing obesity in overweight and obese populations.

Based on the acquired knowledge and newly available products, the CTFPHC Working Group adopted a pragmatic approach to select the review questions, focusing on areas which the scoping review indicated there would be sufficient evidence upon which to formulate recommendations. In addition, to avoid duplication of work already completed, the Working Group directed the McMaster Evidence Review and Synthesis Centre team to:

- update the search of the USPSTF review[5] to examine treatment interventions for those who are already overweight and obese, and,
- conduct a de novo review to address the effectiveness of weight gain prevention interventions for those who are currently of normal weight.

The protocol was registered with PROSPERO (#CRD42012002753).

Analytic Framework and Key Questions

The analytic framework, presented in Figure 1, includes both prevention and treatment of adult overweight/obesity. This review focuses only on the aspects related to prevention; a separate review was conducted to examine treatment (available on the CTFPHC website http://canadiantaskforce.ca/).

The key question (KQ) and sub-questions considered for this prevention focused review are:

KQ1. Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health outcomes or short-term or sustained weight gain prevention, with or without improved physiological measures?

   a. Are there differences in efficacy between patient subgroups [e.g., age 65 years or older, sex, baseline cardiovascular disease (CVD) risk status]?

b. What are the adverse effects of primary care relevant prevention interventions in normal weight adults (e.g., labelling; disordered eating; psychological distress such as anxiety, depression and stigma; nutritional deficits; cost burden)?
c. Are there differences in adverse effects between adult subgroups (e.g., age 65 years or older, sex, baseline CVD risk status)?
d. How well is weight gain prevented or health outcomes maintained after an intervention is completed?
e. What are common elements of efficacious weight gain prevention interventions?

The contextual questions (CQ) considered for both the prevention and the treatment reviews are:

CQ1. Is there evidence that the burden of disease, the risk/benefit ratio of prevention or treatment, the optimal prevention or treatment method/access, and implementation differ in any ethnic subgroups or by age, rural and remote populations, or lower SES populations?
CQ2. What are the resource implications and cost effectiveness of overweight and obesity prevention/treatment in Canada?
CQ3. What are patients' and practitioners' values and screening preferences regarding overweight and obesity prevention/treatment?
CQ4. What are the most effective (accurate and reliable) risk assessment tools identified in the literature to assess future health risk as a result of obesity?

The supplemental questions (SQ) on obesity screening considered for both the prevention and the treatment reviews are:

SQ1. Is there direct evidence that primary care screening programs for adult overweight or obesity improve health outcomes or result in short-term (12 month) or sustained (>12 month) weight loss or improved physiological measures?
a. How well is weight loss maintained after a screening intervention is completed?
b. What is the most effective method of screening for overweight and obesity in adults in primary care?
c. What is the optimal interval/frequency for screening for overweight and obesity in adults in primary care?
d. What is the most effective type of screening (opportunistic vs. organized/systematic) for overweight and obesity in adults in primary care?
e. What are the harms associated with screening for overweight and obesity in adults in primary care?

Search Strategy

For the key and supplemental questions we searched EMBASE, Medline, Cochrane Central Register of Controlled Trials, and PsychINFO from January 1980 to June 27, 2013 using terms such as *obesity prevention*, *health promotion, primary prevention*, *weight control*, *weight maintenance*, *behavior therapy*, *diet*, *exercise, fitness* and *lifestyle*. Reference lists of the included studies of this review and the included studies of other on topic reviews were searched for relevant studies not captured by our search. A separate search was conducted to look for evidence

that would answer the contextual questions; this strategy included three databases (Medline, EMBASE, PsycINFO) and covered the period between January 2007 and August 16, 2013. The full search strategies are provided in Appendix 1. In addition, a focused grey literature search of Canadian sources was undertaken for recent reports on obesity in Canada. All citations were uploaded to a web-based systematic review software program[56] for screening and data extraction.

Study Selection

Titles and abstracts of papers considered for the key question and sub questions were reviewed in duplicate; articles marked for inclusion by either team member went on to full text screening. Full text inclusion was done independently by two people. All disagreements were resolved through discussions rather than relying on a particular level of kappa score to indicate when discussions were no longer necessary. The inclusion results were reviewed by a third person. For papers located in the contextual questions search, title and abstract screening was done by one person.

Inclusion and Exclusion Criteria

Language

The published results of studies had to be available in either English or French.

Populations

Studies had to explicitly state that the sample included normal weight adults (BMI >18 and <25). In the absence of this statement we accepted studies when the baseline mean BMI minus one standard deviation (SD) fell below 25 kg/m^2; we assumed that this result meant there were some normal weight people in the sample. The sample populations were unselected, selected for low CVD risk, or selected for increased risk for specified conditions (CVD, hypertension, dyslipidemia, or T2D). Trials limited to participants with CVD were excluded, but trials with some participants with CVD were included. Studies were excluded if the sample had a condition which predisposed weight gain such as metabolic syndrome, polycystic ovarian disease and niche populations such as those with eating disorders. Pregnant women were excluded but women who were postpartum were included. We also excluded any studies that focused on underweight populations.

Interventions

The focus of the intervention had to be weight gain prevention. Interventions considered for inclusion were behavioural, complementary or alternative. Behavioural interventions could include diet, exercise, diet plus exercise, or lifestyle strategies. Lifestyle strategies were typically referred to as such by the study authors and often included counseling, education or support and environmental changes in addition to diet and/or exercise. Complementary and alternative interventions included strategies such as acupuncture, chiropractic and herbal supplements. Pharmacological and surgical interventions were excluded.

Settings

Trials were conducted in settings generalizable to Canadian primary care, feasible for conducting in primary care or feasible for referral from primary care. Studies conducted in in-patient

hospital settings, institutional settings, school-based programs, occupational settings, faith-based programs, 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 were excluded.

Comparator and Study Design

To answer the questions about the benefits of prevention interventions, only randomized controlled trials (RCTs) were considered for inclusion. More specifically, an acceptable control group could not receive a personalized intervention, at-home workbook materials, and/or advice more frequently than annually, or participate in frequent weigh-ins (<3 months). Provision of healthy lifestyle messages was considered too close to weight loss messages, thus was not considered a valid control group condition. Studies also had to involve at least 30 participants. Case reports, case series and chart reviews were excluded.

Any study design (with or without comparison groups) with any number of participants was considered acceptable to answer the questions about adverse events and the contextual questions.

Outcomes

To answer the questions about the benefits of prevention interventions, only studies that reported data for one or more of the specified weight outcomes were included (i.e., weight in kg, BMI, waist circumference, total % body fat). There was no weight outcome requirement if a study reported data for adverse events of interest (labelling; disordered eating; psychological distress such as anxiety, depression and stigma; nutritional deficits; cost burden). Secondary outcomes of interest included total cholesterol, low density lipoprotein cholesterol (LDL-C), fasting glucose, incidence of T2D, systolic blood pressure (SBP), and diastolic blood pressure (DBP).

Timeframe

There was no intervention duration criterion. However, for the questions regarding intervention effectiveness, studies were only included if they provided outcome data for a minimum of 12 months post baseline assessment.

There was no intervention duration requirement or 12 month minimum expectation for outcome measurements in studies that reported adverse events or for inclusion of studies to address the contextual questions.

Data Abstraction

For each study used to answer the KQ, review team members extracted data about the population, study design, intervention, analysis and results for outcomes of interest. For each study one team member completed full abstraction (study characteristics, risk of bias assessment, outcome data) using electronic forms housed in a web-based systematic review software program.[56] A second team member verified all extracted data and ratings; disagreements were resolved through discussion and/or third party consultation when consensus could not be

reached. Prior to performing meta-analyses, tables were produced for each outcome and all data were checked in a third round of verification.

Unadjusted immediate post assessment data was extracted for most studies. However, for a small number of studies the immediate post intervention data did not meet our minimum 12 months post baseline assessment criterion; in these cases we extracted data at the point closest to the end of the intervention that was ≥12 months post baseline (e.g., intervention duration six months, follow-up six months later). Another small group of studies reported interim results for longer term interventions. Since there was no condition that interventions must be completed to be included in this review, we extracted this interim data.

To answer the adverse effects KQ we selected the more inclusive option and looked for data for all reported adverse events of interest, regardless of whether they were attributed to study participation.

Assessing Risk of Bias

Arriving at a Grading of Recommendations Assessment, Development and Evaluation or GRADE rating for a body of evidence (see next section) requires a preliminary assessment of the risk of bias or study limitations for the individual studies. All RCTs included to answer the KQ of this review were assessed using the Cochrane Risk of Bias tool.[57]

This rating tool covers six domains: sequence generation; allocation concealment; blinding of participants, personnel and outcome assessors; incomplete outcome reporting; selective outcome reporting; and other risk of bias. A few adjustments were made for the purpose of this review: we separated our assessment of blinding of participants and personnel from our assessment of blinding of outcome assessors; we considered objective (total cholesterol, LDL-C, fasting blood glucose, incidence of T2D), subjective (weight, blood pressure, adverse effects) and self-report (weight, adverse effects) outcomes separately under the domains of blinding of outcome assessors and incomplete outcome reporting; we selected study funding, baseline imbalance and selection bias as the three main sources of other risk of bias; and we added an overall risk of bias rating specific to outcome group (objective, subjective, self-report).

Information to determine risk of bias was abstracted from the primary methodology paper for each study and any other relevant published papers. For each study, one team member completed the initial ratings which were then verified by a second person; disagreements were resolved through discussion and/or third party consultation when consensus could not be reached. To assign a high or low risk of bias rating for a particular domain we looked for explicit statements or other clear indications that the relevant methodological procedures were or were not followed. In the absence of such details we assigned unclear ratings to the applicable risk of bias domains. To determine the overall risk of bias rating for an outcome group we considered all domains, however greater emphasis was placed on the assessments of first three areas of randomization, allocation, and blinding of outcome assessment.

Table 3 summarizes the risk of bias ratings applied to the RCTs included in this review.

Assessing Strength or Quality of the Evidence

The strength of the evidence was determined based on the GRADE system of rating the quality of evidence using GRADEPro software.[58,59] This system of assessing evidence is widely used and is endorsed by over 40 major organizations including the WHO, Centers for Disease Control and Prevention, and the Agency for Healthcare Research and Quality.[60] The GRADE system rates the quality of a body of evidence as high, moderate, low or very low; each of the four levels reflects a different assessment of the likelihood that further research will impact the estimate of effect (i.e., high quality: further research is unlikely to change confidence in the estimate of effect; moderate quality: further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate; low quality: further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate; very low quality: the estimate of effect is very uncertain).[60]

A GRADE quality rating is based on an assessment of five conditions: (1) risk of bias (limitations in study designs), (2) inconsistency (heterogeneity) in the direction and/or size of the estimates of effect, (3) indirectness of the body of evidence to the populations, interventions, comparators and/or outcomes of interest, (4) imprecision of results (few participants/events/observations, wide confidence intervals), and (5) indications of reporting or publication bias. Grouped RCTs begin with a high quality rating which may be downgraded if there are serious or very serious concerns across the studies related to one or more of the five conditions. For this review, key data were entered into the GRADEPro software along with the quality assessment ratings to produce two analytic products for each outcome and the comparisons of interest: (1) a GRADE Evidence Profile Table and (2) a GRADE Summary of Findings Table (presented in Evidence Sets 1 to 11).

There was no assessment of the quality of the evidence used to answer the contextual questions.

Data Analysis

To perform meta-analyses, immediate post treatment data (means, standard deviations) were utilized for continous outcomes such as change in weight in kg, BMI and waist circumference while number of events data were utilized for binary outcomes (i.e., incidence of T2D). The DerSimonian and Laird random effects model with inverse variance (IV) method was utilized to generate the summary measures of effect in the form of mean difference (MD) for continous outcomes and risk ratio (RR) for binary outcomes.[61] The random effects model assumes the studies are a sample of all potential studies and incorporates an additional between-study component to the estimate of variability.

MDs were calculated using change from baseline data [i.e., mean difference between pre-treatment (baseline) and post treatment (final/end-point) values along with its standard deviation (SD) for both intervention and control groups]. For studies that did not report SD, we calculated this value from the reported standard error (SE) of the mean, or from the 95% confidence intervals (CI) using equations provided in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions.*[62] For studies that provided neither SD or SE for the follow-up data, we

imputed the SD from either the baseline values or other included studies of similar sample size and for the same outcome. If weight was reported in pounds, we converted values to kg. Similarly, the units of measurement for total cholesterol, LDL-C and fasting glucose, if reported in mg/dL, were converted to Canadian standard units (i.e., mmol/L).

For studies that recruited a single gender or for mixed gender studies that reported results for men and for women, we entered this data separately into the meta-analyses, using alphabetical extensions to identify gender (e.g., Imayama 2011-M, Imayama 2011-F). For all studies with more than one intervention arm, the groups were similar enough to combine (e.g., two arms evaluating the benefits of a diet plus exercise intervention, one using a clinic-based group and one using a correspondence course). We pooled the intervention group data in each study to do a pair-wise comparison with the control group.

We used I^2 statistic to quantify statistical heterogeneity between studies, where $P<0.05$ indicates a high level of statistical heterogenity between studies. Although there are no strict rules for interpreting I^2 a rough guide is that an I^2 >50% may represent substantial heterogeneity.[62]

Sensitivity analyses were performed to evaluate statistical stability and effect on statistical heterogeneity. The sub-group analyses, based on type of intervention (diet, exercise, diet plus exercise, lifestyle), length of intervention (≤12 months, >12 months), gender, participants' baseline CVD risk status (high risk: identified as having CVD risk factors and/or diagnosed with T2D, hypertension, dyslipidemia; low/unknown CVD risk), and study risk of bias rating (high, unclear, low) were performed for weight in kg because this was an outcome that most of the studies reported and, to be consistent, this was the outcome used for sensitivity analyses in the companion review on treatment. One additional sub-group analysis was performed based on baseline mean BMI (<25, ≥25) for the outcome of change in BMI.

Meta-analyses were performed using Review Manager version 5.1.[57] Publication bias for each outcome (with sufficient studies) was assessed with the Egger's test[63] using STATA version 12.[64]

For one secondary outcome (incidence of T2D), if the effect was significant we planned to add the estimate of absolute risk reduction (ARR) and number needed to treat (NNT) to the GRADE table. The NNT would be calculated using the absolute number presented in the GRADE table. GRADE estimates the absolute number per million using the control group event rate and risk ratio with the 95% confidence interval obtained from the meta-analysis.

For studies that provided data that could not be pooled, findings are reported narratively in the respective results sections.

Results presented throughout the body of this review are rounded and/or reported to the second decimal. However, at the request of the CTFPHC, we used four decimals in our calculations and in the presentation of results in the Evidence Sets.

To answer the sub-question about common elements of efficacious interventions it was necessary to first to identify the efficacious interventions. For this review we identified efficacious

interventions from studies included in the weight meta-analyses that showed a statistically significant effect size across all weight outcomes reported by the study. Some of the elements we examined in these interventions were adapted from the features list presented in the 2011 USPSTF review.[5] We also included intervention duration, focus and setting as we believe primary care physicians would want to take such features into consideration when making program recommendations to their patients.

Chapter 3: Results

Summary of the Literature Search for Key Questions

The search and selection process for relevant literature occurred in three stages. Initially we conducted a combined search that included children and adults; prevention and treatment. We believed that some efficiency would be gained in the screening stage if we started with a comprehensive search strategy.

The initial comprehensive search (including both adults and children) located 30,196 unique citations (see Figure 2). These citations were reviewed for title and abstract relevance and were filtered for population (adult or child) and intervention focus (prevention or treatment). A total of 10,914 were excluded at this first level of relevance screening. There were 11,183 citations streamed for adult populations and 8,099 citations streamed for children (further information regarding child-related citations is reported in the child obesity treatment and child obesity prevention reviews available on the CTFPHC website http://canadiantaskforce.ca/).

The second stage involved another round of title and abstract screening and streaming of the 11,183 citations related to adults. At this level 6,711 citations were excluded and 1,152 citations remained for consideration as treatment interventions (these results are further delineated in the adult obesity treatment review available on the CTFPHC website http://canadiantaskforce.ca/) and 3,320 citations remained for consideration as prevention interventions.

Finally, the literature search was updated in June 2013. This updated search was adapted from the original search and any terms referring to children were removed. That search added an additional 1,778 citations for possible inclusion. Another level of title and abstract screening was undertaken where an additional 3,922 citations were excluded. At this point we integrated two studies from in the 2011 USPSTF review[5] that met our definition of a mixed weight population and 13 hand-search located citations for consideration. Full text screening took place on 1,191 citations and 981 were excluded (see list of excluded studies available on the CTFPHC website http://canadiantaskforce.ca/).

One hundred and sixty-two systematic reviews were identified by our team. Upon further examination 51 of these systematic reviews were found to be specific to overweight/obese populations and were excluded. The reference lists of recent (published in 2012 and 2013) and on topic systematic reviews were searched to ensure that we had not missed any relevant studies. Five studies were located in those reference lists that were not found through the database search.

At the end of the search and selection process, 26 studies with 48 papers met the inclusion criteria for this review and were used as data sources for the key questions.

Summary of the Included Studies

A total of 26 RCTs were included to answer the key question and sub-questions in this review.[65-90] As per the inclusion criteria, all studies reported weight outcome data and met the comparison

group and minimum 12 month post baseline assessment requirements. Most (81%) of the studies were rated as having an unclear or a high risk of bias for the weight outcomes, primarily due to the lack of information about or lack of procedures to ensure random sequence generation, allocation concealment and blinding of outcome assessment (see Table 3). Due to the nature of behavioural interventions, there is also a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Although this review focuses on the prevention of overweight and obesity, the population was not restricted to normal weight adults. A single study[73] was found that included only normal weight adults (BMI >18 and <24.9). The criteria were therefore expanded to allow studies that included at least some normal weight adults, with the conditions that at least one study arm had a baseline mean BMI <25 or the baseline mean BMI >25 but minus one SD <25, or the number or percentage of normal weight participants was specified. Four studies were found that reported a baseline mean BMI for at least one study group that fell within the normal range; [68,75,85,88]16 studies reported baseline mean BMIs that fell in the overweight range (25 to 29.9) and in five studies at least one intervention arm had a baseline mean BMI just over the obesity threshold of 30 kg/m^2.[69,83,84,86,87] None of the included studies specifically targeted or recruited seniors (≥65 years). Most studies (n=18) included mixed gender samples; seven targeted only women[67,70,71,74,77,79,86] and the analysis in one study was limited to male participants.[76] Very few studies (n=4) were directed at participants with high CVD risk (i.e., screened/identified as high CVD risk and/or diagnosed with T2D, hypertension and/or dyslipidemia).[65,82,84,90] The intervention duration was one year or less in more than two-thirds of the studies (n=18); in the remaining eight studies the duration ranged from two years to up to 12 years, with half of these interventions (n=4) running for two years. Only three studies were situated in Canada.[68,69,74] Just over one-third of the studies (n=10) were conducted in European countries, many (n=7) were located in the US, several (n=4) were conducted in Australia and/or New Zealand, and two studies took place in Japan. Less than half of the studies (n=11) were published in the last five years (2009-2012); the remaining studies appeared in the literature between 1988 and 2008. The characteristics of the 26 included studies are reported individually in Table 4.

Results for Key Questions

KQ1: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health outcomes or short-term or sustained weight gain prevention, with or without improved physiological measures?

This review is unable to conclusively answer the question regarding whether primary care relevant interventions lead to short-term or sustained weight gain prevention or to improved health outcomes specifically in normal weight adults. As noted above, the search found a single study that included only normal weight adults that met the inclusion criteria of this review.[73] The "Pound of Prevention" study examined the effects of a 12 month, education and incentive-based lifestyle intervention conducted in the US over 25 years ago with approximately 200 normal

weight adults (defined as <115% of ideal weight as indicated by the Metropolitan Life Insurance Company tables for 1983). Results of this pilot study showed that significantly more (P<0.0001) Pound of Prevention participants (82%) maintained their baseline weight or lost weight over the 12 month intervention compared to control group participants (56%). On average, intervention group participants (n=103) lost 2.1 pounds (0.95 kg) whereas control group participants (n=108) lost 0.3 pounds (0.14 kg) (P=0.03). Aside from weight, this study did not report any other outcomes of interest to this review.

Given scant direct evidence to answer the key question of this prevention focused review, the criteria were expanded to allow studies that included some normal weight adults, with the conditions that at least one study arm had a baseline mean BMI <25, or the baseline mean BMI >25 but minus one SD <25, or the number or percentage of normal weight participants was specified. Twenty-five studies were found that met the expanded inclusion criteria for this review. Therefore, the following analyses, based on subgroups of the 26 included RCTs, provide indirect evidence to address the key question and sub-questions.

High level summaries of the included studies and key findings across outcomes with pooled estimates of effect are provided in Tables 5 through 7. Detailed results for each outcome are presented below.

Primary Outcome: Weight

Change in Weight in KG

Evidence Set 1 provides the GRADE Evidence Profile Table (1.1), the GRADE Summary of Findings Table (1.1), the forest plots (1.1 to 1.6), the funnel plots (1.1 to 1.6) and the Egger's test results (for publication bias) generated for the outcome of change in weight as measured in kg for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 19 studies that reported weight loss in kg. Five sub-analyses were conducted to look more closely at this comparison: (1) by type of intervention (diet, exercise, diet plus exercise, lifestyle), (2) by duration of intervention (≤12 months, >12 months), (3) by gender, (4) by participants' baseline CVD risk status (high risk, low/unknown risk), and (7) by study risk of bias rating (high, unclear, low).

1.1 Overall

Nineteen RCTs (n=48,460) of very low GRADE quality (downgraded for risk of bias, indirectness and reporting bias) were included in the meta-analysis on weight change in kg.[65-68,70,71,73,74,76-81,83-85,89,90] Across the 19 studies, baseline BMI ranged from 22.4 to 30.1; in three of the studies the baseline mean BMI of at least one study arm was <25; in 16 studies the baseline means were in the range for overweight/obese. Most studies (n=12) included mixed gender samples; six included only women and one included only men. In three studies (16%) the participants had a high risk of CVD. In terms of type of intervention two were diet, five were exercise, four were diet plus exercise, and eight were lifestyle. Control participants received usual care from their physicians or no intervention; in seven of these studies control participants received a minimal

component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 12 studies and more than 12 months in seven studies. Two studies were conducted in Canada, six in the US, eight in European countries, two in Australia or New Zealand, and one in Japan. About half of the studies (n=9) were published in the last five years (2009-2012); the remaining 10 studies were published between 1988 and 2008. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.73 kg (-0.93, -0.54); I^2=49%].

1.2 Type of Intervention

There was no evidence that the intervention effect differed based on type of intervention (diet, exercise, diet plus exercise, lifestyle) [Chi^2=4.07, df=3 (P=0.25), I^2=26.4%].

Diet

Two diet focused RCTs (n=42,308) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[67,89] Across the two studies, baseline BMI ranged from 25.9 to 29.1. One study included a mixed gender sample and the other study included only women. In both studies the participants had low/unknown risk of CVD. Control participants in both studies received a minimal component (i.e., printed materials on healthy eating and lifestyles). Intervention duration was 12 months in one study and ranged from eight to 12 years in the other study. One study was conducted in the US and the other study was conducted in the UK. One study was published in the last five years (2011); the other study was published in 1997. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.51 kg (-0.65, -0.36); I^2=0%].

Exercise

Five exercise focused RCTs (n=2,024) of low GRADE quality (downgraded for risk of bias and imprecision) were included in the meta-analysis assessing weight change in kg.[66,74,77,79,83] Across the five studies, baseline BMI ranged from 26.6 to 30.1. Two studies (40%) included mixed gender samples; three included only women. In all five studies the participants had low/unknown risk of CVD. Control participants received usual care from their physicians or no intervention. Intervention duration was 12 months or less in all five studies. One study was conducted in Canada, two in the US, one in the Netherlands, and one in New Zealand. Most of the studies (n=4) were published in the last five years (2009-2012); the remaining study was published in 2008. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.88 kg (-1.44, -0.33); I^2=52%].

Diet plus Exercise

Four diet plus exercise focused RCTs (n=748) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[68,70,76,78] Across the four studies, baseline BMI ranged from 22.4 to 29.8; in one study the baseline mean BMI of at least one study arm was <25. Half of the studies (n=2) included mixed gender samples; one included only women and one included only men. In all four studies the participants had low/unknown

risk of CVD. Control participants received usual care from their physicians or no intervention; in three of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in one study and more than 12 months in three studies. One study was conducted in Canada, one in the US, and two in the Netherlands. One study was published in the last five years (2010); the remaining three were published between 2003 and 2007. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.99 kg (-1.90, -0.08); I^2=50%].

Lifestyle

Eight lifestyle focused RCTs (n=3,380) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[65,71,73,80,81,84,85,90] Across the eight studies, baseline BMI ranged from 23.1 to 30.1; in three of the studies the baseline mean BMI of at least one study arm was <25; in five studies the baseline means were in the range for overweight/obese. Most studies (n=7) included mixed gender samples; one included only women. In three studies (38%) the participants had a high risk of CVD. In terms of type of intervention all eight studies were lifestyle focused. Control participants received usual care from their physicians or no intervention; in two of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in five studies and more than 12 months in three studies. Two studies were conducted in the US, four in European countries, one in Australia, and one in Japan. Less than half of the studies (n=3) were published in the last five years (2009-2012); the remaining five were published between 1988 and 2007. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.89 kg (-1.44, -0.34); I^2=60%].

1.3 Duration of Intervention

There was no evidence that the intervention effect differed based on duration of intervention (≤12 months, >12 months) [Chi^2=3.07, df=1 (P=0.08), I^2=67.4%].

Intervention Duration ≤12 Months

Twelve RCTs (n=4,908) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[66,73,74,76,77,79,81,83-85,89,90] Across the 12 studies, baseline BMI ranged from 23.1 to 30.1; in two of the studies the baseline mean BMI of at least one study arm was <25; in 10 studies the baseline means were in the range for overweight/obese. Most studies (n=8) included mixed gender samples; three included only women and one included only men. In two studies (17%) the participants had a high risk of CVD. In terms of type of intervention one was diet, five were exercise, one was diet plus exercise, and five were lifestyle. Control participants received usual care from their physicians or no intervention; in three of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). One study was conducted in Canada, three in the US, five in European countries, two in Australia or New Zealand, and one in Japan. Just over half of the studies (n=7) were published in the last five years (2009-2012); the remaining five studies were

published between 1988 and 2008. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.61 kg (-0.70, -0.51); I^2=2%].

Intervention Duration >12 Months

Seven RCTs (n=43,552) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[65,67,68,70,71,78,80] Across the seven studies, baseline BMI ranged from 22.4 to 29.8; in one study the baseline mean BMI of at least one study arm was <25; in six studies the baseline means were in the range for overweight/obese. Four studies included mixed gender samples; three included only women. In one study the participants had a high risk of CVD. In terms of type of intervention one was diet, three were diet plus exercise, and three were lifestyle. Control participants received usual care from their physicians or no intervention; in four of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). One study was conducted in Canada, three in the US, and three in European countries. Only two studies were published in the last five years (2011, 2012); the remaining five studies were published between 2002 and 2007. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -1.21 kg (-1.88, -0.54); I^2=78%].

1.4 Gender

Ten of the 26 studies provided data for change in weight as measured in kg that was separated by gender.[66,67,70,71,73,74,76,77,79,89] There was no evidence that the intervention effect differed based on gender [Chi^2=1.34, df=1 (P=0.25), I^2=25.3%].

Male

Four RCTs (n=975) of very low GRADE quality (downgraded for risk of bias, indirectness and imprecision) were included in the meta-analysis assessing weight change in kg.[66,73,76,89] Across the four studies, baseline BMI ranged from 23.1 to 29.3; in one study the baseline mean BMI of at least one study arm was <25. Most studies (n=3) included mixed gender samples; one included only men. In all four studies the participants had low/unknown risk of CVD. In terms of type of intervention one was diet, one was exercise, one was diet plus exercise, and one was lifestyle. Control participants received usual care from their physicians or no intervention; in two of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in all four studies. Two studies were conducted in the US and two in European countries. Half of the studies (n=2) were published in the last five years (2010, 2011); the other two studies were published in 1988 and 1997. There was no difference between male intervention and male control group participants in terms of weight change in kg [MD (95% CI) -0.48 kg (-0.99, 0.03); I^2=0%].

Female

Nine RCTs (n=44,390) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[66,67,70,71,73,74,77,79,89] Across the nine

studies, baseline BMI ranged from 23.1 to 29.3; in one study the baseline mean BMI of at least one study arm was <25; in eight studies the baseline means were in the range for overweight/obese. Three studies included mixed gender samples; six included only women. In all eight studies the participants had low/unknown risk of CVD. In terms of type of intervention two were diet, four were exercise, one was diet plus exercise, and two were lifestyle. Control participants received usual care from their physicians or no intervention; in three of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in six studies and more than 12 months in three studies. One study was conducted in Canada, five in the US, two in European countries, and one in New Zealand. About half of the studies (n=4) were published in the last five years (2009-2011); the remaining five studies were published between 1988 and 2008. Female intervention participants had a significantly greater reduction in weight as compared to female control participants [MD (95% CI) -0.82 kg (-1.09, -0.55); I^2=73%].

1.5 Participants' Baseline CVD Risk Status

There was no evidence that the intervention effect differed based on participants' baseline CVD risk status (high, low/unknown) [Chi^2=0.27, df=1 (P=0.60), I^2=0%].

High CVD Risk

Three RCTs (n=1,356) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[65,84,90] Across the three studies, baseline BMI ranged from 28.1 to 30.1. All three studies included mixed gender samples. In terms of type of intervention all three were lifestyle focused. Control participants received usual care from their physicians or no intervention; in one study control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in two studies and more than 12 months in one study. All three studies were conducted in European countries. One study was published in the last five years (2009); the other two studies were published in 1999 and 2002. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.88 kg (-1.45, -0.32); I^2=0%].

Low/Unknown CVD Risk

Sixteen RCTs (n=47,104) of very low GRADE quality (downgraded for risk of bias, indirectness and reporting bias) were included in the meta-analysis assessing weight change in kg.[66-68,70,71,73,74,76-81,83,85,89] Across the 16 studies, baseline BMI ranged from 22.4 to 30.1; in three of the studies the baseline mean BMI of at least one study arm was <25; in 13 studies the baseline means were in the range for overweight/obese. About half of the studies (n=9) included mixed gender samples; six included only women and one included only men. In terms of type of intervention two were diet, five were exercise, four were diet plus exercise, and five were lifestyle. Control participants received usual care from their physicians or no intervention; in six of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 10 studies and more than 12

months in six studies. Two studies were conducted in Canada, six in the US, five in European countries, two in Australia or New Zealand, and one in Japan. Half of the studies (n=8) were published in the last five years (2009-2012); the remaining eight studies were published between 1988 and 2008. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.72 kg (-0.93, -0.52); I^2=54%].

1.6 Study Risk of Bias Rating

There was no evidence that the intervention effect differed based on study risk of bias rating (high, unclear, low) [Chi^2=2.50, df=2 (P=0.29), I^2=20.0%].

High

Two RCTs (n=652) of low GRADE quality (downgraded for risk of bias, indirectness and imprecision) were included in the meta-analysis assessing weight change in kg.[78,80] Across the two studies, baseline BMI ranged from 28.5 to 29.8. Both studies included mixed gender samples. In both studies the participants had low/unknown risk of CVD. In terms of type of intervention one was diet plus exercise and one was lifestyle. Control participants received usual care from their physicians or no intervention and in both of these studies they also received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was more than 12 months in both studies. Both studies were conducted in the Netherlands. One study was published in the last five years (2012); the other study was published in 2003. There was no difference between intervention and control group participants in terms of weight change in kg [MD (95% CI) -1.20 kg (-3.04, 0.64); I^2=75%].

Unclear

Thirteen RCTs (n=45,237) of very low GRADE quality (downgraded for risk of bias, indirectness and reporting bias) were included in the meta-analysis assessing weight change in kg.[65-68,70,73,76,77,83-85,89,90] Across the 13 studies, baseline BMI ranged from 22.4 to 30.1; in three of the studies the baseline mean BMI of at least one study arm was <25; in 10 studies the baseline means were in the range for overweight/obese. Most studies (n=9) included mixed gender samples; three included only women and one included only men. In three studies (23%) the participants had a high risk of CVD. In terms of type of intervention two were diet, three were exercise, three were diet plus exercise, and five were lifestyle. Control participants received usual care from their physicians or no intervention; in five of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in nine studies and more than 12 months in four studies. One study was conducted in Canada, six in the US, and six in European countries. About half of the studies (n=6) were published in the last five years (2009-2012); the remaining seven studies were published between 1988 and 2007. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -0.53 kg (-0.67, -0.40); I^2=0%].

Low

Four RCTs (n=2,571) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing weight change in kg.[71,74,79,81] Across the four studies, baseline BMI ranged from 25 to 29.2. Only one study included a mixed gender sample; three included only women. In all four studies the participants had low/unknown risk of CVD. In terms of type of intervention two were exercise and two were lifestyle. Control participants received usual care from their physicians or no intervention. Intervention duration was 12 months or less in three studies and more than 12 months in one study. One study was conducted in Canada, one in the US, one in Australia, and one in New Zealand. Half of the studies (n=2) were published in the last five years (2011, 2012); the other two studies were published in 2003 and 2008. Intervention participants had a significantly greater reduction in weight as compared to the control group [MD (95% CI) -1.22 kg (-2.16, -0.28); I^2=89%].

Change in Body Mass Index

Evidence Set 2 provides the GRADE Evidence Profile Table (2.1), the GRADE Summary of Findings Table (2.1), the forest plots (2.1, 2.2), the funnel plot (2.1) and the Egger's test results (for publication bias) generated for the outcome of change in BMI for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 20 studies that reported on the outcome of change in BMI. One sub-analysis was conducted to look more closely at this comparison by baseline mean BMI (normal weight BMI<25, overweight/obese BMI≥25).

Overall

Twenty RCTs (n=52,243) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing change in BMI.[66-69,71,72,74-78,80,82,84-90] Across the 20 studies, baseline BMI ranged from 22.4 to 33.2; in four of the studies the baseline mean BMI of at least one study arm was <25; in 16 studies the baseline means were in the range for overweight/obese. Most studies (n=14) included mixed gender samples; five included only women and one included only men. In three studies (15%) the participants had a high risk of CVD. In terms of type of intervention three were diet, four were exercise, four were diet plus exercise, and nine were lifestyle. Control participants received usual care from their physicians or no intervention; in seven of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 14 studies and more than 12 months in six studies. Three studies were conducted in Canada, four in the US, nine in European countries, two in Australia or New Zealand, and two in Japan. About half of the studies (n=9) were published in the last five years (2009-2012); the remaining 11 studies were published between 1997 and 2007. Intervention participants had a significantly greater reduction in BMI as compared to the control group [MD (95% CI) -0.24 kg/m^2 (-0.34, -0.15); I^2=64%]. There is no evidence that the intervention effect differed based on baseline mean BMI (<25, ≥25) [Chi^2=0.06, df=1 (P=0.81), I^2=0%].

Normal Weight: Baseline Mean BMI <25

Four RCTs (n=5,152) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing change in BMI.[68,75,85,88] Across the four studies, baseline BMI ranged from 22.4 to 24.8; all studies included some overweight/obese adults. All studies included mixed gender samples and participants with low/unknown risk of CVD. In terms of type of intervention two were diet and two were lifestyle. Control participants received usual care from their physicians or no intervention. Intervention duration was 12 months or less in two studies and more than 12 months in two studies. One study was conducted in Canada, two in Japan and one in Italy. All of the studies (n=4) were published between 2002 and 2007. Intervention participants had a significantly greater reduction in BMI as compared to the control group [MD (95% CI) -0.27 kg/m^2 (-0.50, -0.05); I^2=47%].

Overweight/Obese: Baseline Mean BMI ≥25

Sixteen RCTs (n=47,091) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing change in BMI.[66,67,69,71,72,74,76-78,80,82,84,86,87,89,90] Across the 16 studies, baseline BMI ranged from 25 to 33.2; all studies included some normal weight adults. Most studies (n=10) included mixed gender samples; five included only women and one included only men. In three studies (19%) the participants had a high risk of CVD. In terms of type of intervention two were diet, four were exercise, three were diet plus exercise, and seven were lifestyle. Control participants received usual care from their physicians or no intervention; in seven of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 12 studies and more than 12 months in four studies. Two studies were conducted in Canada, four in the US, eight in European countries, one in Australia and one in New Zealand. About half of the studies (n=9) were published in the last five years (2009-2012); the remaining seven studies were published between 1997 and 2007. Intervention participants had a significantly greater reduction in BMI as compared to the control group [MD (95% CI) -0.24 kg/m^2 (-0.36, -0.12); I^2=68%].

Change in Waist Circumference

Evidence Set 3 provides the GRADE Evidence Profile Table (3.1), the GRADE Summary of Findings Table (3.1), the forest plot (3.1), the funnel plot (3.1) and the Egger's test results (for publication bias) generated for the outcome of change in waist circumference in centimeters (cm) for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 15 studies that reported on the outcome of waist circumference.

Fifteen RCTs (n=20,796) of very low GRADE quality (downgraded for risk of bias, indirectness and reporting bias) were included in the meta-analysis assessing change in waist circumference.[65-69,71,74,76-80,82-84] Across the 15 studies, baseline BMI ranged from 22.4 to 33.2; in one study the baseline mean BMI of at least one study arm was <25; in 14 studies the baseline means were in the range for overweight/obese. Nine studies included mixed gender samples; five included

only women and one included only men. In three studies (20%) the participants had a high risk of CVD. In terms of type of intervention one was diet, five were exercise, three were diet plus exercise, and six were lifestyle. Control participants received usual care from their physicians or no intervention; in five of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in nine studies and more than 12 months in six studies. Three studies were conducted in Canada, four in the US, seven in European countries, and one in New Zealand. More than half of the studies (n=9) were published in the last five years (2009-2012); the remaining six studies were published between 2002 and 2008. Intervention participants had a significantly greater reduction in waist circumference as compared to the control group [MD (95% CI) -0.95 cm (-1.27, -0.63); I^2=74%].

Change in Total % Body Fat

Evidence Set 4 provides the GRADE Evidence Profile Table (4.1), the GRADE Summary of Findings Table (4.1), the forest plot (4.1), the funnel plot (4.1) and the Egger's test results (for publication bias) generated for the outcome of change in total % body fat for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all six studies that reported on the outcome of total % body fat.

Six RCTs (n=1,663) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing change in total % body fat.[66,71,74,76-78] Across the six studies, baseline BMI ranged from 25 to 29.8. Two studies included mixed gender samples; three included only women and one included only men. In all six studies the participants had low/unknown risk of CVD. In terms of type of intervention three were exercise, two were diet plus exercise, and one was lifestyle. Control participants received usual care from their physicians or no intervention; in two of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in four studies and more than 12 months in two studies. One study was conducted in Canada, two in the US, and three in the Netherlands. Four of the studies were published in the last five years (2009-2011); the remaining two studies were published in 2003. Intervention participants had a significantly greater reduction in total % body fat as compared to the control group [MD (95% CI) -1.27 % (-1.93, -0.61); I^2=80%].

Secondary Outcomes: Lipids

Change in Total Cholesterol

Evidence Set 5 provides the GRADE Evidence Profile Table (5.1), the GRADE Summary of Findings Table (5.1), the forest plot (5.1), the funnel plot (5.1) and the Egger's test results (for publication bias) generated for the outcome of change in total cholesterol for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 15 of the studies that reported on the outcome of total cholesterol.

Fifteen RCTs (n=10,660) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing change in total cholesterol level.[65,67-69,72,75,78,79,82,84-

[87,89,90] Across these studies, baseline BMI ranged from 22.4 to 31.1; in three of the studies the baseline mean BMI of at least one study arm was <25; in 12 studies the baseline means were in the range for overweight/obese. Most studies (n=12) included mixed gender samples; three included only women. In four studies (33%) the participants had a high risk of CVD. In terms of type of intervention two were diet, two were exercise, three were diet plus exercise, and eight were lifestyle. Control participants received usual care from their physicians or no intervention; in five of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 10 studies and more than 12 months in five studies. Two studies were conducted in Canada, two in the US, six in European countries, three in Australia or New Zealand, and two in Japan. About one-third of the studies (n=4) were published in the last five years (2009-2012); the remaining 11 studies were published between 1997 and 2008. Intervention participants had a significantly greater reduction in total cholesterol level as compared to the control group [MD (95% CI) -0.06 mmol/L (-0.11, -0.01); I^2=70%].

Low Density Lipoprotein Cholesterol (LDL-C)

Evidence Set 6 provides the GRADE Evidence Profile Table (6.1), the GRADE Summary of Findings Table (6.1), the forest plot (6.1), the funnel plot (6.1) and the Egger's test results (for publication bias) generated for the outcome of change in LDL-C for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 11 of the studies that reported on the outcome of LDL-C.

Eleven RCTs (n=5,635) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing change in LDL-C level.[65,67,68,71,72,78,82-86] Across these studies, baseline BMI ranged from 22.4 to 31.1; in two of the studies the baseline mean BMI of at least one study arm was <25; in nine studies the baseline means were in the range for overweight/obese. Most studies (n=8) included mixed gender samples; three included only women. In three studies (27%) the participants had a high risk of CVD. In terms of type of intervention one was diet, one was exercise, three were diet plus exercise, and six were lifestyle. Control participants received usual care from their physicians or no intervention; in four of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in six studies and more than 12 months in five studies. One study was conducted in Canada, four in the US, four in European countries, one in Australia, and one in Japan. About half of the studies (n=5) were published in the last five years (2009-2012); the remaining 11 studies were published between 2002 and 2007. Intervention participants had a significantly greater reduction in LDL-C level as compared to the control group [MD (95% CI) -0.06 mmol/L (-0.09, -0.03); I^2=0%].

Secondary Outcomes: Diabetes

Change in Fasting Glucose

Evidence Set 7 provides the GRADE Evidence Profile Table (7.1), the GRADE Summary of Findings Table (7.1), the forest plot (7.1), the funnel plot (7.1) and the Egger's test results (for

publication bias) generated for the outcome of change in fasting glucose for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 10 studies that reported on the outcome of fasting glucose.

Ten RCTs (n=7,189) of low GRADE quality (downgraded for risk of bias and indirectness) were included in the meta-analysis assessing change in fasting glucose level.[67,69,71,74,75,78-80,83,84] Across these studies, baseline BMI ranged from 23.1 to 30.1; in one study the baseline mean BMI of at least one study arm was <25; in nine studies the baseline means were in the range for overweight/obese. Just over half of the studies (n=6) included mixed gender samples; four included only women. In one study (10%) the participants had a high risk of CVD. In terms of type of intervention one was diet, three were exercise, one was diet plus exercise, and five were lifestyle. Control participants received usual care from their physicians or no intervention; in four of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in five studies and more than 12 months in five studies. Two studies were conducted in Canada, three in the US, three in European countries, one in New Zealand, and one in Japan. Half of the studies (n=5) were published in the last five years (2009-2012); the remaining five studies were published between 2002 and 2008. Intervention participants had a significantly greater reduction in fasting glucose level as compared to the control group [MD (95% CI) -0.04 mmol/L (-0.08, -0.0016); I^2=67%].

Incidence of Type 2 Diabetes (T2D)

Evidence Set 8 provides the GRADE Evidence Profile Table (8.1), the GRADE Summary of Findings Table (8.1), the forest plot (8.1), the funnel plot (8.1) and the Egger's test results (for publication bias) generated for the outcome of incidence of T2D for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including both studies that reported on the outcome of T2D incidence.

Two RCTs (n=46,537) of very low GRADE quality (downgraded for risk of bias, indirectness and imprecision) were included in the meta-analysis assessing the risk of T2D.[67,80] Across the two studies, baseline BMI ranged from 28.5 to 29.1; in both studies the baseline means were in the range for overweight/obese. One study included a mixed gender sample while the larger study included only women. In both studies the participants had low/unknown risk of CVD. In terms of type of intervention one was diet and one was lifestyle. Control participants received usual care from their physicians or no intervention as well as a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was more than 12 months in both studies. One study was conducted in the US and one in the Netherlands. Both were recently published studies (2011, 2012). There was no difference between intervention and control group participants in terms of risk of being diagnosed with new onset T2D [RR (95% CI) 0.95 (0.89, 1.02)].

Secondary Outcomes: Hypertension

Change in Systolic Blood Pressure

Evidence Set 9 provides the GRADE Evidence Profile Table (9.1), the GRADE Summary of Findings Table (9.1), the forest plot (9.1), the funnel plot (9.1) and the Egger's test results (for publication bias) generated for the outcome of change in SBP for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 17 studies that reported on the outcome of SBP.

Seventeen RCTs (n=48,493) of very low GRADE quality (downgraded for risk of bias, inconsistency, indirectness, and imprecision) were included in the meta-analysis assessing change in SBP.[65,67,68,71,72,75,76,79,82-90] Across these studies, baseline BMI ranged from 22.4 to 31.1; in four of the studies the baseline mean BMI of at least one study arm was <25; in 13 studies the baseline means were in the range for overweight/obese. Most studies (n=12) included mixed gender samples; four included only women and one included only men. In four studies (24%) the participants had a high risk of CVD. In terms of type of intervention three were diet, three were exercise, three were diet plus exercise, and eight were lifestyle. Control participants received usual care from their physicians or no intervention; in five of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 12 studies and more than 12 months in five studies. One study was conducted in Canada, four in the US, seven in European countries, three in Australia or New Zealand, and two in Japan. About one-third of the studies (n=6) were published in the last five years (2009-2012); the remaining 11 studies were published between 1997 and 2008. There was no difference between intervention and control group participants in terms of change in SBP [MD (95% CI) -0.31 mmHg (-0.84, 0.22); I^2=77%].

Diastolic Blood Pressure

Evidence Set 10 provides the GRADE Evidence Profile Table (10.1), the GRADE Summary of Findings Table (10.1), the forest plot (10.1), the funnel plot (10.1) and the Egger's test results (for publication bias) generated for the outcome of change in DBP for the comparison between intervention participation and usual care or no intervention. An overall analysis was performed including all 15 of the studies that reported on the outcome of DBP.

Fifteen RCTs (n=47,945) of very low GRADE quality (downgraded for risk of bias, inconsistency, indirectness, and imprecision) were included in the meta-analysis assessing change in DBP. [65,67,68,71,72,75,76,79,84-90] Across these studies, baseline BMI ranged from 22.4 to 31.1; in four of the studies the baseline mean BMI of at least one study arm was <25; in 11 studies the baseline means were in the range for overweight/obese. Two-thirds of the studies (n=10) included mixed gender samples; four included only women and one included only men. In three studies (20%) the participants had a high risk of CVD. In terms of type of intervention three were diet, two were exercise, three were diet plus exercise, and seven were lifestyle. Control participants received usual care from their physicians or no intervention; in five of these

studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 10 studies and more than 12 months in five studies. One study was conducted in Canada, three in the US, six in European countries, three in Australia or New Zealand, and two in Japan. About one-quarter of the studies (n=4) were published in the last five years (2009-2012); the remaining 11 studies were published between 1997 and 2008. There was no difference between intervention and control group participants in terms of change in DBP [MD (95% CI) -0.18 mmHg (-0.44, 0.07); I^2=66%].

KQ1a: Are there differences in efficacy between adult subgroups (e.g., age 65 years or older, gender, baseline CVD risk status)?

Subgroup analyses were conducted for the change in weight as measured in kg outcome for gender and baseline CVD risk status and for the change in BMI outcome for baseline mean BMI. Results of these sub-analyses are presented above and in Evidence Sets 1 and 2 (see forest plots 1.4, 1.5 and 2.2). None of the included studies targeted or provided separate results for older adults (≥age 65); therefore no age differentiated subgroup analysis could be performed.

KQ1b: What are the adverse effects of primary care relevant prevention interventions in normal weight adults (e.g., labelling; disordered eating; psychological distress such as anxiety, depression and stigma; nutritional deficits; cost)?

No studies were found that met the inclusion criteria of this review that presented data on the adverse effects of interest (labelling; disordered eating; psychological distress such as anxiety, depression and stigma; nutritional deficits; cost). Therefore, we are unable to provide a direct answer to the questions regarding adverse effects posed in this review. However, six of the 26 included studies did address adverse effects in their results sections.[66,74,79,84,87,88] Four of the studies looked at exercise programs,[66,74,79,87] one examined a lifestyle intervention,[84] and one investigated a very brief primary care delivered education intervention focused on modifying daily diet.[88] The studies involved primarily middle-age adults (sample means ranged across the 40s, 50s and 60s). Half of the six studies noted that no adverse events associated with participation were reported by intervention participants.[74,84,88] The results of two studies showed no significant difference between exercisers and those in the control groups in terms of experiencing injuries, falls or serious adverse events.[66,87] Only one study reported significantly more falls (P<0.001) and injuries (P=0.03) were suffered by those taking part in the exercise program compared to the control group participants.[79]

KQ1c: Are there differences in adverse effects between adult subgroups (e.g., age 65 years or older, gender, baseline CVD risk status)?

It was not possible to examine differences between adult subgroups given that no studies were found that met the inclusion criteria of this review to answer KQ1b regarding adverse effects of primary care relevant prevention interventions in normal weight adults.

KQ1d: How well is weight gain prevented or health outcomes maintained after an intervention is completed?

Nine studies that met the inclusion criteria for this review reported follow-up data for weight outcomes.[70,72,76,79,81,83,84,86,88] For seven studies with intervention durations <12 months, the data point closest to the immediate post and/or ≥12 months post baseline was used in the main analysis for KQ1;[72,79,81,83,84,86,88] this data was not used again to examine maintenance of intervention benefits. Three studies reported follow-up results at either 12 or 15 months post intervention completion;[70,76,79] however as shown in forest plot 1.1 (Evidence Set 1) only one of these studies showed a statistically significant effect in favour of intervention participants for the outcome of weight change in kg at the end of the intervention.[79] Therefore, the study by Lawton et al. (2008) reporting 15 month follow-up data after completion of a nine month exercise intervention is the only piece of evidence available to consider whether weight gain prevention and other health benefits are maintained after interventions are completed. In this study the outcomes that showed significant improvement at the post assessment point and therefore can be examined for long-term maintenance of these benefits were change in: weight in kg, waist circumference, total cholesterol, fasting glucose and SBP.

Evidence Set 11 provides the GRADE Evidence Profile Table (11.1), the GRADE Summary of Findings Table (11.1) and the forest plots (11.1 to 11.5) generated for the primary weight and secondary health outcomes at follow-up for the comparison between intervention participation and usual care. The single RCT (n=1,089) of moderate GRADE quality (downgraded for indirectness) included women with a baseline BMI of 29.2 and low/unknown risk of CVD. Primary care patients in New Zealand received either an exercise prescription with ongoing support to increase physical activity over a nine month period or usual care. Although intervention participants lost significantly more weight than control participants by the end of the intervention [(MD (95% CI) -0.60 kg (-0.63, -0.57), see forest plot 1.1)], there was a statistically significant increase in weight in the intervention group participants as compared to the control group from the point of intervention completion to 15 months later [MD (95% CI) 0.20 kg (0.17, 0.23), see forest plot 11.1]. Intervention participants gained significantly less waist circumference than control participants by the end of the intervention [(MD (95% CI) -0.50 cm (-0.53, -0.47), see forest plot 3.1)], however, there was no statistically significant difference in change in waist circumference in the intervention group participants as compared to the control group from the point of intervention completion to 15 months later [MD (95% CI) 0.00 cm (-0.03, 0.03), see forest plot 11.2]. Similar to the weight change in kg outcome, while intervention participants lowered their total cholesterol level significantly more than control participants by the end of the intervention [(MD (95% CI) -0.04 mmol/L (-0.044, -0.036), see forest plot 5.1)], there was a statistically significant increase in total cholesterol level in the intervention group participants as compared to the control group from the point of intervention completion to 15 months later [MD (95% CI) 0.03 mmol/L (0.027, 0.033), see forest plot 11.3]. Likewise, while intervention participants lowered their fasting glucose level significantly more than control participants by the end of the intervention [(MD (95% CI) -0.05

mmol/L (-0.051, -0.049), see forest plot 7.1)], there was a statistically significant increase in fasting glucose level in the intervention group participants as compared to the control group from the point of intervention completion to 15 months later [MD (95% CI) 0.04 mmol/L (0.038, 0.042), see forest plot 11.4]. Finally, while intervention participants lowered their SBP level significantly more than control participants by the end of the intervention [(MD (95% CI) -0.70 mmHg (-0.76, -0.64), see forest plot 9.1)], there was a statistically significant increase in SBP in the intervention group participants as compared to the control group from the point of intervention completion to 15 months later [MD (95% CI) 0.90 mmHg (0.84, 0.96), see forest plot 11.5].

KQ1e: What are common elements of efficacious weight gain prevention interventions?

Efficacious interventions were identified from studies included in the weight meta-analyses that showed a statistically significant effect size across all weight change outcomes reported by the study (see Evidence Sets 1 to 4). A total of five studies included interventions that resulted in statistically significant effects across all reported weight outcomes at the immediate post intervention assessment point.[65,67,71,74,79] Some of the components we examined in these efficacious interventions were adapted from the features list presented in the 2011 USPSTF review.[5] We also included intervention duration, focus and setting as we believed that primary care physicians would want to take such features into consideration when making program recommendations to their patients. Table 8 offers a summary of the common elements of the five efficacious interventions identified in this review. Our examination revealed that both the length of intervention and the number of sessions varied across these studies. Four of the five studies included an exercise component and provided individual sessions to some or all participants. There was no consistency in terms of context; interventions were delivered in various settings including community, home, primary care and clinics and in four different countries (Canada, Finland, US and New Zealand). It is also of interest to note that four of the five studies targeted only female participants and across all five studies the baseline BMI was in the overweight range.

Results for Contextual Questions

We searched Medline, EMBASE and PsycINFO from January 2007 to August 2013 for any papers, with any study design, that might answer the Contextual Questions (CQ).

CQ1: Is there evidence that the burden of disease, the risk-benefit ratio of prevention or treatment, the optimal prevention or treatment method/access, and implementation differ in any ethnic subgroups or by age, rural and remote populations, or lower SES populations?

Summary of Findings

A total of 79 articles were screened for evidence relating to this question and 20 were included in this review.[20,91-109] All 20 reports were based on Canadian data. International studies were not reported here as relevant Canadian data were available. No evidence relating to prevention

(Canadian or international) was identified. With regard to burden of disease, eight papers[20,93-95,98,99,103,104] considered variation by ethnic group. Two analyses reported estimates of the prevalence of obesity by age,[20,98] four reports discussed disease burden in rural and remote areas,[97,107-109] and eleven papers[20,91,92,96,98-101,105,106,108] considered the impact of SES. One paper[102] discussed optimal treatment in relation to aboriginal populations and to age. There was no information (Canadian or international) regarding optimal treatment method/access and implementation in rural or remote areas, or in relation to SES. Finally, no evidence (Canadian or international) relating to the risk-benefit ratio of treatment was identified.

Burden of Disease

Ethnic Subgroups

Three studies[20,93,94] reported a relatively high prevalence of overweight and obesity among Canada's Aboriginal communities. A diabetes screening study of Manitoba First-Nations adults[93] concluded that the prevalence of obesity in this group was among the highest reported for a Canadian First Nation community living on a reserve (approximately 50% of men and 65% of women as defined by BMI), and substantially higher than off-reserve Aboriginal populations or the Canadian population in general. A cross-sectional survey of three Aboriginal communities in the Northwest Territories[94] reported that 65% of participants were classified as being overweight or obese. A 2011 joint report from the Public Health Agency of Canada and the Canadian Institute for Health Information[20] used data from several surveys to provide a summary of the prevalence of obesity among all First Nations, Inuit, and Métis people in Canada. With the exception of Nunavut, the self-reported prevalence of obesity among Aboriginal peoples aged 18 years and older is higher than that of the general Canadian population in all Provinces and Territories. This difference is statistically significant in Québec, Ontario, Manitoba, Alberta, and in Canada overall. Almost 26% of Aboriginal adults (excluding First Nations on-reserve) were estimated to be obese, with estimates being similar for Inuit (23.9%), Metis (26.4%) and off-reserve First-Nations populations (26.1%). Over one-third (36.0%) of on-reserve First-Nations were estimated to be obese.

Four studies used data from the National Population Health Survey (NPHS) and the Canadian Community Health Survey (CCHS) to assess differences in disease risk factors (obesity included) among immigrant groups to Canada.[95,98,99,104] Chiu et al.[95]examined the age- and sex-standardized prevalence rates of eight cardiovascular risk factors among white, South Asian, Chinese, and black persons living in Ontario, and reported variation in obesity rates among the racial subgroups (Chinese 2.5%, South Asian 8.1%, black 14.1%, white 14.8%). Based on data obtained from the 2005 CCHS, Slater et al.[98] reported a significantly higher relative risk of obesity among white Canadians compared with visible minorities [RR 1.45 (95% CI 1.26, 1.66); P<0.002] and among non-immigrants compared with immigrants who have been in Canada less than 10 years [RR 2.04 (95% CI 1.44, 2.89); P<0.002]. The relative risk estimates for overweight and obesity combined were also higher in white Canadians [RR 1.25 (95% CI 1.17-1.33); P<0.002] and non-immigrants [RR 1.33 (95% CI 1.19, 1.49) P<0.002]. Similar findings were

reported by Bergeron et al.[104] who also used the 2005 CCHS data, looking specifically at persons living in three Canadian metropolitan areas (Toronto, Montréal and Vancouver). Setia et al.[99] assessed whether the BMI of different immigrant groups to Canada converged to Canadian population levels over a 12-year period (1994-2006). They found that the mean BMI of non-white immigrants (male and female) was lower than that of Canadian-born individuals, while the BMI of white immigrant males was similar to that of Canadian-born males at the time of immigration. The BMI of white immigrant females ranged between that of Canadian-born women and non-white immigrant women. After 12 years of follow-up, the mean BMI of all groups increased, however between-group differences (and similarities) remained constant, suggesting that convergence of BMI to Canadian levels may not occur over time in certain immigrant groups. A summary of the data reported in this study are provided in Table 9. Using a joint USA-Canada health survey to explore racial inequities in health,[103] Siddiqi et al. reported significantly higher odds of obesity among native-born American whites versus Canadian whites [OR 1.31 (95% CI 1.12, 1.55); P<0.05] and native-born American non-whites versus native-born Canadian non-whites [OR 2.80 (95% CI 1.75, 4.48); P<0.05], while the USA-Canada comparison of foreign-born whites and non-whites showed inter-country differences were not as pronounced or statistically significant.

Age

A paper by Slater et al.[98] reported age and sex-specific rates of obesity and obesity plus overweight combined, in Canadian adults aged 25-64. The data for this analysis were obtained from the 2005 CCHS and are provided in Table 10. A later analysis that also used data from the CCHS (2007-08)[20] reported that the prevalence of obesity in Canadian adults increases with age in both males and females, and peaks in the 55-64 age group for both sexes. The reported prevalence estimates are provided in Table 11.

Rural and Remote Populations

A provincial report on obesity[108] used data from seven cycles of the NPHS/CCHS to assess differences in obesity between rural and urban areas of Manitoba. Data from 2004 to 2008 showed obesity was lowest in urban areas (24.8-28.5% for males, and 21.7-28.3% for females), higher in rural areas (28.5-38.0% for males and 26.0-38.7% for females), and highest in northern regions (39.8-42.6% for males and 31.7-40.9% for females).

An analysis that used data from the CCHS (2003) to study geography and overweight in Québec[97] reported significantly increased odds of overweight among men living in rural areas [OR 1.17 (95% CI 1.02, 1.33); P<0.05], after adjusting for demographic, socio-economic, and lifestyle characteristics.

A report on the health of rural Canadians[109] used data from four national data sources including the CCHS (2000-01) and found an increased odds of overweight and obesity in rural versus metropolitan regions in Canada [ORs ranged from 1.20 to 1.41 depending on Metropolitan Influence Zone (MIZ) category and gender, and were all statistically significant at P<0.05]. At

the same time, healthy dietary practices such as eating at least five servings of fruits and vegetables per day were lower than in urban areas (31.1-36.5% depending on MIZ category versus 38.2% in urban areas).

Using data from the 2003 CCHS and the 2001 Census, a national study on healthy weights[107] reported that adult Canadians living in locations outside an urban core (i.e., urban fringe, urban area outside census metropolitan area, secondary urban core, rural fringe, and rural areas outside census metropolitan areas) are significantly more likely to report a BMI of 25 and greater (55-57% depending on location compared with 48% in an urban core; all comparisons between various locations and urban core were significant at $P<0.05$ level). One explanation provided was that people living in a city core are more likely to walk or bike, while those living in outer-areas may be more car-dependent.

Socioeconomic Status

Several Canadian studies relating obesity and SES have been conducted using data from the NPHS and the CCHS.[20,91,92,96,98-101,105,108]

An analysis conducted by Slater et al.[98] reported higher odds of obesity among Canadians with lower levels of education (ORs ranged from 1.32 to 1.40 depending on education level, compared with post-secondary graduates, and all comparisons were statistically significant at the $P<0.002$ level), and lower household incomes (ORs ranged from 1.20 to 1.33 depending on income level, compared with ≥$80,000/year, and all comparisons were statistically significant at the $P<0.002$ level). Analyses were adjusted for age and sex.

The authors of one study[91] reported variation across provinces in the relationship between income and BMI, and suggested that a possible contributing factor may be access to fresh produce which can be affected by regional availability, food prices, as well as by differing purchasing power due to variability in taxation rates.

One report[20] of an analysis conducted with data from the 2007-08 CCHS found that obesity tends to decrease as income increases among females, however this pattern was not seen in males, in whom obesity was relatively constant regardless of income. This trend was observed in the general population as well as in Aboriginal peoples. An inverse relationship between education and obesity in Canadian men and women was also reported, in both the general population as well as in Aboriginal peoples.

Godley et al.[92] explored the relationship between BMI and SES as measured by income and education after controlling for sociodemographic variables, and that found their results differed by the measure of SES used and by gender. Education was strongly and consistently inversely related to BMI for both men and women. The relationship between income and BMI was also consistently inverse in women; however men in the highest quartile of income had a higher BMI than men in the lowest income quartile. The authors suggested that cultural factors, as represented by educational attainment, may be more important than material factors, as represented by income, in explaining social class disparities in BMI.

McLaren et al.[96] studied the association between SES and BMI among Canadian men and women in 1978 and 2005. The 1978 data were obtained from the Canada Health Survey. They found an inverse relationship between BMI and education for both genders and at both time points, with no narrowing of this relationship over time. The observed association was stronger among women [ordinary least square regression coefficients for having at least a bachelor's degree versus less than a complete bachelor's degree were -0.78 (95% CI -1.4, -0.17) in 1978 and -0.57 (95% CI -1.05, -0.09) in 2005 among men; for women these coefficients were -0.96 (95% CI -1.8, -0.14) in 1978 and -1.3 (95% CI -1.9, -0.67) in 2005]. There was no clear relationship between BMI and income for men, while this association for women was inverse and changed between the two time periods, with women in the middle income category being heavier according to the 2005 data. The authors suggested that this may be due to changes in women's participation in the workforce between the two time periods.

An analysis that assessed the BMI of adult (aged 18-54 years) immigrant men and women over a 12-year period[99] showed an inverse but not significant relationship between income and BMI, and reported a significantly lower BMI among all higher levels of education (at least secondary education), after adjusting for age, sex, visible minority status, marital status, and other factors.

In another study by McLaren et al.[100] the relationship between BMI and occupational prestige was studied. After adjusting for income and education, the authors found that women in higher-ranking positions tended to have lower BMI scores; however this relationship was not maintained after adjusting for education. Men in supervisory/managerial positions tended to be heavier than men in lower-ranking positions. The authors suggested that males in supervisory roles may benefit from a larger body size.

Combining data from the CCHS (2000-2004) and 2001 Census tract-level neighbourhood data, Matheson et al.[101] explored the relationship between neighbourhood material deprivation and BMI. While they found a positive relationship between these two factors in general [a one-unit increase in the neighbourhood material deprivation scale (scale range: -2 to 6) was associated with an increased BMI score of 0.12 kg/m^2], the effect for men and women was different, with higher mean BMIs reported among men living in more affluent neighbourhoods (1.0 point higher than men in more disadvantaged areas), and women living in poorer neighbourhoods (1.8 points higher compared with less deprived areas).

A study by Lee et al.[105] reported that the prevalence of obesity increased for all levels of income (between 2.8-4.1%, depending on income quartile) between 1993 and 2005.

An analysis of the Manitoba population[108] found decreased odds of obesity among people with at least a high-school education [OR 0.74 (95% CI 0.72, 0.76) $P<1E^{-10}$], and decreased but less pronounced odds of obesity among persons with higher household income (i.e., >$60,000 per year) [OR 0.9988 (95% CI 0.9977, 09988); P<0.01].

Using data from the Ontario Food Survey (1997-98), Ward et al.[106] explored the relationship between socioeconomic variation in lifestyle factors and overweight and obesity. The authors

found a significant inverse relationship between high risk adiposity and income (β=-0.22, P<0.05) and education (β=-0.19, P<0.05) for women, but this relationship did not hold for men. Other potential contributing factors considered in the model included fruit and vegetable intake, long-term physical activity, and smoking status. Only fruit and vegetable intake was a mediator in the inverse relationship between high risk adiposity and education in women.

Optimal Treatment Method/Access and Implementation

Ethnic Subgroups and Age

A study by Schaefer et al.[102] assessed dietary intake and adequacy among Inuit women of childbearing age living in three communities in Nunavut. The authors reported that the prevalence of overweight and obesity among women living in these communities was >70%. There was inadequate consumption of dietary fiber and nutrients in general, and non-nutrient dense foods contributed to more than 30% of energy intake. The authors recommended that strategies be adopted to target the replacement of non-nutrient-dense foods with traditional foods and other nutrient-rich foods such as fruits, vegetables and grains.

CQ2: What are the resource implications and cost-effectiveness of overweight and obesity prevention/treatment in Canada?

Summary of Findings

Twenty-nine articles were screened for evidence relating to the resource implications of obesity and the cost-effectiveness of its treatment in Canada. Five articles relating to the resource implications of obesity treatment in a Canadian context were identified.[20,108,110-112] With regard to cost-effectiveness, no full Canadian economic evaluations were identified. The only economic assessment found was for a lifestyle modification program[113] and it did not report cost-effectiveness ratios. Seven systematic reviews of economic evaluations[114-120] were also identified. Two of the reviews[117,119] also conducted *de novo* economic evaluations; however the vast majority of the studies included in the seven systematic reviews were not conducted from a Canadian perspective. It is difficult to draw conclusions regarding the cost-effectiveness of interventions because assessments were conducted from the perspective of other jurisdictions; however the findings of the reviews have been summarized below for informative purposes.

Resource Implications

Several Canadian studies have used population-attributable fractions obtained from surveys and the literature, together with data from a national burden of illness study **(***Economic Burden of Illness in Canada*) to estimate the economic costs attributable to obesity and overweight.[20,110,111] Moffat et al.[110] estimated the cost of obesity and overweight in Alberta in 2005. They estimated the total direct and indirect costs for that year to be $1.092B, and caregiver costs to be $181.8M, for an annual total of $1.274B. Anis et al.[111] estimated the economic burden of overweight and obesity at the national level, reporting total direct costs of $6.0B in 2006. An analysis done for a national report on obesity[20] also used this methodology to examine the change in the economic

burden of obesity between 2000 and 2008; costs were estimated to have increased from $3.9B ($1.55B direct and $2.33B indirect costs) to $4.6B ($1.98B direct and $2.63B indirect costs) over that time period.

Tarride et al.[112] reported the economic burden associated with BMI in Ontario for 2000-01. Linking data from the CCHS to three administrative databases and using multivariate analyses, the authors found that >50% of adults were overweight or obese, and that hospitalization costs were 40% higher and physician costs were 22% higher among the overweight and obese, compared with the normal weight population.

A Manitoba report[108] examined health care resource use among the adult overweight and obese. The authors considered the use of physician services, prescription drug use, hospitalization rates, inpatient days, rates of specific procedures (i.e., joint replacement, cholecystectomy, cardiac catheterization and revascularization), and home care. The authors reported that the obese group typically had the highest rates of health service use, and any differences between the normal and overweight groups tended to be small. This was the case for most health services examined, with the exception of cholecystectomy rates (similarly high in overweight and obese females), cardiac catheterization and revascularization rates (high in overweight and obese males, and comparatively low in females for all levels of BMI), homecare services (relatively similar across gender and BMI levels), and personal homecare (highest in the normal weight category).

Cost-effectiveness

Gagnon et al.[113] compared the effectiveness and costs of one year of an interdisciplinary intervention consisting of individual counselling every six weeks and 25 group seminars, to group seminars alone. Participants included men and women with a BMI of $\geq$27 kg/m^2. Participants in the intervention group had clinically and statistically significant changes in average weight (4.9 kg) and waist circumference (5 cm), while no significant changes were observed in the group seminar arm. The estimated cost of the combined intervention was CDN$733.06/year, while that of the seminar alone was CDN$81.36/year. The authors concluded that participation in low-cost, moderate-intensity interdisciplinary approaches combined with group seminars leads to clinically important weight loss.

Wieland et al.'s systematic review of computer-based interventions for weight-loss or weight maintenance in the overweight or obese[114] included three American economic evaluations on weight loss, however the authors considered two of the studies to be technologically outdated, and the third was conducted among military personnel and its broader applicability was questioned by the authors. Therefore the details of this review are not reported here.

A systematic review of economic evaluations of adult weight management interventions[115] included 44 articles; 21 of behavioural interventions, 12 of surgical interventions, and 11 of pharmacological plus behavioural interventions. The reviewed studies originated in the United States (n=22), Australia (n=4), the Netherlands (n=4), and various other countries (n=10). The objective of the review was to assess the methods used in each of the studies, and to determine

whether methodology affected the results of the evaluations. While quality of life is an important outcome in assessing the impact of obesity interventions, only 12 studies considered this outcome. Among these 12 studies, the intervention was more cost-effective than standard of care in only three of these analyses, however it is unclear to what extent modelling methods could explain this finding. The authors found that many of the models used in the evaluations were not suitable for chronic diseases with changing health risks, and called for methodological improvements in terms of using recommended practices in economic modelling and a better assessment of the long-term consequences of obesity.

Lehnert et al.[116] conducted a systematic review of the long-term cost-effectiveness (defined as ≥40 years) of obesity prevention interventions. The authors identified 18 cost-utility analyses of 41 interventions (21 behavioural, 12 community, and 8 environmental) that originated in the US, Australia, Mexico, the Netherlands, the UK, New Zealand, and Switzerland. They reported that 24 interventions were shown to be cost-effective. Ten interventions (six community-based and four behavioural) had cost-utility ratios of >$50,000US (generally considered to be not cost-effective). Finally, seven environmentally-targeted interventions were reported to be cost-saving.

Loveman et al.[118] published a systematic review of the clinical and cost-effectiveness of long-term weight management schemes for adults. The authors identified 419 studies in their cost-effectiveness searches, but none met their full inclusion criteria. They included two of these studies in the review, nonetheless, with a cautionary note as to their failure to meet all inclusion criteria (i.e., one study used prescription anti-obesity drugs in some participants, and the other study had a follow-up of less than 18 months). One study was conducted from a US perspective, and the other in the UK. The studies used lifetime chronic disease models and included both the costs and benefits of avoiding chronic illnesses. Both studies used some combination of diet, exercise, pharmacotherapy and behavioural interventions as comparators, and found all the interventions to be cost-effective. The most cost-effective and efficient strategy was a combined intervention of diet, exercise and behavioural modification with a cost per QALY gained of $12,640US. The diet-only strategy was less effective and more costly than routine care, the diet and pharmacotherapy and diet and exercise strategies were less effective and less costly than the triple intervention.

Neovius and Narbro[120] published a systematic review of cost-effectiveness studies of pharmacological plus behavioural anti-obesity treatments. They identified 14 studies (11 cost-utility and three cost-effectiveness analyses), nine of which were on orlistat, four on sibutramine (withdrawn from the Canadian market due to side effects), and one on rimonabant (not approved by the FDA or Health Canada and eventually withdrawn from the UK market). All analyses were conducted in western European countries or the United States. The authors found that all the economic evaluations reported the interventions to be cost-effective, but noted that uncertainty remained regarding weight loss sustainability and long-term health benefits and utility gains associated with weight loss.

A systematic review of the clinical and cost-effectiveness of using drugs to treat obese patients in primary care was conducted by Ara et al.[117] The authors identified 14 published articles on the cost-effectiveness of orlistat, sibutramine, and rimonabant and found that the studies generally reported cost-effective results. The authors then conducted an independent economic evaluation of all three drugs from a UK perspective, which modelled diet and exercise plus one of the pharmacological plus behavioural alternatives or placebo, on changes in body mass and the occurrence of various obesity-related health events and states (e.g., stroke, myocardial infarction, diabetes). All treatment alternatives were found to be highly cost-effective versus placebo (range: £557-£3553 per QALY). Given the dangers subsequently found to be associated with sibutramine and rimonabant, the authors acknowledged that apart from the clinical implications, accounting for the adverse effects later associated with these treatments in the economic analyses would have likely rendered these two treatments not cost-effective.

Bogers et al.[119] explored the relationship between the costs of lifestyle interventions and weight loss in overweight adults. After examining 14 reviews as well as the results of a systematic MEDLINE search, the authors identified and selected 19 randomized trials that described 31 interventions (countries of origin not provided). The regression model that they constructed to explore the relationship between intervention costs and weight loss explained 47% of the variance in weight loss, and reported that clinically-relevant loss of at least 5% of baseline body weight was seen for interventions which cost as little as €110. However the effects on weight loss seemed to level off at about 6%, even with growing costs.

CQ3: What are patients' and practitioners' values and screening preferences regarding overweight and obesity prevention and/or treatment?

Summary of Findings

Six articles were screened and three[121-123] were found to contain relevant information relating to this question.

Patients' Values and Preferences

Garip and Yardley[122] synthesized the findings of 17 qualitative studies (eight from the USA and Canada, five from the UK, three from Europe, and one from Australia) of the views and experiences of overweight and obese persons who participated in weight management programs. A total of 290 people participated in these studies, and the majority (at least 224) were women. The authors derived 11 themes from the reviewed studies, specifically: 1. *Health concerns related to excess weight* were a motivating factor for participation in weight management programs; 2. *Expectations of weight management* varied and may influence weight management attempts; 3. *Attributions for weight gain and the maintenance of excess weight* were often made when people were not trying to manage their weight; 4. *Psychological facilitators* included mental preparedness or understanding one's eating patterns; 5. *Psychological barriers* included lack of will-power, lack of knowledge or skills, psychological problems, or reverting to old dietary habits; 6. *Self-perception and body image* (both negative and positive) were important

factors in motivation; 7. *Stigmatizing experiences relating to excess weight* may hinder some people from taking up public activities to manage their weight; 8. *Socio-cultural factors* (e.g., support vs. pressure from family and friends) may facilitate or hinder weight loss; 9. *Environmental factors* such as barriers to healthy foods and safety (i.e., for physical activity in one's neighbourhood); 10. *Experiences with weight management programs* including support and contact with health professionals and peers, as well as the structure provided by the program, may have a positive influence on outcome; and 11. *Positive outcomes of participating in a weight management program*, such as weight loss, psychosocial benefits, improved mobility, self-acceptance, and relationships with others, may encourage individuals to adhere to weight management efforts.

No evidence on patients' values or preferences for screening was identified. The lack of available evidence may be due to the fact that our search for the contextual questions was limited to the past five years; therefore earlier studies which looked at patient preferences for screening for obesity would not appear in our results.

Practitioners' Values and Preferences

Piccinini-Vallis et al.[121] conducted a survey of practitioners' awareness of and familiarity with the *2006 Canadian Clinical Practice Guidelines on the Management and Prevention of Obesity in Adults and Children,* including the frequency with which practitioners measured weight, calculated BMI, and measured waist circumference in overweight and obese patients. A random sample of 425 general practitioners were selected to complete a mailed questionnaire, and 36.9% (n=157) responded. Almost 38% of the respondents reported being aware of the guidelines, and had a mean familiarity rating of 2.72 (1=not at all familiar, 5=very familiar). Physicians who were aware of the guidelines were more likely to calculate BMI. Other factors that predicted the likelihood of calculating BMI were physician's own BMI and access to an electronic medical record (EMR). Measurement of waist circumference was more likely if the physician was in a group (vs. solo) practice. Physicians in urban practices were significantly more likely to be aware of the guidelines than those in rural practices.

In the *2006 Canadian Clinical Practice Guidelines on the Management and Prevention of Obesity in Adults and Children,*[123] Dent et al. discuss physician-related barriers to weight management and physicians' attitudes toward overweight and obesity. Based on a literature search, they concluded that only 40% of obese people receive recommendations from their physicians regarding weight loss and weight management, even when they have related comorbidities. Based on comparison of surveys conducted before and after 1999, obese people may be subject to negative bias by the medical community, which may in turn be a barrier to the care of these individuals. A tendency to blame patients for their obesity was a consistent view reported across physicians, nurses, medical students, and dieticians.

General Summary of Evidence for CQ1, CQ2 and CQ3

Data Gaps

- Studies relating to the risk-benefit ratio of prevention interventions were not identified;
- Studies regarding optimal prevention method, access, and implementation were not identified, and only limited information was found on treatment (one study);
- Canadian economic evaluations of overweight and obesity interventions are lacking

Findings

- Higher rates of obesity have been observed among Canada's Aboriginal peoples compared with the general Canadian population;
- The rate of overweight and obesity among Inuit women of childbearing age is substantial, and nutritional deficits are common;
- Visible minority immigrants tend to have lower BMIs than the general Canadian population, both at the time of immigration and over time, while the BMIs of non-visible minority immigrants are more similar to those of native-born Canadians;
- Average Canadian overweight and obesity rates increase with age and peak between the ages of 55 and 64, after which time they decline;
- Obesity tends to be higher in rural areas (compared with urban areas) and may be even higher in northern regions. Possible explanations may be differences in dietary practices, food access and physical activity;
- There is a general inverse relationship between obesity and socioeconomic status, however, this relationship has been found to differ by gender and by measure of socioeconomic status, and may be mediated by factors such as regional taxation rates, dietary practices and food access, type of profession, and other societal factors;
- Recent estimates of the economic burden of overweight and obesity in Canada are significant and vary between $4.6B (2008 direct and indirect costs) and $6.0B (2006 direct costs only) per year;
- Costs of healthcare among the overweight and obese combined are higher than those of the general Canadian population; however one provincial study found that obese persons have higher rates of use of some health care services compared with overweight and normal-weight individuals, which tend to be similar;
- A large proportion of international economic evaluations of the prevention and treatment of obesity report these interventions as cost-effective;
- Patients' preferences and values regarding overweight and obesity prevention and treatment are based on multiple and sometimes complex internal and external factors. Practitioners' attitudes towards obesity may influence patients' decisions to seek or access treatment;
- Physicians' measurement of weight or BMI is greatly influenced by awareness of guidelines. Other influences include physicians' personal BMI, access to electronic medical records,

whether the practice is based in an urban or rural area, and whether physicians are in group versus solo practice.

CQ4: What are the most effective (accurate and reliable) risk assessment tools identified in the literature to assess future health risk as a result of obesity?

One study was found that examined a risk assessment tool for obesity[124] and one study was found that looked at assessing mortality risks in already obese adults.[125]

A study conducted with French people assessed the relationship between dietary quality and the development of obesity.[124] The study assessed and compared the predictive value of six different dietary scores on relative weight change and risk of obesity after 13 years of follow-up. The six dietary scores were the French Programme National Nutrition Santé-Guideline Scores (PNNS-GS), the Dietary Guidelines for Americans Index (DGAI), the Diet Quality Index-International (DQI-I), the Mediterranean Diet Scale (MDS), the relative Mediterranean Diet Score (rMED) and the Mediterranean Style Dietary Pattern Score (MSDPS).This study included participants aged 45-60 years at baseline who provided 24-hour dietary records for two years with no missing dietary, anthropometric or covariate data (n=3,151). Among the non-obese men at baseline, 123 became obese and among the 1,385 non-obese women, 84 became obese. For men the odds ratios (OR) of becoming obese after 13 years associated with one standard deviation increase in dietary score values ranged from 0.63 (95% CI 0.51, 0.78) for DGAI to 0.72 (95% CI 0.59, 0.88) for MDS (fully adjusted models), while the MSDPS displayed non-significant associations. In women, no association between the dietary scores and obesity risk were found. A non-significant risk reduction was found for one standard deviation increase of rMED [OR 0.82 (95% CI 0.65, 1.03)], DGAI [OR 0.86 (95% CI 0.68, 1.08)] and PNNS-GS [OR 0.94 (95% CI 0.73, 1.21)].

A study in Texas examined whether the Edmonton Obesity Staging System (EOSS), was helpful to identify obese individuals who are at greater mortality risk.[125] Data from the Aerobics Center Longitudinal Study (n = 29,533) were used to assess mortality risk in obese individuals by EOSS stage [follow-up (SD), 16.2 (7.5) years]. The effect of weight history and lifestyle factors on EOSS classification was explored. Obese participants were categorized, using a modified EOSS definition, as stages 0 to 3, based on the severity of their risk profile and conditions (stage 0, no risk factors or comorbidities; stage 1, mild conditions; and stages 2 and 3, moderate to severe conditions). Compared with normal-weight individuals, obese individuals in stage 2 or 3 had a greater risk of all-cause mortality [stage 2 hazard ratio (HR) (95% CI), 1.6 (1.3, 2.0); stage 3 HR, 1.7 (1.4, 2.0)] and cardiovascular-related mortality [stage 2 HR, 2.1 (1.6, 2.8); stage 3 HR. 2.1 (1.6, 2.8)]. Stage 0/1 was not associated with higher mortality risk. Lower self-ascribed preferred weight, weight at age 21, cardiorespiratory fitness, reported dieting, and fruit and vegetable intake were each associated with an elevated risk for stage 2 or 3. The authors suggest that given the health risk associated with the weight cycling that many obese people experience, physicians should consider promoting weight maintenance as opposed to weight loss especially for patients who score an EOSS stage 0 and 1.

Results for Supplemental Questions

SQ1: Is there direct evidence that primary care screening programs for adult overweight or obesity improve health outcomes or result in short-term (12 month) or sustained (>12 month) weight loss or improved physiological measures?

For the supplemental questions, we did not find any studies that examined primary care screening programs for adult overweight or obesity that met the inclusion criteria for this review.

Chapter 4: Discussion, Limitations and Conclusion

Discussion

To address the questions of interest, this review used a systematic review process and the quality of the included evidence was evaluated using the GRADE system.[59] A substantial body of high level (RCT) but indirect evidence was found to answer most of the key questions. To our knowledge, this is the first systematic review with meta-analyses of prevention of obesity in adults. We are aware of one other recent review that examined a similar question but with different inclusion/exclusion criteria.[126]

Recent evidence from a large cohort study conducted in the United States suggests that non-obese adults gain, on average, 0.8 pounds (about 0.36 kg) per year.[127] The results of this study found that diets high in unhealthy foods, low physical activity levels and other unhealthy lifestyle behaviours are independently associated with long-term weight gain. Gaining less than half a kg over the course of a year may not appear clinically meaningful.[127] Over time however, the accumulated weight can become substantial (estimated at three to four kg over eight years)[128] and with this increase comes greater risk for obesity related health problems.[33-35,38,39] Greater health risks alongside the dramatic increase in the prevalence of obesity in Canadian adults over the last 30 years (approximately 8% in 1980 to approximately 25% in 2011)[18,23] presents a context ripe for prevention.

Weight gain prevention programs targeting normal weight adults would expect to demonstrate weight maintenance in the intervention participants compared to a hypothesized increase in weight[127] in control group participants. In this review we considered four measures of weight gain prevention: weight in kg, BMI, waist circumference, and total % body fat (see Evidence Sets 1 to 4). Across these outcomes and across studies, the programs were successful not only in stabilizing weight but also in producing weight loss by the end of the interventions. In many studies, those in the control groups also lost weight, but a smaller amount than intervention participants. Intervention participants lost 0.73 more kg, lowered their BMI by 0.24 kg/m^2 more, reduced their waist circumference by an additional 0.95 cm, and lost 1.27% more total body fat as compared to control participants at post intervention assessment. For those in an overweight or obese category, these changes do not represent clinically meaningful reductions in weight. However, this was not the goal of these interventions, which was to prevent weight gain. With that goal, the benefits of these interventions could become apparent over time; aside from one study mentioned below, long term follow-up data are not available to draw such conclusions.

Only one study was available to address the key question about the long-term benefits of weight gain prevention programs for the primary outcomes of this review. The results of this research showed that intervention participants actually gained weight and increased their waist circumference following completion of the program (See Evidence Set 11).[79] There was a statistically significant increase in weight in the intervention group as compared to the control group from the point of intervention completion to 15 months later [MD (95% CI) 0.20 kg (0.17,

0.23)]. There was no difference between intervention and control participants in terms of waist circumference from the point of intervention completion to 15 months later [MD (95% CI) 0.00 cm (-0.03, 0.03)]; both groups increased on this measure by 1.4 cm.

Sensitivity analyses performed on studies providing change in weight in kg and BMI data found no significant differences between any sub-groups (see Evidence Sets 1 and 2). None of the specified categorizations (i.e., type of behavioural intervention, duration of intervention, gender, baseline CVD risk status, baseline mean BMI, and study risk of bias rating) explain the variation across this evidence. The moderate to high statistical heterogeneity across studies in most sub-analyses is most likely due to small versus large treatment effects observed across studies.

In addition to the primary weight outcomes we examined the available evidence for changes in six secondary health outcomes: total cholesterol, LDL-C, fasting glucose, incidence of T2D, SBP and DBP (see Evidence Sets 5 to 10). Pooled effect estimates for some of the secondary health outcomes were significant in favour of the interventions. Intervention participants had small but significantly greater reductions in total cholesterol level (0.06 mmol/L), LDL-C level (0.06 mmol/L), and fasting glucose level (0.04 mmol/L) compared to control participants at the post intervention assessment. There was no evidence that intervention and control groups differed in terms of changes in systolic or diastolic blood pressure or on the likelihood of being diagnosed with new onset T2D. Only one study was available to address the key question about the long-term health benefits of weight gain prevention programs.[79] None of the benefits in terms of reduced total cholesterol, fasting glucose and SBP levels that were observed in intervention participants at the end of the nine month exercise program were maintained over the next 15 months. In fact, the intervention group showed significantly greater increases in all three of these outcomes compared to the control group at the follow-up assessment point.

The benefits of program participation must be considered in light of any harm induced by or associated with the intervention. As expected, and consistent with the results of the companion treatment review for the behavioural interventions, very few included studies reported on adverse effects. No harms of interest to this review were reported (labelling; disordered eating; psychological distress such as anxiety, depression and stigma; nutritional deficits; cost). However six of the 26 studies did address adverse effects in their result sections.[66,74,79,84,87,88] Half of these studies reported no adverse events associated with participation in the interventions and two showed no significant differences between exercisers and those in the control groups in terms of injuries, falls or serious adverse events. Only one study found significantly more falls and injuries were sustained by those taking part in the exercise program compared to control group participants.

To answer the key question about common elements of efficacious interventions we identified all studies that showed a significant effect across all reported weight outcomes of interest. Across the 26 included studies, only five met this criterion.[65,67,71,74,79] There were few common elements across these interventions. Four programs included an exercise component and provided individual sessions to some or all participants. Four interventions targeted women only and in all five studies the baseline BMI was in the overweight range. There was variation across the

interventions in terms of length and number of sessions. There was also little consistency in terms of context; interventions were delivered in various settings (community, home, primary care, clinics) and in four different countries (Canada, Finland, US and New Zealand).

Our review of the literature for the contextual questions provided important information for understanding the unique nature and extent of the obesity problem in Canada. However there was limited information available to explore the questions as they relate to prevention of overweight and obesity. No studies relating to the risk-benefit ratio of prevention interventions or regarding optimal prevention methods, access and implementation were identified. Except for one study that assessed and compared the predictive value of six different dietary scores on relative weight change and risk of obesity after 13 years of follow-up, the contextual questions search found little evidence about effective risk assessment tools.

Limitations

Limitations of this review may affect the validity and generalizability of the findings.

This review is unable to conclusively answer the question regarding whether primary care relevant prevention interventions lead to short-term or sustained weight gain prevention or to improved health outcomes in normal weight adults. The search found a single older study that included only normal weight adults that met the inclusion criteria of this review.[73] Given scant direct evidence to answer the key question of this prevention focused review, the criteria were expanded to allow studies that included mixed weight populations, that is groups that included normal weight as well as overweight or obese adults. Twenty-five studies were found that met the expanded inclusion criteria. Therefore, all the analyses in this review provide indirect evidence to address the key question and sub-questions. The use of indirect evidence reduces confidence in the estimates of effect.

Most of the evidence used to answer the key questions was taken from studies that were assessed as having unclear or high risk of bias, primarily due to the lack of information about or lack of procedures to ensure random sequence generation, allocation concealment and blinding of outcome assessment as well as other sources of bias (i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. These circumstances present risk of bias that could impact results and effect sizes. Potential reporting bias was also identified across a number of outcome/comparison-based study groupings. These concerns further reduced the strength of the evidence, resulting in low and sometimes very low quality GRADE ratings which reduce confidence in the pooled estimates of observed effect.

Results presented for the secondary health outcomes (total cholesterol, LDL-C, fasting glucose, blood pressure, incidence of T2D) should be interpreted with caution as we only included interventions that had a focus on weight gain prevention; we did not include studies of, for

example, effectiveness of behavioural interventions on fasting glucose level if the paper did not report weight change outcomes.

There was very little evidence (one study) that met our inclusion criteria to answer the question regarding how well weight gain prevention and improved health outcomes are sustained after interventions are complete. Therefore, results for this question should be interpreted with caution.

Studies were categorized as diet, exercise, diet and exercise or lifestyle, yet each category represents a wide range of intervention approaches. A high degree of heterogeneity was noted in all groups of studies and a review of efficacious interventions revealed many differences, thus providing limited guidance on key components to include in practice.

No studies were found that examined primary care screening programs for adult overweight or obesity that met the inclusion criteria; thus none of the supplemental questions could be answered.

Finally, we restricted our search to papers in English or French, thus we may have missed the opportunity to analyze data from papers written in other languages.

Conclusion

Greater health risks associated with obesity alongside the dramatic increase in the prevalence of obesity in Canadian adults over the last few decades reinforces the need for preventive action. Interpreting the evidence presented in this systematic review is challenging. Adults who were motivated to join a weight gain prevention program not only did not gain weight, but actually lost a small amount of weight. These benefits were also achieved without experiencing adverse effects. For participants who were of normal weight to begin with, we cannot know if this small weight loss was clinically meaningful, except to note that they are not increasing health risks associated with weight gain. It is difficult to know how primary care practitioners might motivate normal weight people to consider participating in such interventions. In summary, this review was unable to conclusively determine if behaviourally-based primary care relevant prevention interventions lead to short-term or sustained weight gain prevention and improved health outcomes in normal weight adults. Intervention research involving normal weight samples with long term follow-up is required to effectively answer this question.

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Figures

Figure 1: Analytic Framework

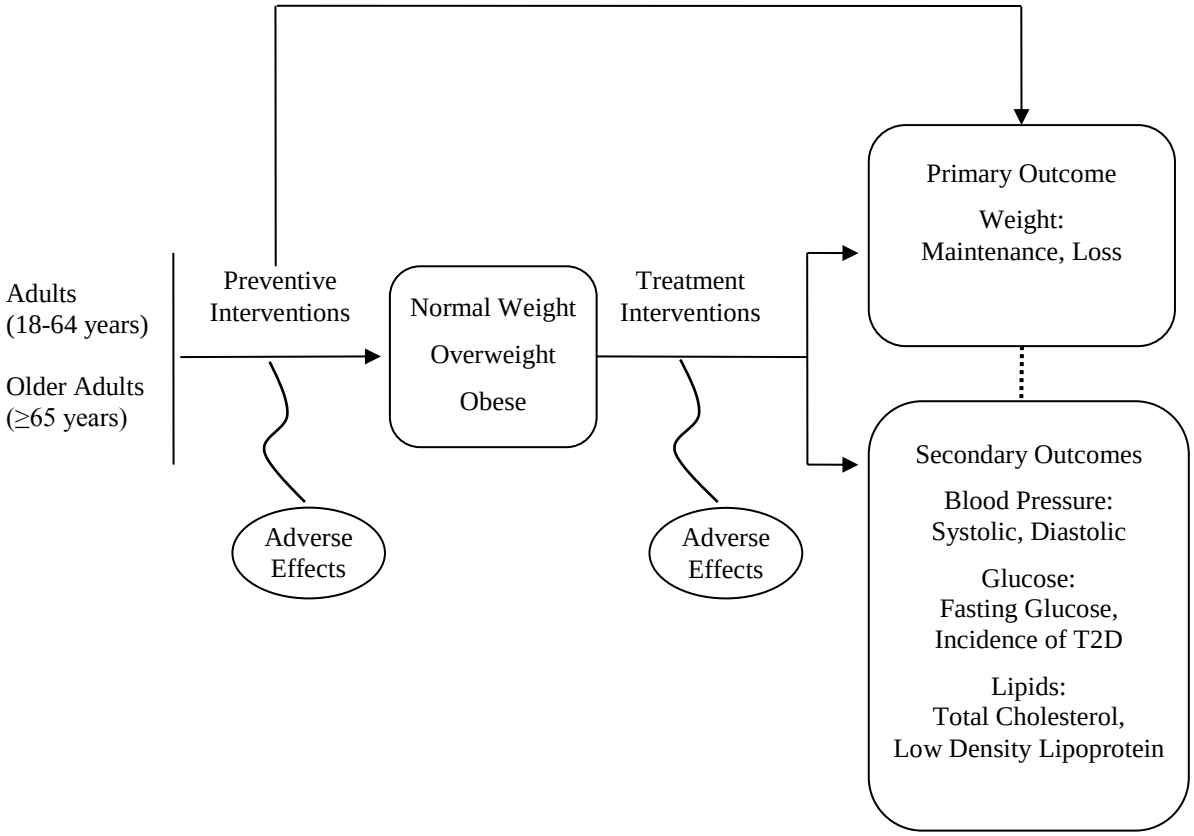
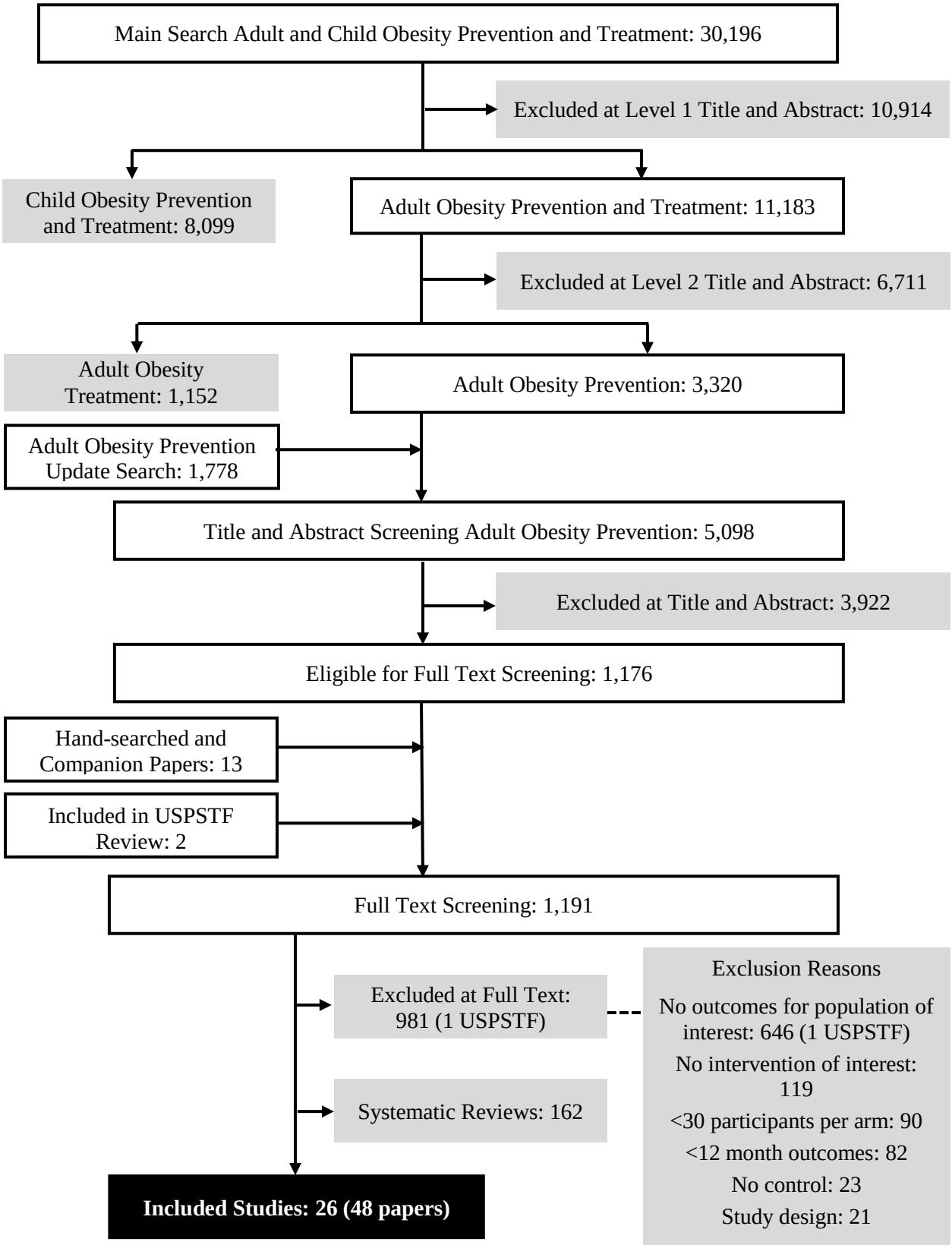


Figure 2: Search Results



Tables

Table 1: Factors Associated with Weight Gain and/or Obesity

Category	Condition/Disease
Neuroendocrine	• Cushing's syndrome[129] • hypothalamic obesity[130] • hypothyroidism[131] • polycystic ovary syndrome[132] • growth hormone deficiency[133] • weight cycling[134]
Congenital	• Prader-Willi syndrome[135] • Lawrence-Moon-Biedle syndrome[136]
Dietary	• overeating relative to energy expenditure[137] • increased dietary fat intake[138] • frequent fast-food consumption[139] • night-eating syndrome[140,141]
Lifestyle	• sedentary lifestyle[28] • decreased physical activity[142] • sleep deprivation[30] • smoking cessation[143] • pregnancy/post-pregnancy[144] • poor diet[145] • skipping meals[145] • snacking[146] • consuming sugary soft drinks[147]
Psychiatric/Psychological/ Psychosocial	• binge eating and other eating disorders[137] • seasonal affective disorder[148] • depression/anxiety[149,150] • boredom[151] • stress[152]
Drugs	• antipsychotics[153] • antidepressants[154] • anticonvulsants[155] • corticosteroids[156]
Biochemical	• genetics[27] • metabolism[27] • injury[157] • mobility issues[158] • intrauterine growth[159]
Socio-Economic Determinants	• education[160] • income[160]

Table 2: Health Consequences of Obesity

Organ System	Condition/Disease
Cardiovascular	• coronary artery disease • hypertension • venous thromboembolism • varicose veins and venous hypertension
Respiratory	• obstructive sleep apnea • hypoventilation syndrome • cor pulmonale
Neurologic	• stroke • intracranial hypertension • meralgia paresthetica
Gastrointestinal	• cholelithiasis • gastroesophageal reflux disease • hepatic steatosis • non-alcoholic steatohepatitis • abdominal and inguinal hernias • colon cancer
Genitourinary	• urinary stress incontinence • hypogonadism • amenorrhea • prostate cancer • breast cancer • uterine cancer
Endocrine/Metabolic	• dyslipidemia • impaired glucose tolerance • type 2 diabetes • metabolic syndrome • infertility • polycystic ovarian syndrome • hypothyroidism • renal disease
Musculoskeletal	• degenerative osteoarthritis • low back strain
Skin	• cellulitis • intertrigo
Psychological	• depression • social and work-related discrimination

Table 3: Summary of Risk of Bias Assessment of Included RCTs

Study	Sequence Generation	Allocation Concealment	Blinding of Outcome Assessors			Incomplete Reporting			Selective Reporting	Other Bias
			OBJ	SUB	S-R	OBJ	SUB	S-R		
Babazono 2007[85]	U	U	L	U		L	L		L	H
Broekhuizen 2012[82]	L	L	L	U		L	L		L	U
Burke 2003[72]	L	U	L	U		H	H		L	U
Carty 2011[67]	L	U	L	L		H	L		L	U
Elley 2003[87]	U	U	L	U		L	L		L	U
Eriksson 2011[84]	L	L	L	U	H	L	L	L	L	U
Forster 1988[73]	U	U		U			L		L	H
Friedenreich 2011[74]	L	L	L	L		L	L		L	H
Harris 2012[81]	L	U		L			L		L	L
Hivert 2007[68]	L	L	L	U		L	L		L	U
Imayama 2011[66]	L	U	L	L		L	L		L	H
Kanaya 2012[83]	L	L	L	U		L	L		L	U
Kastarinen 2002[65]	L	U	L	L		L	L		L	U
Khare 2012[86]	U	U	L	U		H	H		L	H
Lawton 2008[79]	L	L	L	L		L	L		L	U
Levine 2007[70]	U	U		U			L		L	H
Mensink 2003[78]	U	U	L	U		H	H		H	H
Roderick 1997[89]	U	U	L	U		L	L		L	U
Sacerdote 2006[88]	L	U		H			L		L	U
Simkin-Silverman 2003[71]	L	L	L	L		L	L		L	L
Sone 2002[75]	U	U	L	H		L	L		U	U
Steptoe 1999[90]	U	U	L	U		H	H		L	L
Velthuis 2009[77]	U	U	L	U		L	L		H	H
Vermunt 2012[80]	H	H	L	U		H	H		L	H
Werkman 2010[76]	U	L		H			L		L	H
Wister 2007[69]	L	L	L	L	H	L	L	L	L	U

L (green) = Low Risk; U (yellow) = Unclear Risk; H (red) = High Risk; OBJ = Objective Outcome; SUB = Subjective Outcome; S-R = Self-Reported Outcome

Table 4: Characteristics of Included Studies

Study/Location	Babazano 2007[85] Japan
Objective	To determine whether patient-motivated lifestyle changes would better enhance healthcare outcomes compared with usual care
Methods	Design: RCT Selection: participants were members of the National Health Insurance in Umi Town, Fukuoka, Japan. Patients meeting inclusion criteria were sent invitation letters Inclusion criteria: SBP 130-150 mmHg; DBP 85-99 mmHg or HbA1c ≥5.6% Exclusion criteria: Persons with critical need for medical treatment
Participants	Sample n=99 Intervention n=50; Control n=49 Age, Mean (SD) years: Intervention: 64.3 (7.1); Control: 64.5 (7.9) Gender [Female n (%)]: Intervention 29 (58%); Control 28 (51.1%) Loss to follow-up: Intervention n=4; Control n=8
Intervention	Intervention: group had a support team of dietitians, health exercise instructors, and public health nurses who encouraged patients to set goals and to select their own lifestyle improvements. Follow-up support was performed twice during the first year Control: usual care Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Broekhuizen 2012[82] The Netherlands; Companion paper: Broekhuizen[82]
Objective	To evaluate the efficacy of an individualized lifestyle intervention on lipids, systolic blood pressure, glucose, body mass index and waist circumference in people with familial hypercholesterolemia (FH)
Methods	Design: RCT Selection: recruitment by invitation brochures Inclusion criteria: participants diagnosed with FH from Jan 1 2007 to Apr 15 2009; aged 18 to 70 years and with a LDL-C level >75th percentile (age and gender specific) also access to internet; fluency in Dutch and residency <150km from Amsterdam
Participants	Sample: n=340 Intervention n=181; Control n=159 Age, Mean (SD) years: Intervention: 44.7 (12.9); Control: 45.9 (13.0)

	Gender [Female n (%)]: Intervention: 181 (57.1%); Control: 159 (56.3%) Loss to follow-up: Intervention n=11; Control n=14
Intervention	Intervention: personalised health counseling intervention; computer-generated tailored web-based advice and face-to-face counseling with telephone booster session Control: usual care Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Burke 2003[72] Australia; Companion papers: Dzator,[161] Burke[162,163]
Objective	To compare two methods of delivery of a diet and physical activity program for couples with a 1 year follow-up
Methods	Design: RCT Selection: couples recruited by advertisement in the press and through publicity on radio and television programs (did not include couples who took part in the pilot study) Inclusion criteria: couples in Perth, Australia, cohabiting for the first time and for <2 years, intending to reside in Perth for the length of the study, and not planning a pregnancy during the time of the intervention Exclusion criteria: illnesses such as heart disease, diabetes, or severe asthma
Participants	Sample: 137 couples Intervention 1 n=47 couples; Intervention 2 n=47 couples; Control n=43 couples Age, Mean (range) years: Overall women: 29.6 (18-62); men 31.4 (20-61) Gender (Female): 50% Loss to follow-up: 59 couples
Intervention	Interventions: 16-week program consisting of 6 printed modules focused on nutrition (encouraging consumption of foods low in fat, high in fiber, low in salt) and physical activity (encouraging at least 30 minutes of moderate activity most days and incidental activity); information about the benefits of stopping smoking and drinking alcohol Intervention 1 (high-level): modules every 2 weeks, alternating mail-outs with contact sessions at which the facilitators explained the aim of the modules, demonstrated exercise techniques, answered to questions, and reviewed progress Intervention 2 (low-level): after a single contact session at which the first module was delivered, all other modules were mailed every second week Control: no intervention Duration of intervention: 16 weeks Length of follow-up: 36 weeks

Study/Location	Carty 2011[67] US ; Companion papers: Howard,[164,165] Tinker,[166] Women's Health Initiative Study Group,[167] Hays[168]
Objective	To characterize long-term body composition changes associated with a (low-fat) dietary modification trial
Methods	Design: RCT Selection: women aged 50-79 years enrolled between 1993 and 1998 at 40 clinical centers throughout the United States Exclusion criteria: history of breast, colorectal, and other cancers except non-melanoma skin cancer in previous 10 years; medical conditions predictive of a survival time of <3 years; type I diabetes; high risk of lack of retention or intervention non-adherence; consumption of <600 kcal/day or >5,000 kcal/day; consumption of a diet with <32% of total energy from fat; consuming ≥10 main meals/week prepared outside of the home
Participants	Sample: 48,835 Intervention n=19,541 ; Control n=29,294 Age, Mean (SD) years: Overall (SD): 62.3 (6.9) Gender (Female): 100% SES (≥college degree): Intervention: n=7,445 (38.3%); Control n=11,042 (37.9%) Loss to follow-up: Overall n=2,027; Intervention n=727; Control n=1,300
Intervention	Intervention: designed to promote dietary change with the goals of reducing total fat intake to 20% of total energy, increasing vegetable and fruit intake to 5 servings/day and increasing grain intake to 6 servings/day; women received individual fat gram goals and participated in an intensive behavioural modification program consisting of 18 group sessions in the first year and quarterly maintenance sessions until the trial ended in 2005 Control: asked to maintain usual diet and eating patterns, given copy of "Nutrition and Your Health: Dietary Guidelines for Americans" but no contact with study dieticians Duration of intervention: not specified (8-12 years) Length of follow-up: 7.5 years post baseline

Study/Location	Elley 2003[87] New Zealand
Objective	To assess the long term effectiveness of the "green prescription" program, a clinician based initiative in general practice that provides counseling on physical activity
Methods	Design: RCT Selection: all urban and rural general practitioners in the central and eastern Waikato region of New Zealand were invited to participate; all patients aged 40-79 years who attended the participating practices during a five day period received a screening form,

	based on currently recommended levels of physical activity, to establish eligibility Exclusion criteria: patients considered by practice personnel considered as too unwell to participate; patients with debilitating medical condition or unstable cardiac condition; patients who did not understand English, or if they were expecting to leave the region
Participants	Sample n=878 Intervention n=451; Control n=427 Age, Mean (SD) years: Intervention: 57.2 (10.8); Control: 58.6 (11.5) Gender [Female n (%)]: Intervention n=301 (67%); Control n=281 (66%) SES (lower): Intervention: n=205 (45%); Control: n=211 (49%) Loss to follow-up: Intervention n=68; Control n=64
Intervention	Intervention: goals for increasing physical activity discussed and set with primary care professional, written on a green prescription and given to patient as well as faxed to local sports foundation; exercise specialists make at least three calls (10-20 minutes each) to patients over three months to encourage and support using motivational interviewing techniques and give specific advice about exercise or community groups; quarterly newsletters about community exercise initiatives and motivational material; other materials sent to interested participants; general practice staff encouraged to provide feedback to participants on subsequent visits Control: usual care Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Eriksson 2009[84] Sweden *Companion paper*: Eriksson 2006[169]
Objective	To test whether intensive lifestyle modification, shown previously in tightly-controlled clinical trials to be efficacious for diabetes risk-reduction among high-risk individuals, can reduce CVD risk factor levels in the primary care setting
Methods	Design: RCT Selection: catchment area of a primary health care center in the town of Boden in northern Sweden; invited by letter Inclusion criteria: individuals from the clinic aged 18–65 years with a clinically documented diagnosis of hypertension, dyslipidemia, T2D, and/or obesity Exclusion criteria: diagnosis of coronary heart disease, stroke, transient ischemic attack, severe hypertension (SBP>180 or DBP>105 mmHg), dementia or severe psychiatric morbidity
Participants	Sample: n=151 Intervention n=71; Control n=74

	Age, Mean (SD) years: Intervention: 57.7 (6.6); Control: 53.1 (8.2) Gender [Female n (%)]: Intervention: 36 (51%), Control: 47 (63.5%) Loss to follow-up: Intervention n=13; Control n=12
Intervention	Intervention: supervised exercise training and diet counseling, followed by regular group meetings Control: verbal and written information about healthy behaviours, including exercise and diet by the physician, a physiotherapist and a dietician following baseline exam Duration of intervention: 3 months Length of follow-up: 9 months

Study/Location	Forster 1988[73] US
Objective	To evaluate the feasibility and effectiveness of a program for weight gain prevention in normal-weight adults
Methods	Design: RCT Selection: recruited from a list of individuals screened for CVD risk factors as part of the Minnesota Heart Health Program; individuals of normal weight at the time of their visit (before Jan 1986) were sent a letter in Feb 1986 describing the program and requesting that they return a prepaid postcard if they wanted further information Inclusion criteria: no lower weight limit for eligibility for the study
Participants	Sample: 219 Age, Mean years: Overall: 45.9 Gender (Female): 71% Loss to follow-up: NR
Intervention	Intervention: monthly newsletter for 1 year including information relevant to weight control; financial incentive for weight maintenance; offered an optional educational course of four sessions offered midway through the year Control: not contacted between the baseline and follow-up 1 year later Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Friedenreich 2011[74] Canada; Companion papers: Friedenreich[170-172]
Objective	To examine the effects of an aerobic exercise intervention on adiposity outcomes that may be involved in the association between physical activity and breast cancer risk
Methods	Design: RCT

	Selection: targeted mailings to participants in the Alberta Breast Screening Program, posters and brochures distributed to family physicians and media campaigns Inclusion criteria: age 50-74; postmenopausal; no previous cancer diagnosis; no major comorbidities; acceptable baseline fitness test; sedentary (<90 min/week exercise or, if 90-120 min, having a VO2max level <34 kg-1min-1); able to do unrestricted physical activity; normal blood lipid and hormone levels, BMI 22-40; nonsmoker; <14 drinks/week of alcohol; no medications or exogenous hormones that might influence estrogen metabolism, not currently or planning to undertake a weight loss program
Participants	Sample: 320 Intervention n=160 ; Control n=160 Age, Mean (SD) years: Intervention: 61.2 (5.4); Control: 60.6 (5.7) Gender (Female): 100% SES (educated beyond high school): Intervention: 112 (70%); Control: 102 (64%) Loss to follow-up: Overall n=9; Intervention n=5; Control n=4
Intervention	Intervention: exercise prescription was moderate-to-vigorous intensity aerobic exercise for at least 45 min 5 days/week for 1 year; at least three sessions per week were facility based with exercise trainers and remaining sessions were home based; prescription ramped up over the first 3 months starting with 3 weekly sessions of 15-20 min at 50-60% of the heart rate reserve; program individualized to the age and fitness level of each participant; women instructed not to change their usual diet Control: asked to maintain their regular lifestyle Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Harris 2012[81] Australia
Objective	To evaluate the impact of a lifestyle intervention in Australian general practice to reduce the risk of vascular disease
Methods	Design: RCT Selection: recruited from within 30 eligible practices Inclusion criteria: attended practice in past 12 months and were 40-55 years with a diagnosis of hypertension and/or hyperlipidaemia or 56-64 with or without risk factors
Participants	Sample: n=699 Intervention n=384; Control n=315 Age (in 40-55 years range): Intervention n=96 (25.0%); Control n=78 (24.8%) Age (in 56-64 years range): Intervention n=288 (75.0%); Control n=237 (75.2%)

	Gender [Female n(%)]: Intervention: 232 (60.4%); Control: 169 (53.7%) SES (post-secondary education): Intervention: 18.8%; Control: 30.2% Loss to follow-up: Intervention n=29; Control n=15
Intervention	Intervention: initial visit with dietician or exercise physiologist for assessment and goal setting, group education program "CHANGE for HIPS" which comprised four 1.5 hours sessions over 3 months and 2 sessions at 6 and 9 months on education, physical activity (20-30 minutes walking or resistance exercise) and self-management strategies aimed at promoting positive dietary and physical activity changes and weight loss Control: patients attending practices allocated to control group received usual general practice care for their risk factors, including routine pharmacological management Duration of intervention: 9 months Length of follow-up: 3 months

Study/Location	Hivert 2007[68] Canada
Objective	To explore the efficacy of a seminar based educational and behavioural program aimed at improving lifestyle in newly admitted undergraduate students
Methods	Design: RCT Selection: recruitment by written advertisements, notices in lecture rooms and information tables in corridors of the university among two incoming student cohorts Inclusion criteria: full-time first or second year students at Faculte de Medecine et des Sciences de la santé de l'Universite de Sherbrooke (FMSSUS); left parental home for <2 years; BMI between 18-30 kg/m^2 Exclusion criteria: any medical condition; regular use of any medication except oral contraceptives; being pregnant or planning a pregnancy during the two years of the study
Participants	Sample: 115 Intervention n=58; Control n=57 Age, Mean (SD) years: Intervention: 19.9 (0.2); Control: 19.5 (0.2) Gender [Female n (%)]: Intervention n=47 (81.0%); Control n=47 (82.4%) Loss to follow-up: Overall n=19; Intervention n=10; Control n=9
Intervention	Intervention: small group interactive educational/behavioural seminars approximately 45 minutes offered every 2 weeks for the first 2 months of the academic calendar and every month thereafter for the remaining 2 years (23 seminars in 2 years) Control: no intervention Duration of intervention: 24 months Length of follow-up: immediate post

Study/Location	Imayama 2011[66] US; Companion paper: McTiernan[173]
Objective	To assess, in a randomized, controlled clinical trial, the effect of a 12-month moderate-to-vigorous intensity exercise program on weight, anthropometrics, and body composition and abdominal fat in women and men
Methods	Design: RCT Selection: recruited to a trial that examined the effects of exercise on colon cancer biomarkers (not a trial specifically focused on obesity prevention); recruited through gastroenterology practices, media placements, flyers, a study website and referrals Inclusion criteria: 40 to 75 years old; colonoscopy within past 3 years; engaged in <90 minutes/week of moderate-to-vigorous intensity exercise during past 3 months (or low-fitness on VO2max testing); <two servings of alcohol/day; no history of invasive cancer or high risk for colon cancer (e.g., familial polyposis, ulcerative colitis) or other serious medical conditions; normal response to maximal exercise tolerance test; normal complete blood count and chemistries, no contraindications for colon biopsy
Participants	Sample: 202 Intervention n=100; Control n=102 Age, Mean (SD, range) years: Intervention women: 54.4 (7.1, 43-73), men 56.2 (6.7, 40-69); Control women: 53.7 (5.6, 42-65); men 56.6 (7.6, 40-74) Gender [Female n (%)]: Intervention n=49 (49.0%); Control n=51 (50.0%) SES (college degree): Intervention n=61 (61.0%); Control n=62 (60.8%) Loss to follow-up: Intervention n=6; Control n=2
Intervention	Intervention: goal 60 min/day, 6 days/week of moderate-to vigorous intensity aerobic exercise, with gradual increase over first 12 weeks; required to exercise 3 times/week at one of four facilities under supervision of exercise specialists, provided with heart rate monitors and advised to exercise at 60-85% of maximal heart rate on baseline VO2max test; exercise at home or at facilities 3 days/week with same instructions Control: asked not to change exercise or diet habits during trial Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Kanaya 2012[83] USA
Objective	To evaluate a community-based, translational lifestyle program to reduce diabetes risk in lower–socioeconomic status and ethnic minority adults
Methods	Design: RCT Selection: recruitment began with community- based, educational outreach to identify

	individuals at risk for diabetes in 4 distinct low-income neighborhoods Inclusion criteria: capillary blood glucose value 106-160 mg/dL who had a moderate to high diabetes risk appraisal score; 25 years or older Exclusion criteria: diabetes (physician diagnosis, use of insulin or other diabetes medications); diagnosis (<6 months) of myocardial infarction, congestive heart failure, or stroke; heart procedure or heart surgery (<6 months); implanted defibrillator; hip or knee replacement (<3 months); insufficient cognitive functioning; pregnancy; not conversant in English or Spanish; plans to move out of area in 1 year; spouse or partner already enrolled
Participants	Sample: n=238 Intervention n=119; control n=119 Age, Mean (SD) years: Intervention: 58 (16); Control (SD): 55 (17) Gender (Female): Intervention: 73%; Control: 74% Race/Ethnicity: African American 23%, Non-Hispanic White 22.5%, Hispanic 37% SES (education): <High school 23%, High school 15.5% Loss to follow-up: Intervention n=14; Control n=12
Intervention	Intervention: 6-month active intervention and 6-month maintenance phase; trained health department counselors provided education and skills training to modify diet and physical activity through primarily telephone counseling (12 calls) with 2 in person sessions and 5 optional group workshops Control: wait list Duration of intervention: 6 months Length of follow-up: 6 months

Study/Location	Kastarinen 2002[65] Finland
Objective	To assess whether lifestyle counseling is effective in non-pharmacological treatment of hypertension in primary health care
Methods	Design: RCT Selection: The Lifestyle Intervention against Hypertension in Eastern Finland (LIHEF) study was conducted in 10 municipal primary health care centres in eastern Finland, mainly in North Karelia; participants enrolled between Feb 1996 and June 1997 Inclusion: men and women aged 25–74 years with SBP 140–179 mmHg and/or DBP 90–109 mmHg or on antihypertensive drug therapy Exclusion criteria: secondary hypertension, mental or physical illness serious enough to potentially influence compliance with study procedures, alcoholism, type 1 diabetes, current or planned pregnancy, recent myocardial infarction or stroke
Participants	Sample n=715 Intervention n=360; Control n=355

	Age, Mean (SD) years: Intervention: 54.4 (10.1); Control: 54.2 (9.9) Gender [Female n (%)]: Intervention n=187 (52%); Control n=192 (54%) Loss to follow-up: Intervention n=58; Control n=71
Intervention	Intervention: 4 visits to local public health nurses during the first year of the follow-up (1, 3, 6, 9 months), 3visits during the second year (15, 18, 21 months); instructed to change health behaviour primarily on the basis of their individual situation; 2 hour group sessions on reduction of salt intake and overweight at 6 and 18 months Control: visit own physicians and public health nurses according to usual practices Duration of intervention: 24 months Length of follow-up: immediate post

Study/Location	Khare 2012[86] USA; Companion paper: Khare[174]
Objective	To reduce CVD risk factors among uninsured and underinsured women who are participants in the Illinois Breast and Cervical Cancer Program (IBCCP), an early detection and screening program for low-income women
Methods	Design: RCT Selection: recruited from Illinois Breast and Cervical Cancer Program (IBCCP) using family info sessions, personal phone calls, fliers and advertisements Inclusion: underinsured and uninsured women aged 40 to 64 years enrolled in the Illinois Breast and Cervical Cancer Program (IBCCP)
Participants	Sample n=833 Intervention n=418; Control n=415 Age, Mean (SD) years: Overall: 52.5 (7.0); Intervention: 52.4 (7.0); Control: 52.5 (6.9) Gender (Female): 100% Race/Ethnicity: Intervention: Non-Hispanic White 84.1%; Control: Non-Hispanic White 84.2% SES (Education grades 9-12): Intervention: 60%; Control: 58.9% Loss to follow-up: Intervention n=193; Control n=135
Intervention	Intervention: received CVD risk factor screening, CVD-related educational materials, referrals to physician care as needed, 12-week lifestyle intervention, follow-up contacts for 24 months from the baseline screening Control: received CVD risk factor screening and CVD-related educational materials Duration of intervention: 12 weeks Length of follow-up: 40 weeks

Study/Location	Lawton 2008[79] New Zealand
Objective	To assess the effectiveness of a primary care based program of exercise on prescription among relatively inactive women over a two year period
Methods	Design: RCT Selection: recruited from an existing cohort of 50-74 year old women recruited by invitation letter from GP to a previous study of postmenopausal women from 10 primary care practices in Wellington; remainder recruited from 13 primary care practices, including two Maori health clinics; GPs identified women in the age group from their practice register, excluding patients deemed inappropriate for a physical activity trial, letters sent inviting them to participate in a lifestyle study Inclusion criteria: women, 40-74 years; physically inactive, as determined by a one question screening tool Exclusion criteria: women with a medical condition that might be adversely affected by increasing physical activity, as determined by the physical activity readiness questionnaire (PAR-Q) and subsequent assessment by their GP
Participants	Sample: 1,089 Intervention n=544 ; Control n=545 Age, Mean (SD) years: Intervention: 59.1 (6.8); Control: 58.7 (6.9) Gender (Female): 100% SES (lower): Intervention n=87 (16%), Control n=75 (14%) Loss to follow-up: 7% at 12 months, 11% at 24 months
Intervention	Intervention: primary care nurse briefly counsels (7-13 minutes) patients using motivational interviewing techniques to increase physical activity (goal was moderate intensity physical activity such as brisk walking, achieving 30 minutes five days/week); follow-up was telephone calls over 9 months (average of 5 calls, each lasting 15 minutes) with an added 30 minute visit with the primary care nurse at 6 months Control: usual care from primary care practice Duration of intervention: 9 months Length of follow-up: 3 months, 15 months

Study/Location	Levine 2007[70] US
Objective	To evaluate the efficacy of two interventions in preventing weight gain among normal or overweight women and to identify demographic, behavioural, and psychosocial factors related to weight gain prevention
Methods	Design: RCT Selection: recruited through local television, radio, and newspaper advertisements,

	direct-market mailings, and announcements to employees of a local medical center Inclusion criteria: 25-44 years of age; self-reported good health; BMI 21-30 Exclusion criteria: pregnant; pregnant or participated in a weight loss program in past year; receiving treatment for a psychiatric disorder; taken medication affecting body weight during past 3 months; planning to relocate within the next 36 months; unable to engage in moderate physical activity or make modest changes in dietary intake
Participants	Sample: 284 Intervention 1 (clinic) n=97; Intervention 2 (correspondence) n=94; Control n=93 Age, Mean (SD) years: Intervention 1: 36.4 (5.7); Intervention 2: 35.0 (6.1); Control: 35.4 (5.3) Gender (Female): 100% SES (% college graduate): Intervention 1: 52.6%; Intervention 2: 74.5%; Control: 66.3% Loss to follow-up: year 1: n= 62; year 2: n=74; year 3: n=79
Intervention	Intervention 1 (clinic-based): 15 group meetings over 24-months led by trained nutritionists and behavioural interventionists; biweekly for first 2 months and bimonthly for next 22 months Intervention 2 (correspondence): 15 lessons by mail over 24-months; lessons identical in content to clinic group, contained a brief homework assignment to be completed and returned by mail Control: received a booklet containing information about the benefits of weight maintenance, low-fat eating, and regular physical activity Duration of intervention: 24 months Length of follow-up: immediate post, 12 months

Study/Location	Mensink 2009[78] The Netherlands
Objective	To evaluate the impact of a 2-year combined diet and physical activity intervention program on glucose tolerance in Dutch subjects at increased risk for developing diabetes
Methods	Design: RCT Selection: patients selected from existing cohort Inclusion criteria: high risk of glucose intolerance, i.e., age >40 years and family history of diabetes or a BMI ≥25 Exclusion criteria: overt or previously diagnosed diabetes (not gestational); medication use known to interfere with glucose tolerance; participation in regular vigorous exercise or an intensive weight reduction program during past year; any (chronic) disease interfering with participation in a lifestyle program; improbability of 5-year survival

Participants	Sample: 114 Intervention: n=55; Control n=59 Age, Mean (SD) years: Intervention: 55.6 (0.9); Control: 57.8 (1.0) Gender [Female n (%)]: 50 (44%) Loss to follow-up: Intervention n=14; Control n=11
Intervention	Intervention: dietary and physical activity components Control: received oral and written information about benefits of a healthy diet, weight loss, and increased physical activity; no individual advice or programs provided Duration of intervention: 2 years Length of follow-up: immediate post

Study/Location	Roderick 1997[89] UK
Objective	To compare the effectiveness of structured dietary advice by practice nurses with standard health education in changing serum cholesterol, weight and diet.
Methods	Design: RCT Selection: 8 practices from the Medical Research Centre's general practice research framework selected in pairs with one pair from each of 4 geographical areas Inclusion: aged 35-59 attending surgery who did not have contra-indications, i.e., known causes of secondary hyperlipidaemia, severe psychiatric illness, pregnancy, terminal illness, or already attending a coronary heart disease health promotion clinic
Participants	Sample n=956 Intervention n=473; Control n=483 Age, Mean years: Intervention: 47.2; Control: 47.4 Gender [Female n (%)]: Intervention n=246 (52%); Control n=232 (48%) Loss to follow-up: Intervention n=66; Control n=126
Intervention	Intervention: standard health education from the leaflets Guides to Healthy Eating, Giving up Smoking, Look After Your Heart, Heart Disease, and Exercise, Why Bother?; dietary advice aimed for food substitution after review of the type, quantity and frequency of key foods consumed; specially designed dietary sheets given out according to whether weight loss required; all foods classified as 'to eat plentifully', 'in moderation' or 'on special occasions only'; overweight patients (BMI >25) given special advice, including a self-monitoring chart and choice of a calorie-restricted diet Control: standard health education from the same leaflets Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Sacerdote 2006[88] Italy
Objective	To investigate the effectiveness of a non-structured 15-min educational intervention by general practitioners (GPs) on modifications of daily diet among healthy adults
Methods	Design: RCT Selection: GPs selected through professional organizations as most motivated in the trial. All patients aged 18–65 years attending 33 selected GPs (Torino and Asti, Italy) Inclusion: aged 18–65 years, not obese (BMI <30), no chronic or severe diseases, not attending GP for reasons related to gastrointestinal problems, no dietary restrictions
Participants	Sample n=3,179 Intervention n=1,592; Control n=1,587 Age, Mean (SD) years: Intervention: 44.7 (12.6); Control: 44.2 (12.1) Gender [Female n (%)]: Intervention: n=797 (50.1%); Control: n=794 (50.0%) Loss to follow-up: Intervention n=104; Control n=98
Intervention	Intervention: GP administered 15-min personalized nutritional intervention, based on a brochure that summarized Italian Guidelines for a Correct Nutrition 1998. Control: 'sham' intervention, i.e. a simpler and non-personalized conversation without the use of a brochure. Duration of intervention: 15 minutes Length of follow-up: 12 months

Study/Location	Simkin-Silverman 1998[71] US; Companion papers: Simkin-Silverman,[175] Salamone,[176] Klem,[177] Kuller,[178] Park[179]
Objective	To report the 54-month results of a lifestyle dietary and physical activity program on weight, body composition, physical activity, diet, and other CVD risk factors.
Methods	Design: RCT Selection: mailings targeted at registered voters in Allegheny, Pennsylvania Inclusion criteria: women aged 44-50; premenopausal; not taking hormone replacement therapy; BMI 20-34, fasting total cholesterol 140-260 mg/dL, fasting LDL-C 80-160 mg/dL, fasting glucose levels <140 mg/dL and DBP <95 mmHg Exclusion criteria: taking lipid-lowering medication, antihypertensive medication, insulin, thyroid medication, or psychotropic medications
Participants	Sample: 535 Intervention n=260; Control n=275 Age Range, years: Overall 44 to 50

	Gender (Female): 100% Loss to follow-up: Intervention n=14; Control n=12
Intervention	Intervention: 5-year dietary and physical activity program conducted in 2 phases; Phase 1 (weeks 1-20): 15 group meetings, presentation, handouts, homework assignments, low-fat/reduced-calorie meal plan, suggested increase in physical activity (moderate-intensity aerobic activity and purposeful lifestyle activities), with ongoing consultation , monitoring and written feedback; Phase 2 (months 6-54): additional behavioural skills, support, motivation, group meetings, refresher programs, mail and telephone follow-up, incentives and group competitions Control: assessment-only Duration of intervention: 54 months Length of follow-up: immediate post

Study/Location	Sone 2002[75] Japan
Objective	To determine whether long-term lifestyle intervention can improve glycemic control and prevent complications in patients with T2D
Methods	Design: RCT Selection: patients previously diagnosed with T2D with HbA1c levels >6.5% from all over Japan were recruited from 59 institutes specializing in diabetes care
Participants	Sample n=2,205 Intervention n=1,105; Control n=1,100 Age, Mean (SD) years: Intervention: 59.4 (7.5); Control: 59.4 (7.4) Gender (Female): Intervention n=495; Control n=505 SES (college degree or higher): Intervention n=240; Control n=238 Unemployed: Intervention n=681; Control n=353 Co-morbidities: Diabetes Loss to follow-up: Overall n=232; Intervention n=115; Control n=117
Intervention	Intervention: lifestyle modification with intensive lifestyle management at each visit and telephone counseling by trained nurse educators at least once every 2 weeks Control: conventional care Duration of intervention: not specified Length of follow-up: 36 months post initiation

Study/Location	Steptoe 1999[90] UK
Objective	To measure the effect of behavioural counseling in general practice on healthy behaviour and biological risk factors in patients at risk of coronary heart disease
Methods	Design: RCT Selection: 42 training practices linked with the Department of General Practice at St. George's Hospital Medical School and within the South Thames region were invited to participate by means of letters outlining the study aims Inclusion criteria: ≥1 modifiable CVD risk factors: regular smoking (>1 cigarette/day), high serum cholesterol (6.5-9.0 mmol/L), high BMI (25-35) plus low physical activity (<12 episodes vigorous or moderate exercise for at least 20 minutes in past 4 weeks) Exclusion criteria: active follow-up or drugs for coronary heart disease, CVD or peripheral vascular disease, serious chronic illness, prescribed special diet, lipid lowering drugs
Participants	Sample n=883 Intervention n=316; Control n=567 Age, Mean (SE) years: Overall: 46.7 (0.4) Gender [Female n (%)]: 477 (54.0%) Loss to follow-up: Overall n=365; Intervention n=148; Control n=217
Intervention	Intervention: 3 counseling sessions if 2 risk factors and 2 sessions if only 1 risk factor; sessions lasted ≤20 minutes, between sessions nurse contacted patient by telephone one or two times to consolidate the counselling and to encourage behaviour change Control: usual care Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Velthuis 2009[77] The Netherlands; Companion paper: Monninkhof[180]
Objective	To investigate the effect of a 12-month moderate-to-vigorous exercise program combining aerobic and muscle strength training on body composition among sedentary, postmenopausal women
Methods	Design: RCT Selection: random selection out of municipality registries Inclusion criteria: post-menopausal women; 50-69 years old; sedentary (<2 hours/week in moderate sport activities); non-smokers for ≥12 months; not abusing alcohol or drugs; not planning strict diet; no diabetes or other endocrine related diseases, no disease or disorder (locomotor, optical, neurological, mental) that might impede participation in exercise program; BMI 22-40; fluent in Dutch; last menses ≥12 months ago; no hormone

	replacement or oral contraceptives in the past 6 months; not diagnosed with breast cancer or other cancers in the past 5 years; not using cortico steroids or beta-blockers
Participants	Sample: 189 Intervention n=96; Control n=93 Age, Mean (SD) years: Intervention: 58.9 (4.6); Control: 58.4 (4.2) Gender (Female): 100% Loss to follow-up: Overall n=6; Intervention n=1; Control n=5
Intervention	Intervention: one-year moderate to vigorous exercise program including 2 supervised group sessions of 1 hour/week and a home-based individual session of 30 min/week Control: requested to retain habitual exercise patterns Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Vermunt 2012[80] The Netherlands; Companion paper*:* Vermunt[181]
Objective	To determine the effectiveness of a 2.5-year lifestyle intervention for T2D prevention in Dutch general practice compared with usual care
Methods	Design: RCT Selection: recruited by 48 GPs from 14 general practices Inclusion criteria: Age 40 to 70, score of ≥13 on Dutch translation of the FINDRISC
Participants	Sample: n=1,065 Intervention n=479 and Control n=446 Age, Range, years: 40-70 Loss to follow-up: Intervention n=70; Control n=59
Intervention	Intervention: 11 consultations of 20 min over 2.5 years alternately with nurse practitioner and GP; 5 group meetings to provide more information on diet and exercise; 1 hour consultation with dietician, in which 3-day food record discussed Control: oral and written information on T2D and healthy lifestyle provided Duration of intervention: 2.5 years Length of follow-up: immediate post

Study/Location	Werkman 2010[76] The Netherlands
Objective	To investigate the effect of a one year low-intensity computer-tailored energy balance program among recent retirees on waist circumference, body weight and body composition, blood pressure, physical activity and dietary intake

Methods	Design: RCT Selection: recruited from pre-retirement workshops as offered by employers to approximately 10% of the Dutch retiring population; approximately 1,100 workshop attendees were invited to participate Inclusion criteria: recent retirees (retirement ≤6 months before or after baseline); 55-65 years; not undergoing medical treatments that might affect body composition.
Participants	Sample: n=415 Intervention n=174; Control n=178 Age, Mean (SD) years: Intervention: 59.5 (2.5); Control: 59.4 (2.3) Gender (Female): some female intervention participants but analyses only for men SES (% low education): Intervention: 25%; Control: 23% Loss to follow-up: Intervention n=27; Control n=24
Intervention	Intervention: 5 on-line modules, newsletters every 2-3 months containing information about diet and physical activity and encouragements to use the modules Control: newsletters with general information about the study, such as study progress, and information about art exhibitions and city trips; they could not login to the website Duration of intervention: 12 months Length of follow-up: immediate post and 12 months

Study/Location	Wister 2007[69] Canada
Objective	To test the efficacy of a low intensity lifestyle intervention aimed at reducing the risk of CVD among mid-life individuals
Methods	Design: RCT Selection: population based recruitment 2002-2004 via ads in local newspapers, interviews on radio, posters for workplaces Inclusion criteria: aged 45–64 years, residence in the Fraser Health region and CVD risk profile according to the literature for primary and secondary prevention
Participants	Sample: n=611 Intervention 1 (primary prevention) n=157; Control 1 (primary prevention) n=158; Intervention 2 (secondary prevention) n=153; Control 2 (secondary prevention) n=143 Age, Mean (SD) years: Intervention 1: 55.8 (5.5); Control 1: 55.1 (5.2); Intervention 2: 56.6 (5.1) ; Control 2: 57.2 (5.0) Gender [Female n (%)]: Intervention 1: n= 86 (54.8%); Control 1: n= 98 (62.0%); Intervention 2: n=52 (34.0%); Control 2: n=40 (28.0%) Loss to follow-up: Overall n=79 ; Intervention 1 n=20; Control 1 n=17; Intervention 2

	n=15; Control 2 n=27
Intervention	Intervention: report card (sent to the participant and his or her family doctor) showing the person's CVD risk profile, coupled with a Telehealth-guided self-care management system; Telehealth counseling occurred within 10 days of the patient receiving the annual report card and every 6 months thereafter for approximately 30 minutes per session, up to 60 minutes per year Control: usual care Duration of intervention: 12 months Length of follow-up: immediate post

Table 5: Broad Features of the Available Evidence

Designs	• 26 RCTs
Populations	• Indirect for weight: 1 study included normal weight adults; 25 studies included mixed weight (normal weight and overweight and/or obese) adults • No interventions targeted seniors (≥65 years) • 20 studies included men and women; 5 studies included only women; 1 study reported data only for men • 4 studies (15%) were directed at high CVD risk populations
Interventions	• All studies included behavioural intervention arms (3 diet, 6 exercise, 5 diet plus exercise, 12 lifestyle) • 18 interventions (69%) were 12 months or less in duration
Quality Assessment	• 21 RCTs (80%) rated as having unclear or high risk of bias for the weight outcomes • Most outcomes received low GRADE ratings (downgraded for risk of bias and indirectness); occasional very low GRADE ratings applied due to added concerns regarding imprecision or reporting bias
Study Locations	• 3 studies in Canada, 7 in the US, 10 in European countries, 4 in Australia or New Zealand, 2 in Japan
Publication Dates	• 11 studies (42%) were published in the last 5 years; 15 were published between 1988 and 2008

Table 6: Key Findings of Overall and Sub-group Analyses for Continuous Outcomes (Weight in kg, BMI, Waist Circumference, Total % Body Fat, Total Cholesterol, LDL-C, Fasting Glucose, SBP, DBP)

Group or Sub-group	Meta-analysis, MD (95% CI); I^2	Sub-group Differences P-Value, I^2-Value	No. Participants	No. Studies	GRADE Rating
Outcome: Change in Weight in kg					
Overall	-0.73 (-0.93 to -0.54); 49%	na	48,460	19	Very Low
Diet	-0.51 (-0.65 to -0.36); 0%	0.25, 26.4%	42,308	2	Low
Exercise	-0.88 (-1.44 to -0.33); 52%		2,024	5	Low
Diet plus Exercise	-0.99 (-1.90 to -0.08); 50%		748	4	Low
Lifestyle	-0.89 (-1.44 to -0.34); 60%		3,380	8	Low
≤ 12 Months	-0.61 (-0.70 to -0.51); 2%	0.08, 67.4%	4,908	12	Low
> 12 Months	-1.21 (-1.88 to -0.54); 78%		43,552	7	Low
Male	-0.48 (-0.99 to 0.03); 0%	0.25, 25.3%	975	4	Very Low
Female	-0.82 (-1.09 to -0.55); 73%		44,390	9	Low
High CVD Risk	-0.88 (-1.45 to -0.32); 0%	0.60, 0%	1,356	3	Low
Low/Unknown CVD Risk	-0.72 (-0.93 to -0.52); 54%		47,104	16	Very Low
High Risk of Bias	-1.20 (-3.04 to 0.64); 75%	0.29, 20.0%	652	2	Very Low
Unclear Risk of Bias	-0.53 (-0.67 to -0.40); 49%		45,237	13	Very Low
Low Risk of Bias	-1.22 (-2.16 to -0.28); 89%		2,571	4	Low
Outcome: Change in BMI (kg/m^2)					
Overall	-0.24 (-0.34 to -0.15); 64%	na	52,243	20	Low
Baseline Mean BMI <25	-0.27 (-0.50 to -0.05); 47%	0.81, 0%	5,152	4	Low
Baseline Mean BMI ≥25	-0.24 (-0.36 to -0.12); 68%		47,091	16	Low
Outcome: Change in Waist Circumference (cm)					
Overall	-0.95 (-1.27 to -0.63); 74%	na	20,796	15	Very Low
Outcome: Change in Total % Body Fat					
Overall	-1.27 (-1.93 to -0.61); 80%	na	1,663	6	Low

Group or Sub-group	Meta-analysis, MD (95% CI); I^2	Sub-group Differences P-Value, I^2-Value	No. Participants	No. Studies	GRADE Rating
Outcome: Change in Total Cholesterol (mmol/L)					
Overall	-0.06 (-0.11 to -0.01); 70%	na	10,660	15	Low
Outcome: Change in LDL-C (mmol/L)					
Overall	-0.06 (-0.09 to -0.03); 0%	na	5,635	11	Low
Outcome: Change in Fasting Glucose (mmol/L)					
Overall	-0.04 (-0.08 to -0.0016); 67%	na	7,189	10	Low
Outcome: Change in SBP (mmHg)					
Overall	-0.31 (-0.84 to 0.22); 77%	na	48,493	17	Very Low
Outcome: Change in DBP (mmHg)					
Overall	-0.18 (-0.44 to -0.07); 66%	na	47,945	15	Very Low

Table 7: Key Findings of Overall Analyses for Dichotomous Outcomes (T2D)

Group or Sub-group	Effect		No. Participants	No. Studies	GRADE Rating
	RR (95% CI); I^2	Absolute Number per Million (Range)			
Outcome: Incidence of T2D					
Overall	0.95 (0.89 to 1.02); 0%	3,417 fewer (7,989 fewer to 1,461 more)	46,537	2	Very Low

Table 8: Summary of Features of Efficacious Interventions

Study	Intervention Duration	Estimated Number of Sessions	Intervention Focus	Intervention Setting	Includes Group Sessions	Includes Individual Sessions
Carty 2011[67]	8-12 years	18	Diet	Community	Yes	
Friedenreich 2011[74]	12 months	260	Exercise	Multi-setting		Yes
Kastarinen 2002[65]	24 months	7	Lifestyle	Primary Care		Yes
Lawton 2008[79]	9 months	7	Exercise	Primary Care		Yes
Simkin-Silverman 2003[71]	54 months	21 sessions + 6 week refresher	Lifestyle	Clinic	Yes	Yes (some received based on LDL-C level, weight gain or activity lapse)

Table 9: Mean BMI by Immigrant Status and Sex, Canada 1994 and 2006[99]

Immigrant Status	1994		2006	
	Males n=2,504	**Females** n=2,906	**Males** n=2,386	**Females** n=2,865
Canadian-born	26.2 (3.9)	24.9 (5.2)	27.9 (4.3)	26.9 (5.9)
White immigrants	26.3 (4.0)	24.3 (4.7)	28.0 (4.8)	26.2 (5.7)
Non-white immigrants	24.3 (3.4)	23.2 (4.1)	25.7 (3.8)	24.5 (3.9)

Estimates in brackets are standard deviation units

Table 10: Prevalence of Self-reported Obesity and Obesity and Overweight in Canada, by Age and Sex 2005[98]

Gender	Age Group				
	25-34	35-44	45-54	55-64	All Ages
Obese					
Males	15.42	17.76	20.36	21.98	18.77
Females	12.81	13.83	17.55	19.42	15.79
Overweight and Obese Combined					
Males	53.78	62.11	64.83	67.10	61.92
Females	33.63	38.76	46.25	55.65	43.17

Table 11: Prevalence of Self-reported Obesity in Canada, by Age and Sex, 2007-08[20]

Gender	Age Group							
	18-19	20-24	25-34	35-44	45-54	55-64	65-74	75+
Males	7.2	11.1	15.9	19.4	20.6	23.3	21.2	12.0
Females	5.5	8.4	13.3	16.0	17.5	21.4	20.2	14.3

EVIDENCE SETS

- Evidence Set 1: Weight – Change in KG
- Evidence Set 2: Weight – Change in BMI
- Evidence Set 3: Weight – Change in Waist Circumference
- Evidence Set 4: Weight – Change in Total % Body Fat
- Evidence Set 5: Health/Physiological Outcomes – Change in Total Cholesterol
- Evidence Set 6: Health/Physiological Outcomes – Change in LDL-C
- Evidence Set 7: Health/Physiological Outcomes – Change in Fasting Glucose
- Evidence Set 8: Health/Physiological Outcomes – Incidence of T2D
- Evidence Set 9: Health/Physiological Outcomes – Change in SBP
- Evidence Set 10: Health/Physiological Outcomes – Change in DBP
- Evidence Set 11: Weight Gain Prevention and Health Outcomes at Follow-up

Evidence Set 1: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to short-term or sustained weight gain prevention (kg)?

- Summary of Weight Change in KG Evidence
- GRADE Evidence Profile Table 1.1: Effect of Weight Gain Prevention Interventions on Weight in KG
- GRADE Summary of Findings Table 1.1: Effect of Weight Gain Prevention Interventions on Weight in KG
- Forest Plots 1.1 to 1.6: Effect of Weight Gain Prevention Interventions on Weight in KG
    - 1.1: Overall
    - 1.2: Type of Intervention (Diet, Exercise, Diet plus Exercise, Lifestyle)
    - 1.3: Duration of Intervention (≤ 12 Months, >12 Months)
    - 1.4: Gender
    - 1.5: Participants' Baseline CVD Risk Status (High Risk, Low/Unknown Risk)
    - 1.6: Study Risk of Bias Rating (High, Unclear, Low)
- Funnel Plots 1.1 to 1.6: Effect of Weight Gain Prevention Interventions on Weight in KG
    - Same as bulleted list above
- Egger's Test Results (for Publication Bias)

Summary of Weight Change in KG Evidence

1.1 Overall

- 19 studies; 48,460 participants
- Statistically significant reduction (P<0.00001) in weight in the intervention group as compared to the control group [MD (95% CI) -0.73 kg (-0.93, -0.54)]
- Moderate statistical heterogeneity across studies [Chi^2=40.95, df=21 (P=0.006), I^2=49%]

1.2 Type of Intervention

Test for subgroup differences is not significant [Chi^2=4.07, df=3 (P=0.25), I^2=26.4%]; type of intervention does not explain variation across studies

Diet

- 2 studies; 42,308 participants
- Statistically significant reduction (P<0.00001) in weight in the intervention group as compared to the control group [MD (95% CI) -0.51 kg (-0.65, -0.36)]
- Low statistical heterogeneity across studies [Chi^2=0.25, df=2 (P=0.88), I^2=0%]

Exercise
- 5 studies; 2,024 participants
- Statistically significant reduction (P=0.002) in weight in the intervention group as compared to the control group [MD (95% CI) -0.88 kg (-1.44, -0.33)]
- Moderate statistical heterogeneity across studies [Chi^2=10.39, df=5 (P=0.06), I^2=52%]

Diet plus Exercise
- 4 studies; 748 participants
- Statistically significant reduction (P=0.03) in weight in the intervention group as compared to the control group [MD (95% CI) -0.99 kg (-1.90, -0.08)]
- Moderate statistical heterogeneity across studies [Chi^2=6.05, df=3 (P=0.11), I^2=50%]

Lifestyle
- 8 studies; 3,380 participants
- Statistically significant reduction (P=0.001) in weight in the intervention group as compared to the control group [MD (95% CI) -0.89 kg (-1.44, -0.34)]
- Moderate statistical heterogeneity across studies [Chi^2=19.80, df=8 (P=0.01), I^2=60%]

1.3 Duration of Intervention

Test for subgroup differences is not significant [Chi^2=3.07, df=1 (P=0.08), I^2=67.4%]; duration of intervention does not explain variation across studies

≤12 Months
- 12 studies; 4,908 participants
- Statistically significant reduction (P<0.00001) in weight in the intervention group as compared to the control group [MD (95% CI) -0.61 kg (-0.70, -0.51)]
- Low statistical heterogeneity across studies [Chi^2=14.22, df=14 (P=0.43), I^2=2%]

>12 Months
- 7 studies; 43,552 participants
- Statistically significant reduction (P=0.0004) in weight in the intervention group as compared to the control group [MD (95% CI) -1.21 kg (-1.88, -0.54)]
- Moderate statistical heterogeneity across studies [Chi^2=26.71, df=6 (P=0.0002), I^2=78%]

1.4 Gender

Test for subgroup differences is not significant [Chi^2=1.34, df=1 (P=0.25), I^2=2.35%]; gender does not explain variation across studies

Male
- 4 studies; 975 participants
- No significant reduction (P=0.06) in weight in the intervention group as compared to the control group [MD (95% CI) -0.48 kg (-0.99, 0.03)]
- Low statistical heterogeneity across studies [Chi^2=2.43, df=3 (P=0.49), I^2=0%]

Female
- 9 studies; 44,390 participants
- Statistically significant reduction (P<0.00001) in weight in the intervention group as compared to the control group [MD (95% CI) -0.82 kg (-1.09, -0.55)]
- High statistical heterogeneity across studies [Chi^2=29.79, df=8 (P=0.0002), I^2=73%]

1.5 Participants' Baseline CVD Risk Status

Test for subgroup differences is not significant [Chi^2=0.27, df=1 (P=0.60), I^2=0%]; participants' baseline CVD risk status does not explain variation across studies

High Risk

- 3 studies; 1,356 participants
- Statistically significant reduction (P=0.002) in weight in the intervention group as compared to the control group [MD (95% CI) -0.88 kg (-1.45, -0.32)]
- Low statistical heterogeneity across studies [Chi^2=1.22, df=2 (P=0.54), I^2=0%]

Low/Unknown Risk or Unselected Population or Risk Status Not Available

- 16 studies; 47,104 participants
- Statistically significant reduction (P<0.00001) in weight in the intervention group as compared to the control group [MD (95% CI) -0.72 kg (-0.93, -0.52)]
- Moderate statistical heterogeneity across studies [Chi^2=38.75, df=18 (P=0.003), I^2=54%]

1.6 Study Risk of Bias Rating

Test for subgroup differences is not significant [Chi^2=2.50, df=2 (P=0.29), I^2=20.0%]; study risk of bias rating does not explain variation across studies

High Risk

- 2 studies; 652 participants
- No significant reduction (P=0.20) in weight in the intervention group as compared to the control group [MD (95% CI) -1.20kg (-3.04, 0.64)]
- High statistical heterogeneity across studies [Chi^2=3.96, df=1 (P=0.05), I^2=75%]

Unclear Risk

- 13 studies; 45,237 participants
- Statistically significant reduction (P<0.00001) in weight in the intervention group as compared to the control group [MD (95% CI) -0.53 kg (-0.67, -0.40)]
- Low statistical heterogeneity across studies [Chi^2=8.49, df=15 (P=0.90), I^2=0%]

Low Risk

- 4 studies; 2,571 participants
- Statistically significant reduction (P=0.01) in weight in the intervention group as compared to the control group [MD (95% CI) -1.22 kg (-2.16, -0.28)]
- High statistical heterogeneity across studies [Chi^2=27.30, df=3 (P<0.00001), I^2=89%]

GRADE Evidence Profile Table 1.1: Effect of Weight Gain Prevention Interventions on Weight in KG *

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Weight Change in KG: Overall (Better indicated by lower values)											
19	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	reporting bias[7]	19,825	28,635	0.7335 lower (0.9273 to 0.5397 lower)	⊕OOO VERY LOW	CRITICAL
Weight Change in KG: by Type of Intervention - Diet (Better indicated by lower values)											
2	randomized trials[8]	serious risk[9]	no serious inconsistency[10]	serious indirectness[4,11]	no serious imprecision[12]	none[13]	16,770	25,538	0.5072 lower (0.6520 to 0.3624 lower)	⊕⊕OO LOW	CRITICAL
Weight Change in KG: by Type of Intervention - Exercise (Better indicated by lower values)											
5	randomized trials[14]	serious risk[15]	no serious inconsistency[16]	serious indirectness[4,17]	no serious imprecision[18]	none[19]	1,012	1,012	0.8846 lower (1.4432 to 0.3260 lower)	⊕⊕OO LOW	CRITICAL
Weight Change in KG: by Type of Intervention - Diet plus Exercise (Better indicated by lower values)											
4	randomized trials[20]	serious risk[21]	no serious inconsistency[22]	serious indirectness[4,23]	no serious imprecision[24]	none[25]	400	348	0.9915 lower (1.8999 to 0.0830 lower)	⊕⊕OO LOW	CRITICAL
Weight Change in KG: by Type of Intervention - Lifestyle (Better indicated by lower values)											
8	randomized trials[26]	serious risk[27]	no serious inconsistency[28]	serious indirectness[4,29]	no serious imprecision[30]	none[31]	1,643	1,737	0.8895 lower (1.4352 to 0.3439 lower)	⊕⊕OO LOW	CRITICAL
Weight Change in KG: by Length of Interventions ≤12 Months (Better indicated by lower values)											
12	randomized trials[32]	serious risk[33]	no serious inconsistency[34]	serious indirectness[4,35]	no serious imprecision[36]	none[37]	2,383	2,525	0.6056 lower (0.6989 to 0.5122 lower)	⊕⊕OO LOW	CRITICAL
Weight Change in KG: by Length of Interventions >12 Months (Better indicated by lower values)											
7	randomized trials[38]	serious risk[39]	no serious inconsistency[40]	serious indirectness[4,41]	no serious imprecision[42]	none[43]	17,442	26,110	1.2095 lower (1.8786 to 0.5403 lower)	⊕⊕OO LOW	CRITICAL
Weight Change in KG: by Gender - Male (Better indicated by lower values)											
4	randomized trials[44]	serious risk[45]	no serious inconsistency[46]	serious indirectness[4,47]	serious imprecision[48]	none[49]	475	500	0.4790 lower (0.9850 lower to 0.0270 higher)	⊕OOO VERY LOW	CRITICAL
Weight Change in KG: by Gender - Female (Better indicated by lower values)											
9	randomized trials[50]	serious risk[51]	no serious inconsistency[52]	serious indirectness[4,53]	no serious imprecision[54]	none[55]	17,845	26,545	0.8177 lower (1.0882 to 0.5472 lower)	⊕⊕OO LOW	CRITICAL

Weight Change in KG: by CVD Risk in Interventions - High Risk (Better indicated by lower values)											
3	randomized trials[56]	serious risk[57]	no serious inconsistency[58]	serious indirectness[4,59]	no serious imprecision[60]	none[61]	588	768	0.8849 lower (1.4512 to 0.3186 lower)	⊕⊕OO LOW	CRITICAL
Weight Change in KG: by CVD Risk in Interventions – Low/Unknown Risk (Better indicated by lower values)											
16	randomized trials[62]	serious risk[63]	no serious inconsistency[64]	serious indirectness[4,65]	no serious imprecision[66]	reporting bias[67]	19,237	27,867	0.7242 lower (0.9333 to 0.5151 lower)	⊕OOO VERY LOW	CRITICAL
Weight Change in KG: by Study Risk of Bias Rating - High (Better indicated by lower values)											
2	randomized trials[68]	very serious risk[69]	no serious inconsistency[70]	serious indirectness[4,71]	serious imprecision[72]	none[73]	345	307	1.2001 lower (3.0388 lower to 0.6385 higher)	⊕OOO VERY LOW	CRITICAL
Weight Change in KG: by Study Risk of Bias Rating – Unclear (Better indicated by lower values)											
13	randomized trials[74]	serious risk[75]	no serious inconsistency[76]	serious indirectness[4,77]	no serious imprecision[78]	reporting bias[79]	18,175	27,062	0.5339 lower (0.6655 to 0.4023 lower)	⊕OOO VERY LOW	CRITICAL
Weight Change in KG: by Study Risk of Bias Rating – Low (Better indicated by lower values)											
4	randomized trials[80]	no serious risk[81]	serious inconsistency[82]	serious indirectness[4,83]	no serious imprecision[84]	none[85]	1,305	1,266	1.2204 lower (2.1586 to 0.2822 lower)	⊕⊕OO LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 1.1: Effect of Weight Gain Prevention Interventions on Weight in KG

Outcome: Weight Change in KG	Compared to the control group, the mean weight in kg (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
Overall	**0.7335 lower** (0.9273 to 0.5397 lower)	48,460 (19 studies[1])	⊕⊖⊖⊖ **very low**[2,3,4,5,6,7]
By Type of Intervention - Diet	**0.5072 lower** (0.6520 to 0.3624 lower)	42,308 (2 studies[8])	⊕⊕⊖⊖ **low**[4,9,10,11,12,13]
By Type of Intervention - Exercise	**0.8846 lower** (1.4432 to 0.3260 lower)	2,024 (5 studies[14])	⊕⊕⊖⊖ **low**[4,15,16,17,18,19]
By Type of Intervention - Diet plus Exercise	**0.9915 lower** (1.8999 to 0.0830 lower)	748 (4 studies[20])	⊕⊕⊖⊖ **low**[4,21,22,23,24,25]
By Type of Intervention - Lifestyle	**0.8895 lower** (1.4352 to 0.3439 lower)	3,380 (8 studies[26])	⊕⊕⊖⊖ **low**[4,27,28,29,30,31]
By Length of Interventions ≤12 Months	**0.6056 lower** (0.6989 to 0.5122 lower)	4,908 (12 studies[32])	⊕⊕⊖⊖ **low**[4,33,34,35,36,37]
By Length of Interventions >12 Months	**1.2095 lower** (1.8786 to 0.5403 lower)	43,552 (7 studies[38])	⊕⊕⊖⊖ **low**[4,39,40,41,42,43]
By Gender - Male	**0.4790 lower** (0.9850 lower to 0.0270 higher)	975 (4 studies[44])	⊕⊖⊖⊖ **very low**[4,45,46,47,48,49]
By Gender - Female	**0.8177 lower** (1.0882 to 0.5472 lower)	44,390 (9 studies[50])	⊕⊕⊖⊖ **low**[4,51,52,53,54,55]
By CVD Risk - High Risk	**0.8849 lower** (1.4512 to 0.3186 lower)	1,356 (3 studies[56])	⊕⊕⊖⊖ **low**[4,57,58,59,60,61]
By CVD Risk – Low/Unknown Risk	**0.7242 lower** (0.9333 to 0.5151 lower)	47,104 (16 studies[62])	⊕⊖⊖⊖ **very low**[4,63,64,65,66,67]
By Study Risk of Bias Rating - High	**1.2001 lower** (3.0388 lower to 0.6385 higher)	652 (2 studies[68])	⊕⊖⊖⊖ **very low**[4,69,70,71,72,73]
By Study Risk of Bias Rating - Unclear	**0.5339 lower** (0.6655 to 0.4023 lower)	45,237 (13 studies[74])	⊕⊖⊖⊖ **very low**[4,75,76,77,78,79]
By Study Risk of Bias Rating - Low	**1.2204 lower** (2.1586 to 0.2822 lower)	2,571 (4 studies[80])	⊕⊕⊖⊖ **low**[4,81,82,83,84,85]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Weight in KG

[1] The 19 studies are:[65-68,70,71,73,74,76-81,83-85,89,90] Immediate post assessment for all but 5 studies; for these 5 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] provides 9 month follow-up data post completion of a 3 month intervention; Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Lawton[79] and Harris[81] provide 3 month follow-up data post completion of 9 month interventions; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 13 studies (68%) were rated as unclear risk, 2 studies (11%) were rated as high risk, and 4 studies (21%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (47%), allocation concealment (63%), blinding of outcome assessors (63%) and other sources of bias (84%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] Although the statistical heterogeneity is moderate and significant [Chi^2=40.95, df=21 (P=0.006); I^2=49%] the direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 19 studies, baseline BMI ranged from 22.4 to 30.1; in 3 of the studies the baseline mean BMI of at least one study arm was <25; in 16 studies the baseline means were in the range for overweight/obese. Most studies (n=12) included mixed gender samples; 6 included only women and 1 included only men. In 3 studies (16%) the participants had a high risk of CVD. In terms of type of intervention 2 were diet, 5 were exercise, 4 were diet plus exercise, and 8 were lifestyle. Control participants received usual care from their physicians or no intervention; in 7 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 12 studies and more than 12 months in 7 studies. Two studies were conducted in Canada, 6 in the US, 8 in European countries, 2 in Australia or New Zealand, and 1 in Japan. About half of the studies (n=9) were published in the last 5 years (2009-2012); the remaining 10 studies were published between 1988 and 2008.

[6] The sample size is adequate (19,825 intervention arm, 28,635 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.7335 kg (-0.9273, -0.5397)]. This body of evidence was not downgraded for imprecision.

[7] The funnel plot for these studies and this outcome is asymmetrical. The Egger's test was conducted to detect publication bias; results were significant (p=0.003). This body of evidence was downgraded for strongly suspected publication bias.

[8] The 2 studies are:[67,89] Immediate post assessment for one study and the data point closest to the immediate post and ≥12 months post baseline was selected (Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[9] Using Cochrane's Risk of Bias tool, for this outcome both studies were rated as unclear risk. There was a lack of certainty (unclear ratings) associated with sequence generation (50%), allocation concealment (100%), blinding of outcome assessors (50%) and other sources of bias (100%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given all of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[10] Statistical heterogeneity is low and not significant [Chi^2=0.25, df=2 (P=0.88); I^2=0%]. The direction of the effect is consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

[11] Across the 2 studies, baseline BMI ranged from 25.9 to 29.1. One study included a mixed gender sample and the other study included only women. In both studies the participants had low/unknown risk of CVD. In terms of type of intervention both studies were diet focused. Control participants in both studies received a minimal component (i.e., printed materials on healthy eating and lifestyles). Intervention duration was 12 months in 1 study and ranged from 8 to 12 years in the other study. One study was conducted in the US and the other study was conducted in the UK. One study was published in the last 5 years (2011); the other study was published in 1997.

[12] The sample size is adequate (16,770 intervention arm, 25,538 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.5072 kg (-0.6520, -0.3624)]. This body of evidence was not downgraded for imprecision.

[13] There were too few studies (n<10) to assess publication bias.

[14] The 5 studies are:[66,74,77,79,83] Immediate post assessment for all but 2 studies; for these 2 studies the data point closest to the immediate post and ≥12 months post baseline was selected (Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Lawton[79] provides 3 month follow-up data post completion of a 9 month intervention).

[15] Using Cochrane's Risk of Bias tool, for this outcome 3 studies (60%) were rated as unclear risk and 2 studies (40%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (20%), allocation concealment (40%), blinding of outcome assessors (40%) and other sources of bias (100%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[16] The statistical heterogeneity is moderate but not significant [Chi^2=10.39, df=5 (P=0.06); I^2=52%]. The direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[17] Across the 5 studies, baseline BMI ranged from 26.6 to 30.1. Two studies (40%) included mixed gender samples; 3 included only women. In all 5 studies the participants had low/unknown risk of CVD. In terms of type of intervention all 5 were exercise focused. Control participants received usual care from their

physicians or no intervention. Intervention duration was 12 months or less in all 5 studies. One study was conducted in Canada, 2 in the US, 1 in the Netherlands, and 1 in New Zealand. Most of the studies (n=4) were published in the last 5 years (2009-2012); the remaining study was published in 2008.

[18] The sample size is adequate (1,012 intervention arm, 1,012 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.8846 kg (-1.4432, -0.3260)]. This body of evidence was not downgraded for imprecision.

[19] There were too few studies (n<10) to assess publication bias.

[20] The 4 studies are:[68,70,76,78] Immediate post assessment for all studies.

[21] Using Cochrane's Risk of Bias tool, for this outcome 3 studies (75%) were rated as unclear risk and 1study (25%) was rated as high risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (75%), allocation concealment (50%), blinding of outcome assessors (100%) and other sources of bias (100%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at moderate to high risk of bias, this body of evidence was downgraded for serious study limitations.

[22] The statistical heterogeneity is moderate but not significant [Chi^2=6.05, df=3 (P=0.11); I^2=50%]. The direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[23] Across the 4 studies, baseline BMI ranged from 22.4 to 29.8; in 1 study the baseline mean BMI of at least one study arm was <25. Half of the studies (n=2) included mixed gender samples; 1 included only women and 1 included only men. In all 4 studies the participants had low/unknown risk of CVD. In terms of type of intervention all 4 studies were diet plus exercise focused. Control participants received usual care from their physicians or no intervention; in 3 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 1 study and more than 12 months in 3 studies. One study was conducted in Canada, 1 in the US, and 2 in the Netherlands. One study was published in the last 5 years (2010); the remaining 3 studies were published between 2003 and 2007.

[24] The sample size is adequate (400 intervention arm, 348 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.9915 kg (-1.8999, -0.0830)]. This body of evidence was not downgraded for imprecision.

[25] There were too few studies (n<10) to assess publication bias.

[26] The 8 studies are:[65,71,73,80,81,84,85,90] Immediate post assessment for all but 2 studies; for these 2 studies the data point closest to the immediate post and ≥12 months post baseline was selected (Eriksson[84] provides 9 month follow-up data post completion of a 3 month intervention; Harris[81] provides 3 month follow-up data post completion of a 9 month intervention).

[27] Using Cochrane's Risk of Bias tool, for this outcome 5 studies (62.5%) were rated as unclear risk, 1 study (12.5%) was rated as high risk, and 2 studies (25%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (75%), blinding of outcome assessors (62.5%) and other sources of bias (62.5%; i.e., industry funding, imbalance in baseline characteristics and/or

selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[28] Although the statistical heterogeneity is moderate and significant [Chi^2=19.80, df=8 (P=0.01); I^2=60%] the direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[29] Across the 8 studies, baseline BMI ranged from 23.1 to 30.1; in 3 of the studies the baseline mean BMI of at least one study arm was <25; in 5 studies the baseline means were in the range for overweight/obese. Most studies (n=7) included mixed gender samples; 1 included only women. In 3 studies (38%) the participants had a high risk of CVD. In terms of type of intervention all 8 studies were lifestyle focused. Control participants received usual care from their physicians or no intervention; in 2 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 5 studies and more than 12 months in 3 studies. Two studies were conducted in the US, 4 in European countries, 1 in Australia, and 1 in Japan. Less than half of the studies (n=3) were published in the last 5 years (2009-2012); the remaining 5 studies were published between 1988 and 2007.

[30] The sample size is adequate (1,643 intervention arm, 1,737 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.8895 kg (-1.4352, -0.3439)]. This body of evidence was not downgraded for imprecision.

[31] There were too few studies (n<10) to assess publication bias.

[32] The 12 studies are:[66,73,74,76,77,79,81,83-85,89,90] Immediate post assessment for all but 4 studies; for these 4 studies the data point closest to the immediate post and ≥12 months post baseline was selected (Eriksson[84] provides 9 month follow-up data post completion of a 3 month intervention; Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Lawton[79] and Harris[81] provide 3 month follow-up data post completion of 9 month interventions).

[33] Using Cochrane's Risk of Bias tool, for this outcome 9 studies (75%) were rated as unclear risk and 3 studies (25%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (58%), blinding of outcome assessors (67%) and other sources of bias (83%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[34] The statistical heterogeneity is low [Chi^2=14.22, df=14 (P=0.43); I^2=2%], the direction of the effect is consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

[35] Across the 12 studies, baseline BMI ranged from 23.1 to 30.1; in 2 of the studies the baseline mean BMI of at least one study arm was <25; in 10 studies the baseline means were in the range for overweight/obese. Most studies (n=8) included mixed gender samples; 3 included only women and 1 included only men. In 2 studies (17%) the participants had a high risk of CVD. In terms of type of intervention 1 was diet, 5 were exercise, 1 was diet plus exercise, and 5 were

lifestyle. Control participants received usual care from their physicians or no intervention; in 3 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in all 12 studies. One study was conducted in Canada, 3 in the US, 5 in European countries, 2 in Australia or New Zealand, and 1 in Japan. Just over half of the studies (n=7) were published in the last 5 years (2009-2012); the remaining 5 studies were published between 1988 and 2008.

[36] The sample size is adequate (2,383 intervention arm, 2,525 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.6056 kg (-0.6989, -0.5122)]. This body of evidence was not downgraded for imprecision.

[37] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (p=0.053). This body of evidence was not downgraded for suspected publication bias.

[38] The 7 studies are:[65,67,68,70,71,78,80] Immediate post assessment for all but 1 study; for the one exception the data point closest to the immediate post and ≥12 months post baseline was selected (Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[39] Using Cochrane's Risk of Bias tool, for this outcome 4 studies (57%) were rated as unclear risk, 2 studies (29%) were rated as high risk, and 1 study (14%) was rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (43%), allocation concealment (71%), blinding of outcome assessors (57%) and other sources of bias (86%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate and high risk of bias, this body of evidence was downgraded for serious study limitations.

[40] Although the statistical heterogeneity is high and significant [Chi^2=26.71, df=6 (P=0.0002); I^2=78%] the direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[41] Across the 7 studies, baseline BMI ranged from 22.4 to 29.8; in 1 study the baseline mean BMI of at least one study arm was <25; in 6 studies the baseline means were in the range for overweight/obese. Four studies included mixed gender samples; 3 included only women. In 1 study (14%) the participants had a high risk of CVD. In terms of type of intervention 1 was diet, 3 were diet plus exercise, and 3 were lifestyle. Control participants received usual care from their physicians or no intervention; in 4 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was more than 12 months in all 7 studies. One study was conducted in Canada, 3 in the US, and 3 in European countries. Only 2 studies were published in the last 5 years (2011, 2012); the remaining 5 studies were published between 2002 and 2007.

[42] The sample size is adequate (17,442 intervention arm, 26,110 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-1.2095 kg (-1.8786, -0.5403)]. This body of evidence was not downgraded for imprecision.

[43] There were too few studies (n<10) to assess publication bias.

[44] The 4 studies are:[66,73,76,89] Immediate post assessment for all studies.

[45] Using Cochrane's Risk of Bias tool, for this outcome all 4 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (75%), allocation concealment (75%), blinding of outcome assessors (75%) and other sources of bias (100%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[46] The statistical heterogeneity is low [Chi^2=2.43, df=3 (P=0.49); I^2=0%] the direction of the effect is consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

[47] Across the 4 studies, baseline BMI ranged from 23.1 to 29.3; in 1 study the baseline mean BMI of at least one study arm was <25. Most studies (n=3) included mixed gender samples; 1 included only men. In all 4 studies the participants had low/unknown risk of CVD. In terms of type of intervention 1 was diet, 1 was exercise, 1 was diet plus exercise, and 1 was lifestyle. Control participants received usual care from their physicians or no intervention; in 2 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in all 4 studies. Two studies were conducted in the US and 2 in European countries. Half of the studies (n=2) were published in the last 5 years (2010, 2011); the other two studies were published in 1988 and 1997.

[48] The sample size is adequate (475 intervention arm, 500 control arm) but the pooled effect estimate is not precise with a confidence interval that includes the no effect value [MD -0.4790 kg (-0.9850, 0.0270)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[49]There were too few studies (n<10) to assess publication bias.

[50] The 9 studies are:[66,67,70,71,73,74,77,79,89] Immediate post assessment for all but 2 studies; for these 2 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Lawton[79] provides 3 month follow-up data post completion of a 9 month intervention; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[51] Using Cochrane's Risk of Bias tool, for this outcome 6 studies (67%) were rated as unclear risk and 3 studies (33%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (44%), allocation concealment (67%), blinding of outcome assessors (44%) and other sources of bias (89%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[52] Although the statistical heterogeneity is high and significant [Chi^2=29.79, df=8 (P=0.0002); I^2=73%] the direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[53] Across the 9 studies, baseline BMI ranged from 23.1 to 29.3; in 1 study the baseline mean BMI of at least one study arm was <25; in 8 studies the baseline means were in the range for overweight/obese. Three studies included mixed gender samples; 6 included only women. In all 8 studies the participants had

low/unknown risk of CVD. In terms of type of intervention 2 were diet, 4 were exercise, 1 was diet plus exercise, and 2 were lifestyle. Control participants received usual care from their physicians or no intervention; in 3 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 6 studies and more than 12 months in 3 studies. One study was conducted in Canada, 5 in the US, 2 in European countries, and 1 in New Zealand. About half of the studies (n=4) were published in the last 5 years (2009-2011); the remaining 5 studies were published between 1988 and 2008.

[54] The sample size is adequate (17,845 intervention arm, 26,545 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.8177 kg (-1.0882, -0.5472)]. This body of evidence was not downgraded for imprecision.

[55] There were too few studies (n<10) to assess publication bias.

[56] The 3 studies are:[65,84,90] Immediate post assessment for all but 1 study; for the exception the data point closest to the immediate post and ≥12 months post baseline was selected (Eriksson[84] provides 9 month follow-up data post completion of a 3 month intervention).

[57] Using Cochrane's Risk of Bias tool, for this outcome all 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) associated with sequence generation (33%), allocation concealment (67%), blinding of outcome assessors (67%) and other sources of bias (67%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[58] The statistical heterogeneity is low [Chi^2=1.22, df=2 (P=0.54); I^2=0%], the direction of the effect is consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

[59] Across the 3 studies, baseline BMI ranged from 28.1 to 30.1. All 3 studies included mixed gender samples. In all 3 studies the participants had a high risk of CVD. In terms of type of intervention all 3 were lifestyle focused. Control participants received usual care from their physicians or no intervention; in 1 study control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 2 studies and more than 12 months in 1 study. All 3 studies were conducted in European countries. One study was published in the last 5 years (2009); the other 2 studies were published in 1999 and 2002.

[60] The sample size is adequate (588 intervention arm, 768 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.8849 kg (-1.4512, -0.3186)]. This body of evidence was not downgraded for imprecision.

[61] There were too few studies (n<10) to assess publication bias.

[62] The 16 studies are:[66-68,70,71,73,74,76-81,83,85,89] Immediate post assessment for all but 4 studies; for these 4 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Lawton[79] and Harris[81] provide 3 month follow-up data post completion of 9 month interventions; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[63] Using Cochrane's Risk of Bias tool, for this outcome 10 studies (63%) were rated as unclear risk, 2 studies (12.5%) were rated as high risk, and 4 studies (25%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (63%), blinding of outcome assessors (63%) and other sources of bias (88%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate and high risk of bias, this body of evidence was downgraded for serious study limitations.

[64] Although the statistical heterogeneity is moderate and significant [Chi^2=38.75, df=18 (P=0.003); I^2=54%] the direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[65] Across the 16 studies, baseline BMI ranged from 22.4 to 30.1; in 3 of the studies the baseline mean BMI of at least one study arm was <25; in 13 studies the baseline means were in the range for overweight/obese. About half of the studies (n=9) included mixed gender samples; 6 included only women and 1 included only men. In all 16 studies the participants had low/unknown risk of CVD. In terms of type of intervention 2 were diet, 5 were exercise, 4 were diet plus exercise, and 5 were lifestyle. Control participants received usual care from their physicians or no intervention; in 6 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 10 studies and more than 12 months in 6 studies. Two studies were conducted in Canada, 6 in the US, 5 in European countries, 2 in Australia or New Zealand, and 1 in Japan. Half of the studies (n=8) were published in the last 5 years (2009-2012); the remaining 8 studies were published between 1988 and 2008.

[66] The sample size is adequate (19,237 intervention arm, 27,867 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.7242 kg (-0.9333, -0.5151)]. This body of evidence was not downgraded for imprecision.

[67] The funnel plot for these studies and this outcome is asymmetrical. The Egger's test was conducted to detect publication bias; results were significant (p=0.009). This body of evidence was downgraded for strongly suspected publication bias.

[68] The 2 studies are:[78,80] Immediate post assessment for both studies.

[69] Using Cochrane's Risk of Bias tool, for this outcome both studies were rated high risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (100%), allocation concealment (100%), blinding of outcome assessors (100%) and other sources of bias (100%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at high risk of bias, this body of evidence was downgraded for very serious study limitations.

[70] Although the statistical heterogeneity is high and significant [Chi^2=3.96, df=1 (P=0.05); I^2=75%] the direction of the effect is consistent across studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[71] Across the 2 studies, baseline BMI ranged from 28.5 to 29.8. Both studies included mixed gender samples. In both studies the participants had low/unknown risk of CVD. In terms of type of intervention 1 was diet plus exercise and 1 was lifestyle. Control participants received usual care from their physicians or no intervention and in both of these studies they also received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was more than 12 months in both studies. Both studies were conducted in the Netherlands. One study was published in the last 5 years (2012); the other study was published in 2003.

[72] The sample size is adequate (345 intervention arm, 307 control arm) but the pooled effect estimate is not precise with a confidence interval that includes the no effect value [MD -1.2001 kg (-3.0388, 0.6385)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[73] There were too few studies (n<10) to assess publication bias.

[74] The 13 studies are:[65-68,70,73,76,77,83-85,89,90] Immediate post assessment for all but 3 studies; for these 3 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] provides 9 month follow-up data post completion of a 3 month intervention; Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[75] Using Cochrane's Risk of Bias tool, for this outcome all 13 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (54%), allocation concealment (69%), blinding of outcome assessors (77%) and other sources of bias (92%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[76] The statistical heterogeneity is low [Chi^2=8.49, df=15 (P=0.90); I^2=0%] the direction of the effect is consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

[77] Across the 13 studies, baseline BMI ranged from 22.4 to 30.1; in 3 of the studies the baseline mean BMI of at least one study arm was <25; in 10 studies the baseline means were in the range for overweight/obese. Most studies (n=9) included mixed gender samples; 3 included only women and 1 included only men. In 3 studies (23%) the participants had a high risk of CVD. In terms of type of intervention 2 were diet, 3 were exercise, 3 were diet plus exercise, and 5 were lifestyle. Control participants received usual care from their physicians or no intervention; in 5 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 9 studies and more than 12 months in 4 studies. One study was conducted in Canada, 6 in the US, and 6 in European countries. About half of the studies (n=6) were published in the last 5 years (2009-2012); the remaining 7 studies were published between 1988 and 2007.

[78] The sample size is adequate (18,175 intervention arm, 27,062 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.5339 kg (-0.6655, -0.4023)]. This body of evidence was not downgraded for imprecision.

[79] The funnel plot for these studies and this outcome is asymmetrical. The Egger's test was conducted to detect publication bias; results were significant (p=0.022). This body of evidence was downgraded for strongly suspected publication bias.

[80] The 4 studies are:[71,74,79,81] Immediate post assessment for 2 studies and for the other 2 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Lawton[79] and Harris[81] provide 3 month follow-up data post completion of 9 month interventions).

[81] Using Cochrane's Risk of Bias tool, for this outcome all 4 studies were rated as low risk. All ratings were low except 1 study had unclear allocation concealment and 2 studies had problems with other sources of bias (i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at low risk of bias, this body of evidence was not downgraded for serious study limitations.

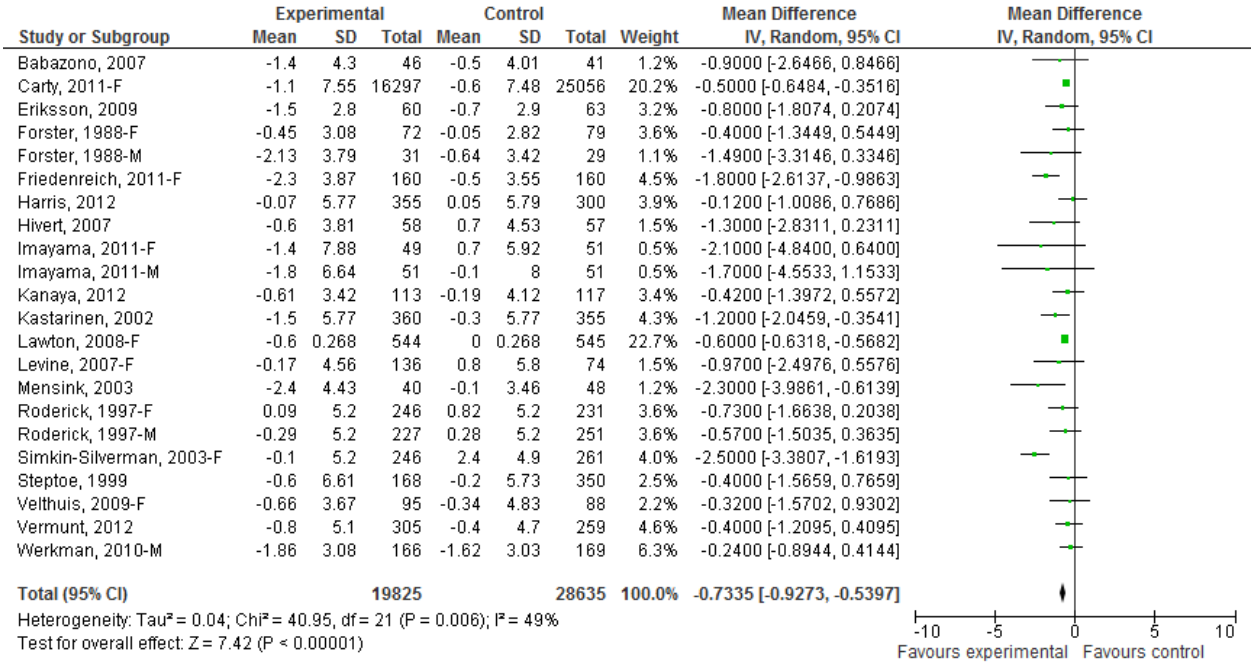
[82] The statistical heterogeneity is high and significant [Chi^2=27.30, df=3 (P<0.00001); I^2=89%]. While the direction of the effect is consistent across studies, there is some concern about the amount of overlap across confidence intervals. This body of evidence was downgraded for inconsistency.

[83] Across the 4 studies, baseline BMI ranged from 25 to 29.2. Only 1 study included a mixed gender sample; 3 included only women. In all 4 studies the participants had low/unknown risk of CVD. In terms of type of intervention 2 were exercise and 2 were lifestyle. Control participants received usual care from their physicians or no intervention. Intervention duration was 12 months or less in 3 studies and more than 12 months in 1 study. One study was conducted in Canada, 1 in the US, 1 in Australia, and 1 in New Zealand. Half of the studies (n=2) were published in the last 5 years (2011, 2012); the other 2 studies were published in 2003 and 2008.

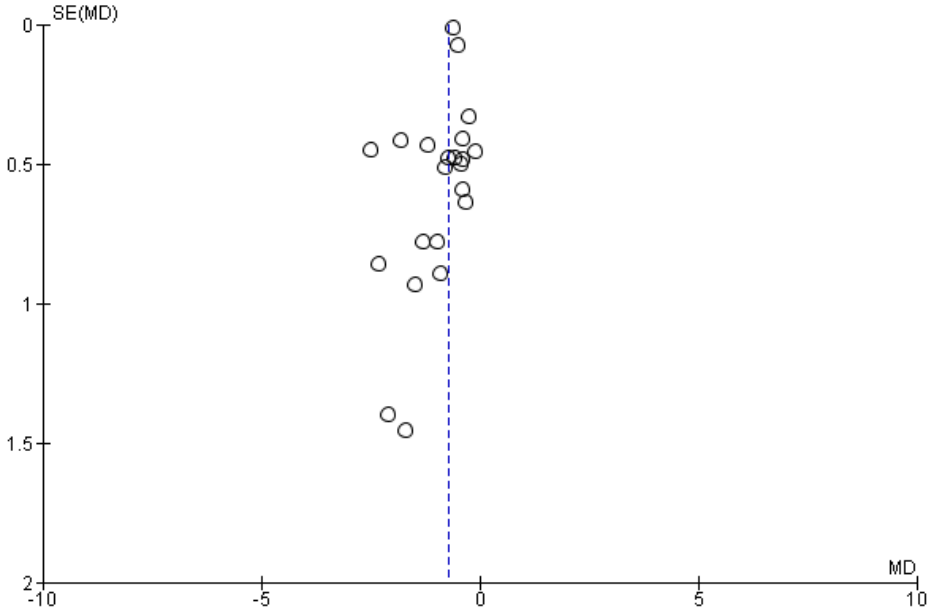
[84] The sample size is adequate (1,305 intervention arm, 1,266 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-1.2204 kg (-2.1586, -0.2822)]. This body of evidence was not downgraded for imprecision.

[85] There were too few studies (n<10) to assess publication bias.

Forest Plot 1.1: Effect of Weight Gain Prevention Interventions on Weight in KG – Overall



Funnel Plot 1.1: Effect of Weight Gain Prevention Interventions on Weight in KG – Overall

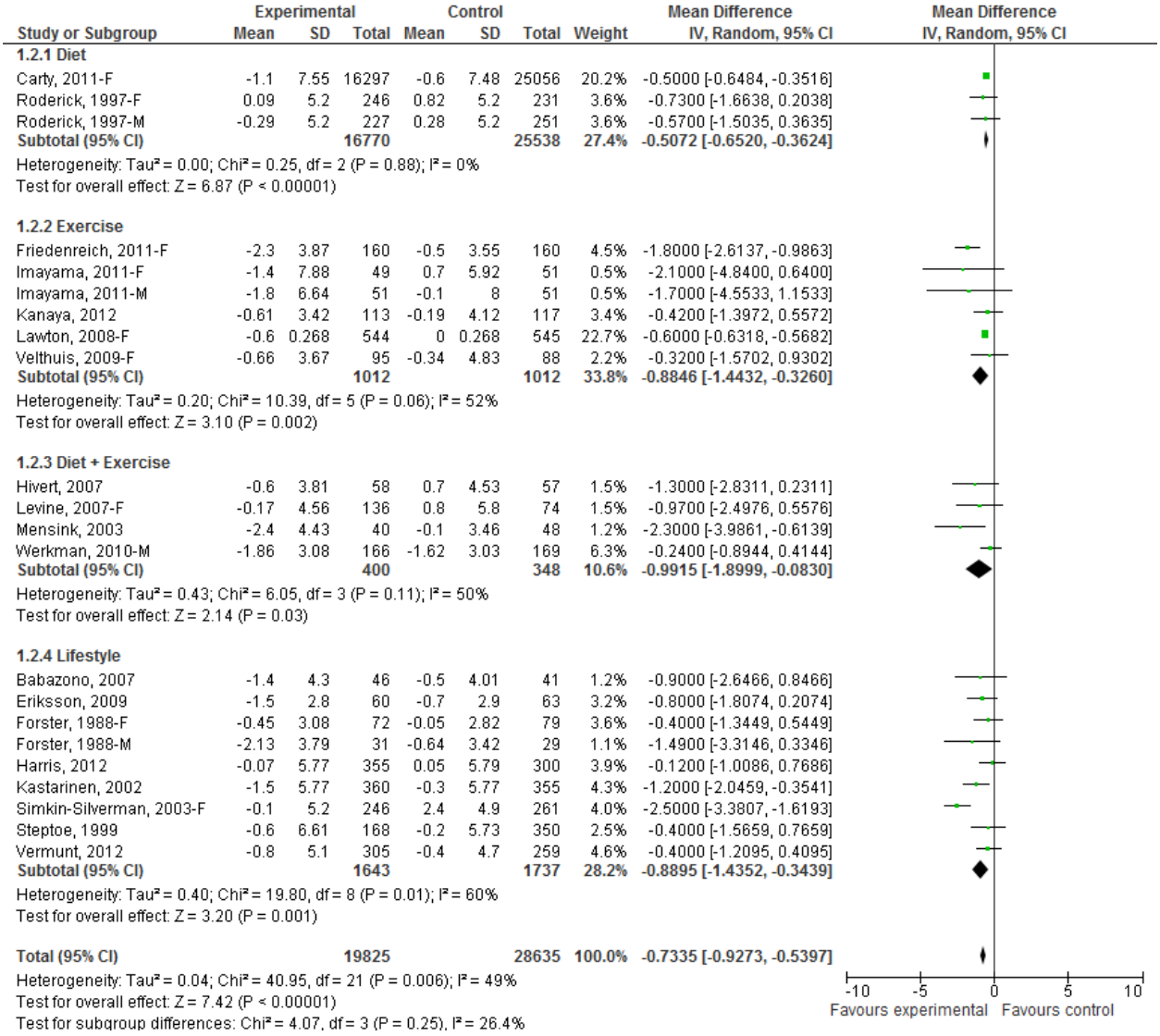


Egger's Test to Detect Publication Bias: Weight Change in KG – Overall

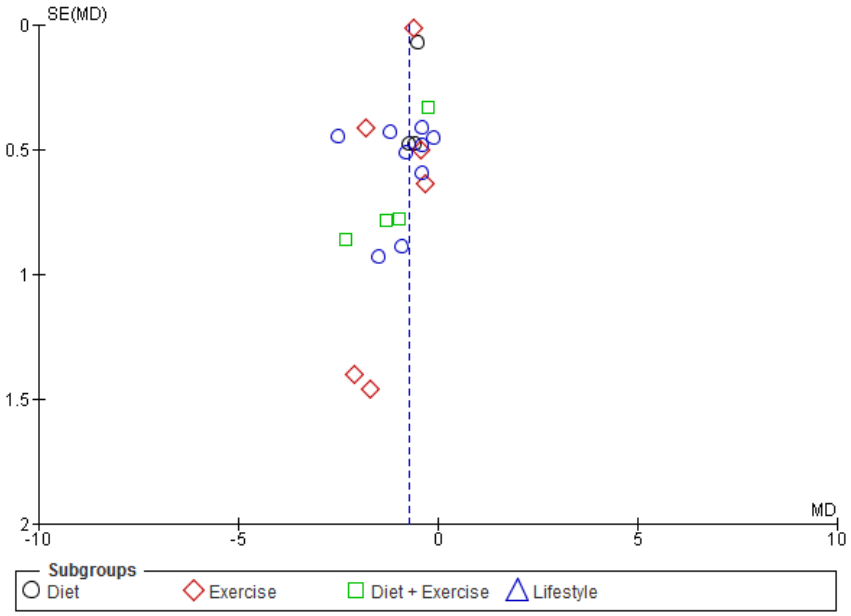
Included Studies	P-value
Overall	0.003*

* Significant p≤0.05

Forest Plot 1.2: Effect of Weight Gain Prevention Interventions on Weight in KG – by Type of Intervention (Diet, Exercise, Diet plus Exercise, Lifestyle)



Funnel Plot 1.2: Effect of Weight Gain Prevention Interventions on Weight in KG – by Type of Intervention (Diet, Exercise, Diet plus Exercise, Lifestyle)

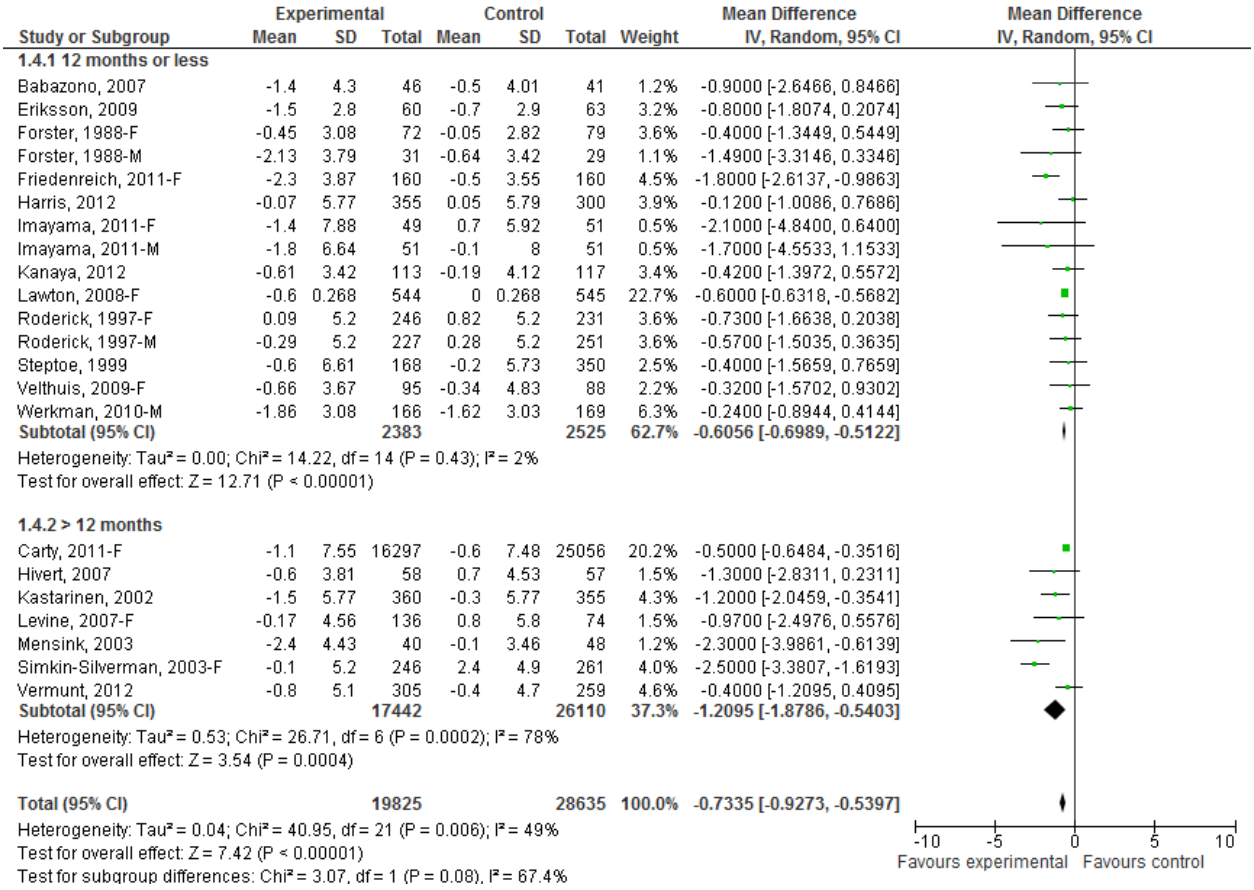


Egger's Test to Detect Publication Bias: Weight Change in KG – by Type of Intervention (Diet, Exercise, Diet plus Exercise, Lifestyle)

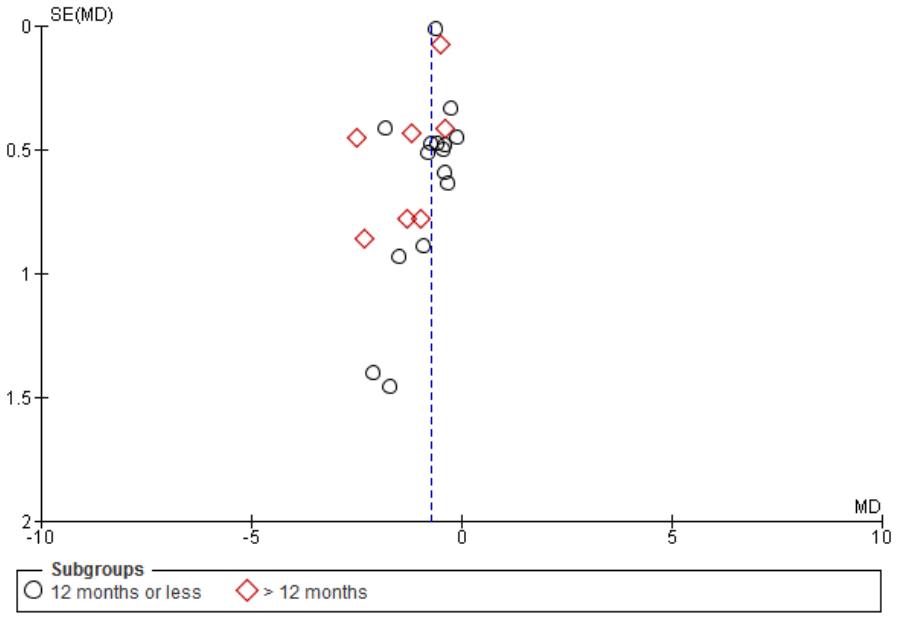
Included Studies	P-value
Diet	**
Exercise	**
Diet plus Exercise	**
Lifestyle	**

** Too few studies (n<10) to assess

Forest Plot 1.3: Effect of Weight Gain Prevention Interventions on Weight in KG – by Duration of Intervention (≤ 12 Months, >12 Months)



Funnel Plot 1.3: Effect of Weight Gain Prevention Interventions on Weight in KG – by Duration of Intervention (≤ 12 Months, >12 Months)

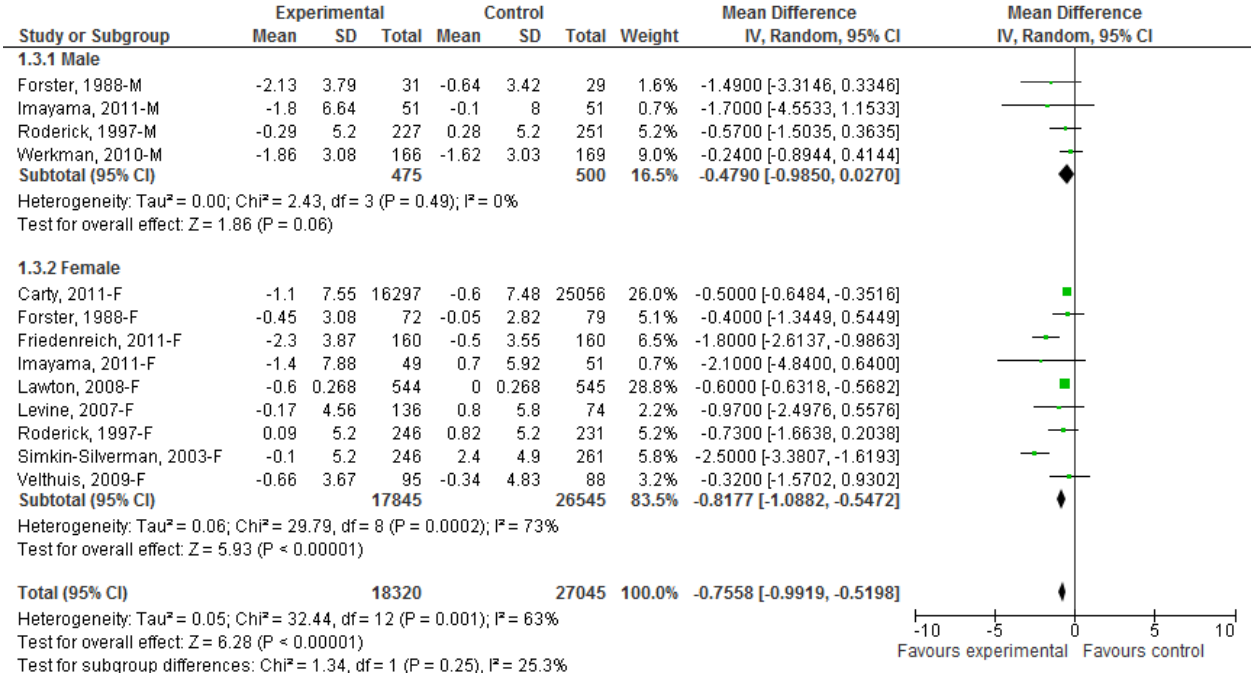


Egger's Test to Detect Publication Bias: Weight in KG – by Duration of Intervention (≤ 12 Months, >12 Months)

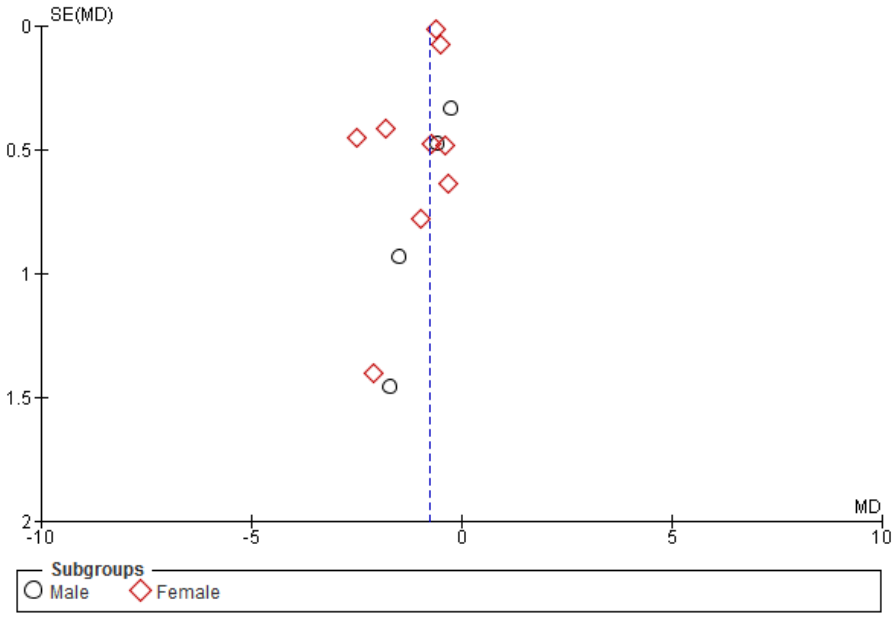
Included Studies	P-value
≤12 Months	0.053
>12 Months	**

** Too few studies (n<10) to assess

Forest Plot 1.4: Effect of Weight Gain Prevention Interventions on Weight in KG – by Gender



Funnel Plot 1.4: Effect of Weight Gain Prevention Interventions on Weight in KG – by Gender

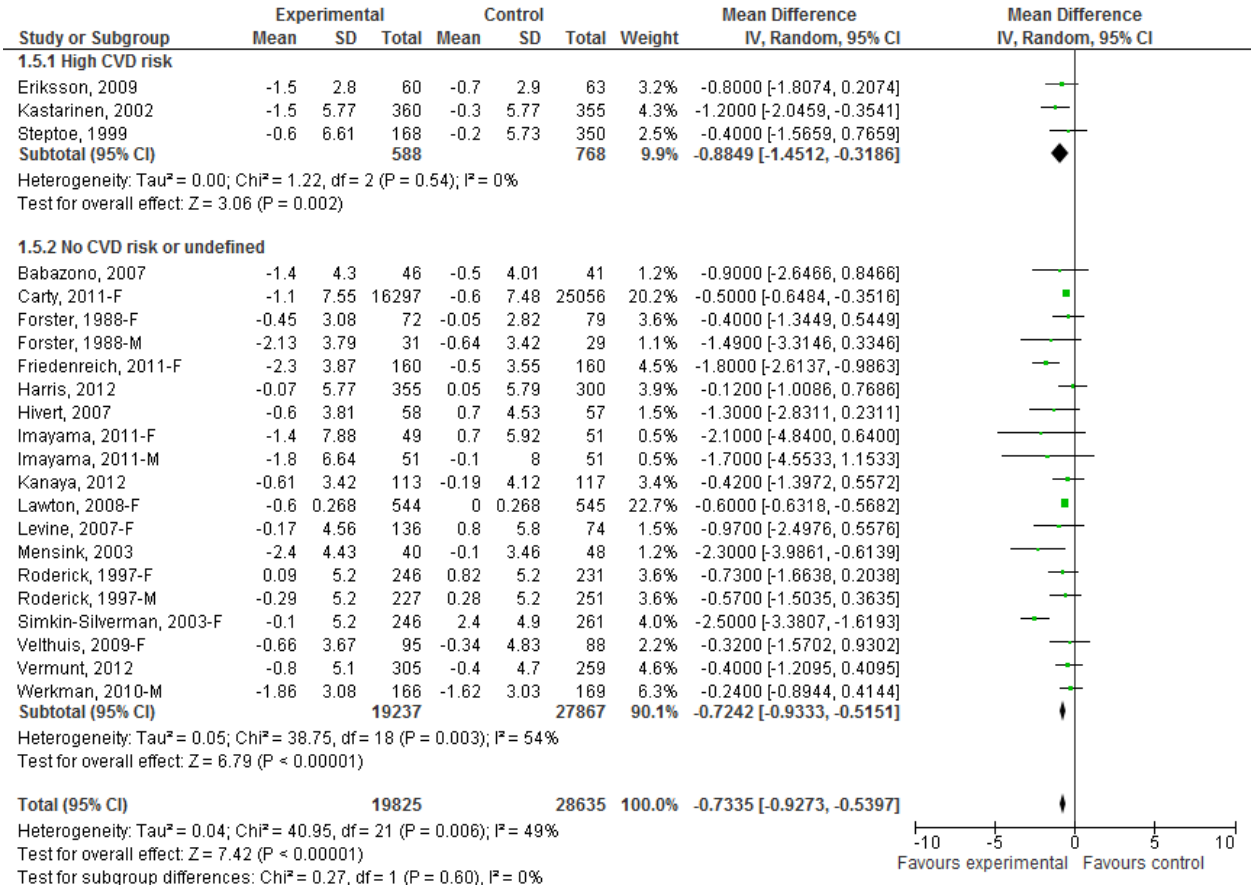


Egger's Test to Detect Publication Bias: Weight Change in KG – by Gender

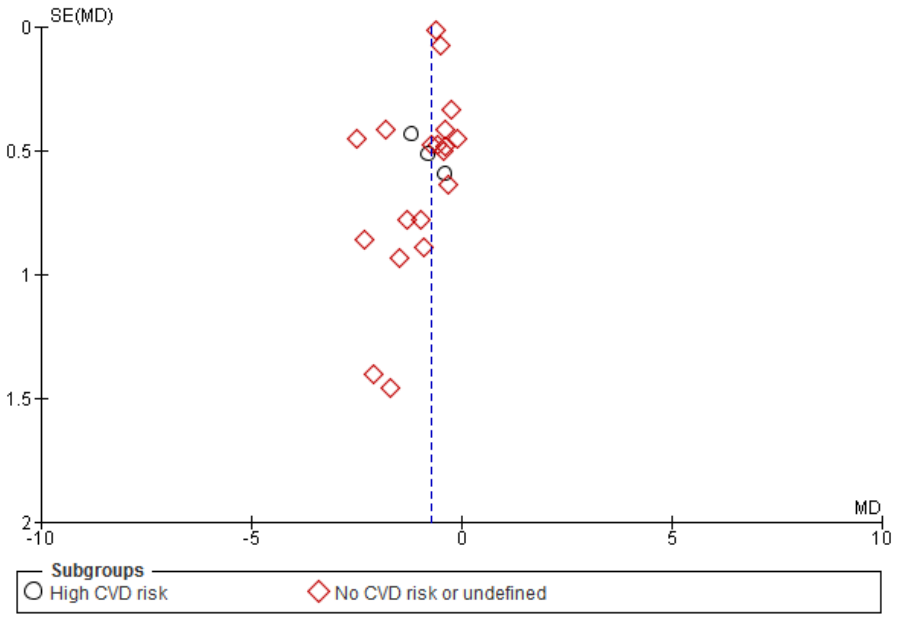
Included Studies	P-value
Male	**
Female	**

** Too few studies (n<10) to assess

Forest Plot 1.5: Effect of Weight Gain Prevention Interventions on Weight in KG – by Participants' Baseline CVD Risk Status (High Risk, Low/Unknown Risk)



Funnel Plot 1.5: Effect of Weight Gain Prevention Interventions on Weight in KG – by Participants' Baseline CVD Risk Status (High Risk, Low/Unknown Risk)



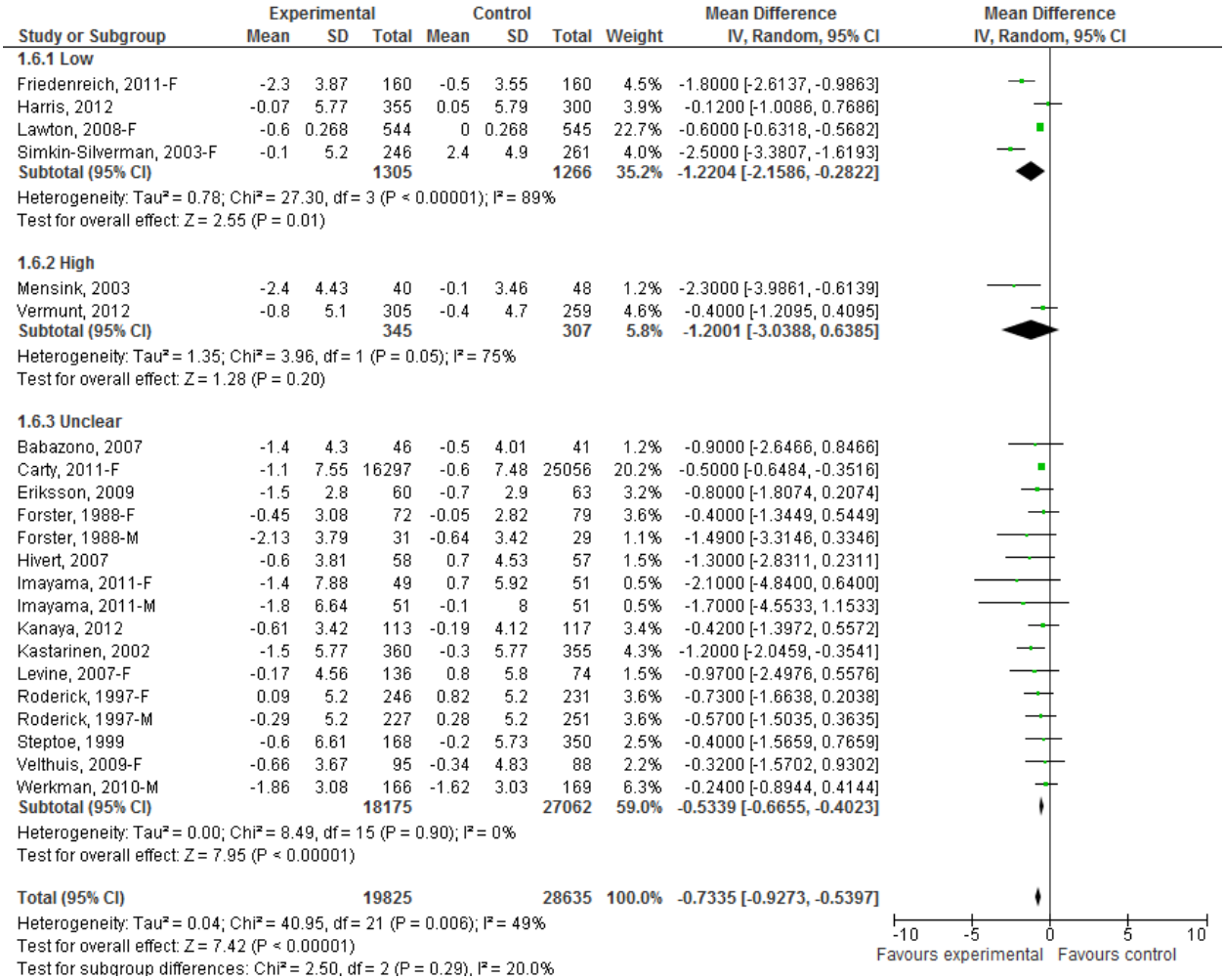
Egger's Test to Detect Publication Bias: Weight Change in KG – by Participants' Baseline CVD Risk Status (High Risk, Low/Unknown Risk)

Included Studies	P-value
High CVD Risk	**
Low/Unknown CVD Risk	0.009*

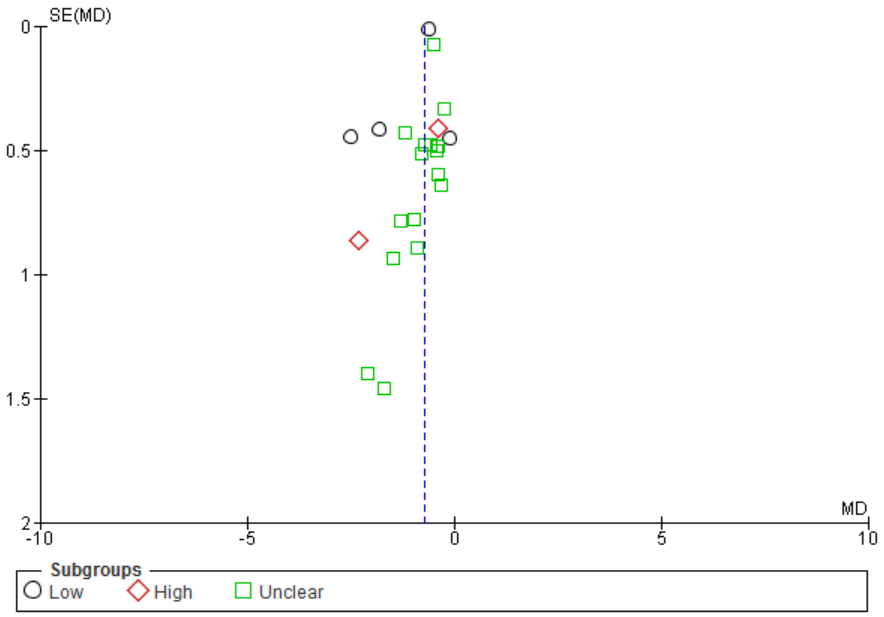
* Significant p≤0.05

** Too few studies (n<10) to assess

Forest Plot 1.6: Effect of Weight Gain Prevention Interventions on Weight in KG – by Study Risk of Bias Rating (High, Unclear, Low)



Funnel Plot 1.6: Effect of Weight Gain Prevention Interventions on Weight in KG – by Study Risk of Bias Rating (High, Unclear, Low)



Egger's Test to Detect Publication Bias: Weight Change in KG – by Study Risk of Bias Rating (High, Unclear, Low)

Included Studies	P-value
High Risk	**
Unclear Risk	0.022*
Low Risk	**

* Significant p≤0.05

** Too few studies (n<10) to assess

Evidence Set 2: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to short-term or sustained weight gain prevention (BMI)?

- Summary of Change in BMI Evidence
- GRADE Evidence Profile Table 2.1: Effect of Weight Gain Prevention Interventions on BMI
- GRADE Summary of Findings Table 2.1: Effect of Weight Gain Prevention Interventions on BMI
- Forest Plot 2.1: Effect of Weight Gain Prevention Interventions on BMI
- Forest Plot 2.2: Effect of Weight Gain Prevention Intervention on BMI – by Baseline Mean BMI
- Funnel Plot 2.1: Effect of Weight Gain Prevention Interventions on BMI
- Egger's Test Results (for Publication Bias)

Summary of Change in BMI Evidence

Overall

- 20 studies; 52,243 participants
- Statistically significant reduction (P<0.00001) in BMI in the intervention group as compared to the control group [MD (95% CI) -0.24 kg/m^2 (-0.34, -0.15)]
- Moderate statistical heterogeneity across studies [Chi^2=55.70, df=20 (P<0.0001), I^2=64%]

Test for subgroup differences is not significant [Chi^2=0.06, df=1 (P=0.81), I^2=0%]; baseline mean BMI does not explain variation across studies

By Baseline Mean BMI – Normal Weight (<25 kg/m^2)

- 4 studies; 5,152 participants
- Statistically significant reduction (P=0.02) in BMI in the intervention group as compared to the control group [MD (95% CI) -0.27 kg/m^2 (-0.50, -0.05)]
- Moderate statistical heterogeneity across studies [Chi^2=5.68, df=3 (P=0.13), I^2=47%]

By Baseline Mean BMI – Overweight/Obese (≥25 kg/m^2)

- 16 studies; 47,091 participants
- Statistically significant reduction (P<0.0001) in BMI in the intervention group as compared to the control group [MD (95% CI) -0.24 kg/m^2 (-0.36, -0.12)]
- Moderate statistical heterogeneity across studies [Chi^2=49.64, df=16 (P<0.0001), I^2=68%]

GRADE Evidence Profile Table 2.1: Effect of Weight Gain Prevention Interventions on BMI *

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in BMI: Overall (Better indicated by lower values)											
20	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	none[7]	21,761	30,482	0.2448 lower (0.3443 to 0.1453 lower)	⊕⊕OO LOW	CRITICAL
Change in BMI: by Baseline Mean BMI – Normal Weight (<25 kg/m^2) ((Better indicated by lower values)											
4	randomized trials[8]	serious risk[9]	no serious inconsistency[10]	serious indirectness[4,11]	no serious imprecision[12]	none[13]	2,582	2,570	0.2732 lower (0.4967 to 0.0497 lower)	⊕⊕OO LOW	CRITICAL
Change in BMI: by Baseline Mean BMI – Overweight/Obese (≥25 kg/m^2) (Better indicated by lower values)											
16	randomized trials[14]	serious risk[15]	no serious inconsistency[16]	serious indirectness[4,17]	no serious imprecision[18]	none[19]	19,179	27,912	0.2417 lower (0.3625 to 0.1210 lower)	⊕⊕OO LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 2.1: Effect of Weight Gain Prevention Interventions on BMI

Outcome: Change in BMI	Compared to the control group, the mean reduction in BMI (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in BMI	**0.2448 lower** (0.3443 to 0.1453 lower)	52,243 (20 studies[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6,7]
By Baseline Mean BMI – Normal Weight (<25 kg/m^2)	**0.2732 lower** (0.4967 to 0.0497 lower)	5,152 (4 studies[8])	⊕⊕⊖⊖ **low**[4,9,10,11,12,13]
By Baseline Mean BMI – Overweight/Obese (≥25 kg/m^2)	**0.2417 lower** (0.3625 to 0.1210 lower)	47,091 (16 studies[14])	⊕⊕⊖⊖ **low**[4,15,16,17,18,19]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on BMI

[1] The 20 studies are:[66-69,71,72,74-78,80,82,84-90] Immediate post assessment for all but 5 studies; for these 5 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] and Khare[86] provide 9 month follow-up data post completion of 3 month interventions; Sacerdote[88] provides 12 month follow-up for a 15 minute intervention; Sone[75] presents outcomes at 36 months post baseline assessment for an intervention of unspecified duration; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 15 studies (75%) were rated as unclear risk, 2 studies (10%) were rated as high risk, and 3 studies (15%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (65%), blinding of outcome assessors (75%) and other sources of bias (90%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] Although the statistical heterogeneity is moderate and significant [Chi^2=55.70, df=20 (P<0.0001); I^2=64%] the direction of the effect is consistent across all but one study and aside from this one exception the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 20 studies, baseline BMI ranged from 22.4 to 33.2; in 4 of the studies the baseline mean BMI of at least one study arm was <25; in 16 studies the baseline means were in the range for overweight/obese. Most studies (n=14) included mixed gender samples; 5 included only women and 1 included only men. In 3 studies (15%) the participants had a high risk of CVD. In terms of type of intervention 3 were diet, 4 were exercise, 4 were diet plus exercise, and 9 were lifestyle. Control participants received usual care from their physicians or no intervention; in 7 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 14 studies and more than 12 months in 6 studies. Three studies were conducted in Canada, 4 in the US, 9 in European countries, 2 in Australia or New Zealand, and 2 in Japan. About half of the studies (n=9) were published in the last 5 years (2009-2012); the remaining 11 studies were published between 1997 and 2007.

[6] The sample size is adequate (21,761 intervention arm, 30,482 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.2448 (-0.3443, -0.1453)]. This body of evidence was not downgraded for imprecision.

[7] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (p=0.280). This body of evidence was not downgraded for suspected publication bias.

[8] The 4 studies are:[68,75,85,88] Immediate post assessment for 2 studies; for the other 2 studies the data point closest to the immediate post and ≥12 months post baseline was selected (Sacerdote[88] provides 12 month follow-up for a 15 minute intervention; Sone[75] presents outcomes at 36 months post baseline assessment for an intervention of unspecified duration).

[9] Using Cochrane's Risk of Bias tool, for this outcome all 4 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (75%), blinding of outcome assessors (100%) and other sources of bias (100%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[10] The statistical heterogeneity is moderate and not significant [Chi^2=5.68, df=3 (P=0.13); I^2=47%], the direction of the effect is consistent across all studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

[11] Across the 4 studies, baseline BMI ranged from 22.4 to 24.8; all studies included some overweight/obese adults. All studies included mixed gender samples and participants with low/unknown risk of CVD. In terms of type of intervention 2 were diet and 2 were lifestyle. Control participants received usual care from their physicians or no intervention. Intervention duration was 12 months or less in 2 studies and more than 12 months in 2 studies. One study was conducted in Canada, 2 in Japan and 1 in Italy. All of the studies (n=4) were published between 2002 and 2007.

[12] The sample size is adequate (2,582 intervention arm, 2,570 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.2732 (-0.4967, -0.0497)]. This body of evidence was not downgraded for imprecision.

[13] There were too few studies (n<10) to assess publication bias.

[14] The 16 studies are:[66,67,69,71,72,74,76-78,80,82,84,86,87,89,90] Immediate post assessment for all but 3 studies; for these 3 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] and Khare[86] provide 9 month follow-up data post completion of 3 month interventions; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[15] Using Cochrane's Risk of Bias tool, for this outcome 11 studies (69%) were rated as unclear risk, 2 studies (12%) were rated as high risk, and 3 studies (19%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (63%), blinding of outcome assessors (69%) and other sources of bias (88%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[16] Although the statistical heterogeneity is moderate and significant [Chi^2=49.64, df=16 (P<0.0001); I^2=68%] the direction of the effect is consistent across all but one study and aside from this one exception the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[17] Across the 16 studies, baseline BMI ranged from 25 to 33.2. Most studies (n=10) included mixed gender samples; 5 included only women and 1 included only men. In 3 studies (19%) the participants had a high risk of CVD. In terms of type of intervention 2 were diet, 4 were exercise, 3 were diet plus exercise, and 7 were lifestyle. Control participants received usual care from their physicians or no intervention; in 7 of these studies control participants received a minimal

component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 12 studies and more than 12 months in 4 studies. Two studies were conducted in Canada, 4 in the US, 8 in European countries, 1 in Australia and 1 in New Zealand. About half of the studies (n=9) were published in the last 5 years (2009-2012); the remaining 7 studies were published between 1997 and 2007.

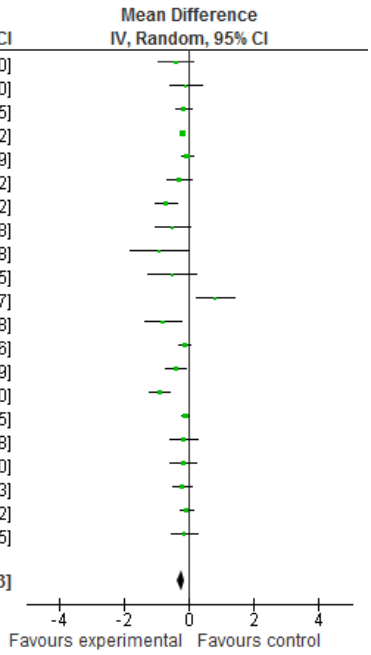
[18] The sample size is adequate (19,179 intervention arm, 27,912 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.2417 (-0.3625, -0.1210)]. This body of evidence was not downgraded for imprecision.

[19] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (p=0.504). This body of evidence was not downgraded for suspected publication bias.

Forest Plot 2.1: Effect of Weight Gain Prevention Interventions on BMI

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Babazono, 2007	-0.5	1.43	46	-0.1	1.1	41	2.6%	-0.4000 [-0.9330, 0.1330]
Broekhuizen, 2012	-0.1	1.99	167	0	2.38	147	3.0%	-0.1000 [-0.5890, 0.3890]
Burke, 2003	0.15	0.97	188	0.3	0.93	86	6.6%	-0.1500 [-0.3905, 0.0905]
Carty, 2011-F	-0.1	2.69	16230	0.1	2.64	24943	10.4%	-0.2000 [-0.2528, -0.1472]
Elley, 2003	-0.11	1.46	451	-0.05	1.32	427	7.8%	-0.0600 [-0.2439, 0.1239]
Eriksson, 2009	-0.5	1	60	-0.2	1.1	63	4.3%	-0.3000 [-0.6712, 0.0712]
Friedenreich, 2011-F	-0.9	1.61	160	-0.2	1.61	160	4.6%	-0.7000 [-1.0528, -0.3472]
Hivert, 2007	-0.3	1.52	58	0.2	1.51	57	2.5%	-0.5000 [-1.0538, 0.0538]
Imayama, 2011-F	-0.6	2.42	49	0.3	2.25	51	1.1%	-0.9000 [-1.8168, 0.0168]
Imayama, 2011-M	-0.5	1.71	51	0	2.12	51	1.5%	-0.5000 [-1.2475, 0.2475]
Khare, 2012-F	1.2	3.38	225	0.4	3.4	280	2.2%	0.8000 [0.2053, 1.3947]
Mensink, 2003	-0.8	1.26	40	0	1.39	48	2.5%	-0.8000 [-1.3542, -0.2458]
Roderick, 1997	0.01	1.32	407	0.14	1.32	357	7.7%	-0.1300 [-0.3176, 0.0576]
Sacerdote, 2006	-0.41	4.72	1488	0	3.84	1489	5.3%	-0.4100 [-0.7191, -0.1009]
Simkin-Silverman, 2003-F	0.05	2	260	0.96	1.8	275	5.0%	-0.9100 [-1.2330, -0.5870]
Sone, 2002	-0.1	1.39	990	0	1.34	983	9.2%	-0.1000 [-0.2205, 0.0205]
Steptoe, 1999	-0.23	2.38	168	-0.07	2.1	350	3.7%	-0.1600 [-0.5818, 0.2618]
Velthuis, 2009-F	-0.25	1.3	95	-0.07	1.61	88	3.6%	-0.1800 [-0.6060, 0.2460]
Vermunt, 2012	-0.3	1.8	305	-0.1	1.7	259	5.6%	-0.2000 [-0.4893, 0.0893]
Werkman, 2010-M	-0.49	1.01	166	-0.43	0.98	169	7.2%	-0.0600 [-0.2732, 0.1532]
Wister, 2007	-0.47	1.95	157	-0.33	1.8	158	3.7%	-0.1400 [-0.5545, 0.2745]
Total (95% CI)			**21761**			**30482**	**100.0%**	**-0.2448 [-0.3443, -0.1453]**

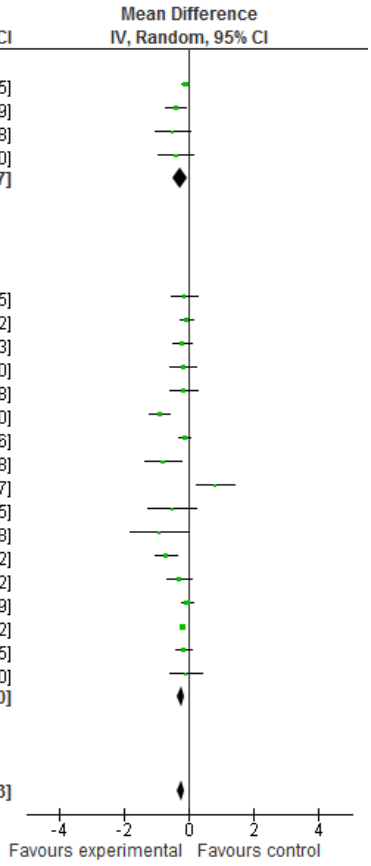
Heterogeneity: Tau² = 0.02; Chi² = 55.70, df = 20 (P < 0.0001); I² = 64%
Test for overall effect: Z = 4.82 (P < 0.00001)



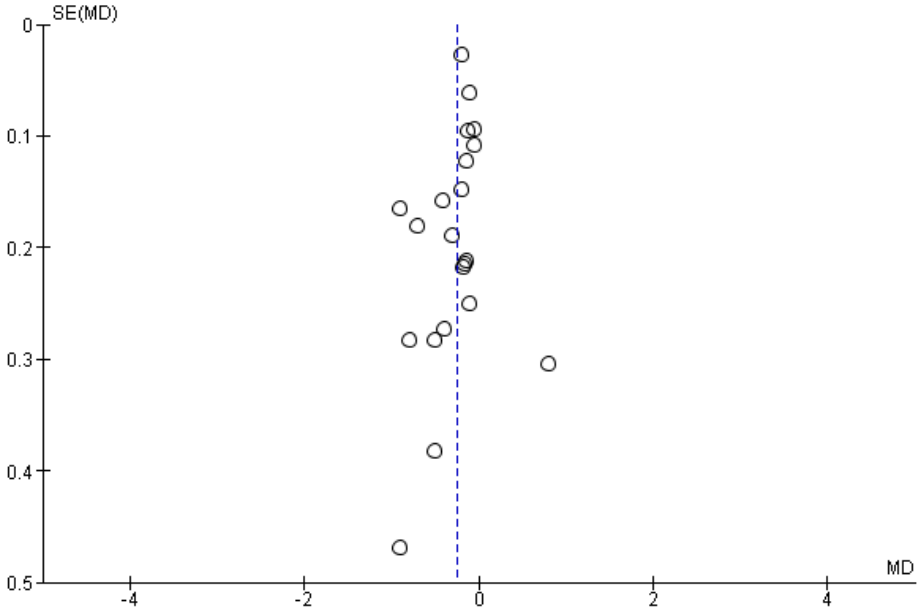
Forest Plot 2.2: Effect of Weight Gain Prevention Interventions on BMI – by Baseline Mean BMI

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.1.1 Baseline BMI < 25 kg/m2								
Sone, 2002	-0.1	1.39	990	0	1.34	983	9.2%	-0.1000 [-0.2205, 0.0205]
Sacerdote, 2006	-0.41	4.72	1488	0	3.84	1489	5.3%	-0.4100 [-0.7191, -0.1009]
Hivert, 2007	-0.3	1.52	58	0.2	1.51	57	2.5%	-0.5000 [-1.0538, 0.0538]
Babazono, 2007	-0.5	1.43	46	-0.1	1.1	41	2.6%	-0.4000 [-0.9330, 0.1330]
Subtotal (95% CI)			**2582**			**2570**	**19.6%**	**-0.2732 [-0.4967, -0.0497]**
Heterogeneity: Tau² = 0.02; Chi² = 5.68, df = 3 (P = 0.13); I² = 47%								
Test for overall effect: Z = 2.40 (P = 0.02)								
2.1.2 Baseline BMI => 25 kg/m2								
Wister, 2007	-0.47	1.95	157	-0.33	1.8	158	3.7%	-0.1400 [-0.5545, 0.2745]
Werkman, 2010-M	-0.49	1.01	166	-0.43	0.98	169	7.2%	-0.0600 [-0.2732, 0.1532]
Vermunt, 2012	-0.3	1.8	305	-0.1	1.7	259	5.6%	-0.2000 [-0.4893, 0.0893]
Velthuis, 2009-F	-0.25	1.3	95	-0.07	1.61	88	3.6%	-0.1800 [-0.6060, 0.2460]
Steptoe, 1999	-0.23	2.38	168	-0.07	2.1	350	3.7%	-0.1600 [-0.5818, 0.2618]
Simkin-Silverman, 2003-F	0.05	2	260	0.96	1.8	275	5.0%	-0.9100 [-1.2330, -0.5870]
Roderick, 1997	0.01	1.32	407	0.14	1.32	357	7.7%	-0.1300 [-0.3176, 0.0576]
Mensink, 2003	-0.8	1.26	40	0	1.39	48	2.5%	-0.8000 [-1.3542, -0.2458]
Khare, 2012-F	1.2	3.38	225	0.4	3.4	280	2.2%	0.8000 [0.2053, 1.3947]
Imayama, 2011-M	-0.5	1.71	51	0	2.12	51	1.5%	-0.5000 [-1.2475, 0.2475]
Imayama, 2011-F	-0.6	2.42	49	0.3	2.25	51	1.1%	-0.9000 [-1.8168, 0.0168]
Friedenreich, 2011-F	-0.9	1.61	160	-0.2	1.61	160	4.6%	-0.7000 [-1.0528, -0.3472]
Eriksson, 2009	-0.5	1	60	-0.2	1.1	63	4.3%	-0.3000 [-0.6712, 0.0712]
Elley, 2003	-0.11	1.46	451	-0.05	1.32	427	7.8%	-0.0600 [-0.2439, 0.1239]
Carty, 2011-F	-0.1	2.69	16230	0.1	2.64	24943	10.4%	-0.2000 [-0.2528, -0.1472]
Burke, 2003	0.15	0.97	188	0.3	0.93	86	6.6%	-0.1500 [-0.3905, 0.0905]
Broekhuizen, 2012	-0.1	1.99	167	0	2.38	147	3.0%	-0.1000 [-0.5890, 0.3890]
Subtotal (95% CI)			**19179**			**27912**	**80.4%**	**-0.2417 [-0.3625, -0.1210]**
Heterogeneity: Tau² = 0.03; Chi² = 49.64, df = 16 (P < 0.0001); I² = 68%								
Test for overall effect: Z = 3.92 (P < 0.0001)								
Total (95% CI)			**21761**			**30482**	**100.0%**	**-0.2448 [-0.3443, -0.1453]**

Heterogeneity: Tau² = 0.02; Chi² = 55.70, df = 20 (P < 0.0001); I² = 64%
Test for overall effect: Z = 4.82 (P < 0.00001)
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%



Funnel Plot 2.1: Effect of Weight Gain Prevention Interventions on BMI



Egger's Test to Detect Publication Bias: Change in BMI

Included Studies	P-value
All Studies Reporting Change in BMI	0.280
Normal Weight: Baseline Mean BMI <25	**
Overweight/Obese: Baseline Mean BMI ≥25	0.504

** Too few studies (n<10) to assess

Evidence Set 3: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to short-term or sustained weight gain prevention (waist circumference)?

- Summary of Change in Waist Circumference Evidence
- GRADE Evidence Profile Table 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference
- GRADE Summary of Findings Table 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference
- Forest Plot 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference
- Funnel Plot 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference
- Egger's Test Results (for Publication Bias)

Summary of Change in Waist Circumference Evidence

- 15 studies; 20,796 participants
- Statistically significant reduction (P<0.00001) in waist circumference in the intervention group as compared to the control group [MD (95% CI) -0.95 cm (-1.27, -0.63)]
- High statistical heterogeneity across studies [Chi^2=57.39, df=15 (P<0.00001), I^2=74%]

GRADE Evidence Profile Table 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference *

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in Waist Circumference (cm): Overall (Better indicated by lower values)											
15	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	reporting bias[7]	8,737	12,059	0.9466 lower (1.2664 to 0.6267 lower)	⊕OOO VERY LOW	CRITICAL

***** Footnotes appear after Summary of Findings Table

GRADE Summary of Findings Table 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference

Outcome: Change in Waist Circumference (cm)	Compared to the control group, the mean reduction in waist circumference (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in Waist Circumference	**0.9466 lower** (1.2664 to 0.6267 lower)	20,796 (15 studies[1])	⊕⊖⊖⊖ **very low**[2,3,4,5,6,7]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Waist Circumference

[1] The 15 studies are:[65-69,71,74,76-80,82-84] Immediate post assessment for all but 4 studies; for these 4 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] provides 9 month follow-up data post completion of a 3 month intervention; Kanaya[83] presents 6 month follow-up data post completion of a 6 month intervention; Lawton[79] provides 3 month follow-up data post completion of a 9 month intervention; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 9 studies (60%) were rated as unclear risk, 2 studies (13%) were rated as high risk, and 4 studies (27%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (27%), allocation concealment (40%), blinding of outcome assessors (53%) and other sources of bias (93%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] Although the statistical heterogeneity is high and significant [Chi^2=57.39, df=15 (P<0.00001); I^2=74%] the direction of the effect is consistent across all but one study and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

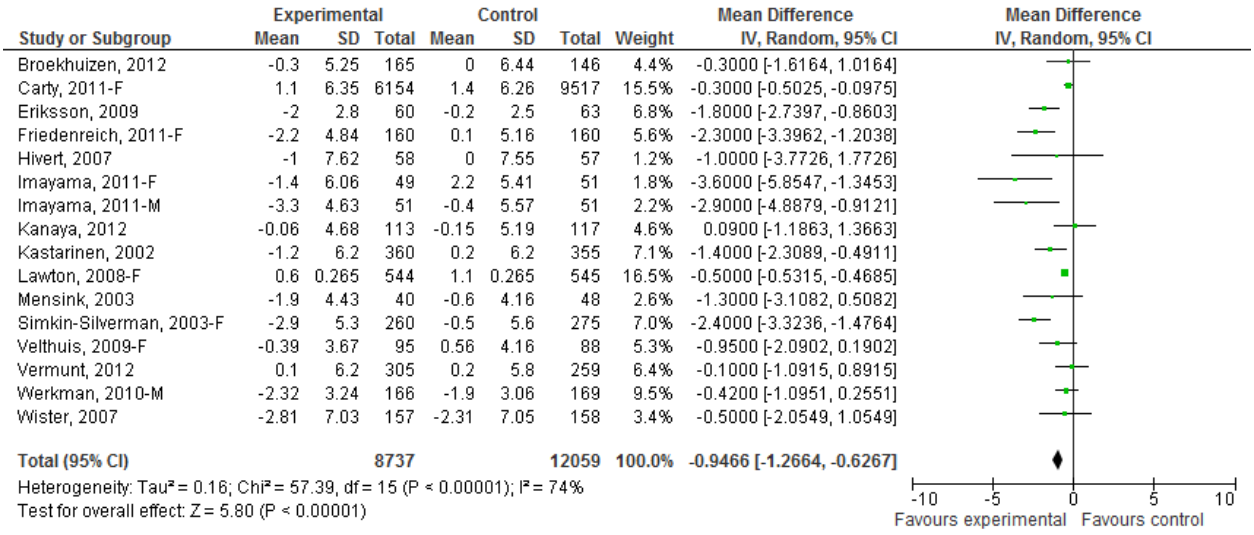
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 15 studies, baseline BMI ranged from 22.4 to 33.2; in 1 study the baseline mean BMI of at least one study arm was <25; in 14 studies the baseline means were in the range for overweight/obese. Nine studies included mixed gender samples; 5 included only women and 1 included only men. In 3 studies (20%) the participants had a high risk of CVD. In terms of type of intervention 1 was diet, 5 were exercise, 3 were diet plus exercise, and 6 were lifestyle. Control participants received usual care from their physicians or no intervention; in 5 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 9 studies and more than 12 months in 6 studies. Three studies were conducted in Canada, 4 in the US, 7 in European countries, and 1 in New Zealand. More than half of the studies (n=9) were published in the last 5 years (2009-2012); the remaining 6 studies were published between 2002 and 2008.

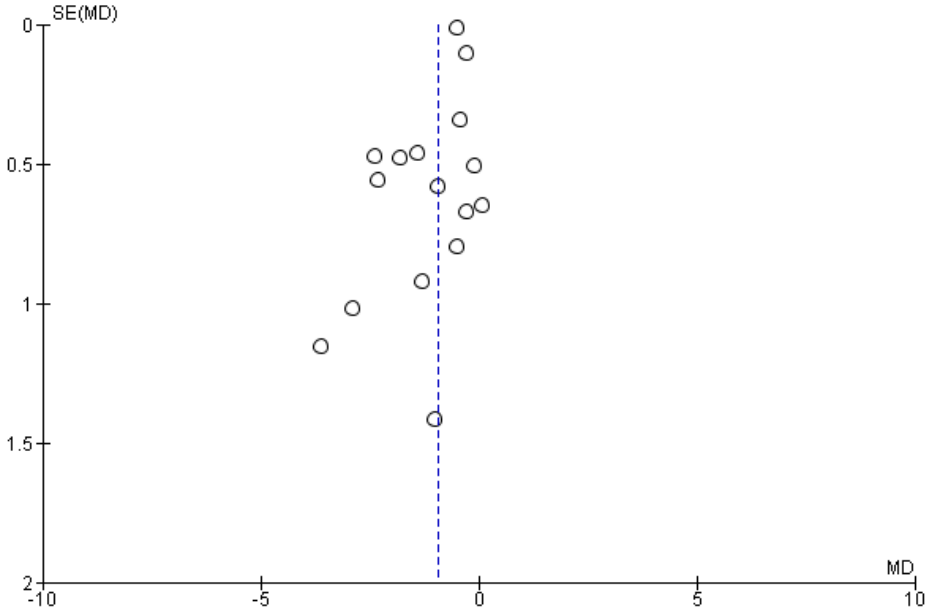
[6] The sample size is adequate (8,737 intervention arm, 12,059 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.9466 cm (-1.2664, -0.6267)]. This body of evidence was not downgraded for imprecision.

[7] The funnel plot for these studies and this outcome is asymmetrical. The Egger's test was conducted to detect publication bias; results were significant (p=0.039). This body of evidence was downgraded for strongly suspected publication bias.

Forest Plot 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference



Funnel Plot 3.1: Effect of Weight Gain Prevention Interventions on Waist Circumference



Egger's Test to Detect Publication Bias: Change in Waist Circumference

Included Studies	P-value
All Studies Reporting Change in Waist Circumference	0.039*

* Significant p≤0.05

Evidence Set 4: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to short-term or sustained weight gain prevention (total % body fat)?

- Summary of Change in Total % Body Fat Evidence
- GRADE Evidence Profile Table 4.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat
- GRADE Summary of Findings Table 5.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat
- Forest Plot 4.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat
- Funnel Plot 4.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat
- Egger's Test Results (for Publication Bias)

Summary of Change in Total % Body Fat Evidence

- 6 studies; 1,663 participants
- Statistically significant reduction (P=0.0002) in total % body fat in the intervention group as compared to the control group [MD (95% CI) -1.27 % (-1.93, -0.61)]
- High statistical heterogeneity across studies [Chi^2=30.23, df=6 (P<0.0001), I^2=80%]

GRADE Evidence Profile Table 4.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat *

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in Total % Body Fat: Overall (Better indicated by lower values)											
6	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	none[7]	821	842	1.2720 lower (1.9329 to 0.6111 lower)	⊕⊕OO LOW	CRITICAL

***** Footnotes appear after Summary of Findings Table

GRADE Summary of Findings Table 4.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat

Outcome: Change in Total % Body Fat	Compared to the control group, the mean reduction in total % body fat (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in Total % Body Fat	**1.2720 lower** (1.9329 to 0.6111 lower)	1,663 (6 studies[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6,7]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Total % Body Fat

[1] The 6 studies are:[66,71,74,76-78] Immediate post assessment for all studies.

[2] Using Cochrane's Risk of Bias tool, for this outcome 3 studies (50%) were rated as unclear risk, 1 study (17%) was rated as high risk, and 2 studies (33%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (50%), blinding of outcome assessors (50%) and other sources of bias (83%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate and high risk of bias, this body of evidence was downgraded for serious study limitations.

[3] Although the statistical heterogeneity is high and significant [Chi^2=30.23, df=6 (P<0.0001); I^2=80%] the direction of the effect is consistent across all but one study and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

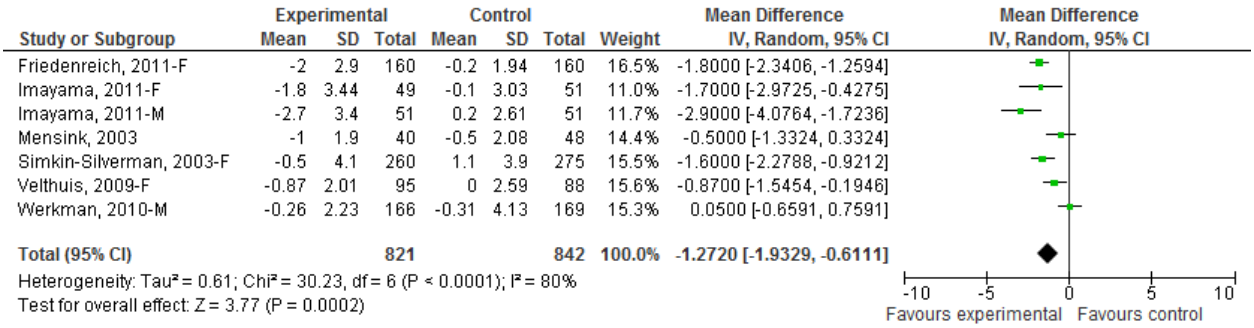
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 6 studies, baseline BMI ranged from 25 to 29.8. Two studies included mixed gender samples; 3 included only women and 1 included only men. In all 6 studies the participants had low/unknown risk of CVD. In terms of type of intervention 3 were exercise, 2 were diet plus exercise, and 1 was lifestyle. Control participants received usual care from their physicians or no intervention; in 2 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 4 studies and more than 12 months in 2 studies. One study was conducted in Canada, 2 in the US, and 3 in the Netherlands. Four of the studies were published in the last 5 years (2009-2011); the remaining 2 studies were published in 2003.

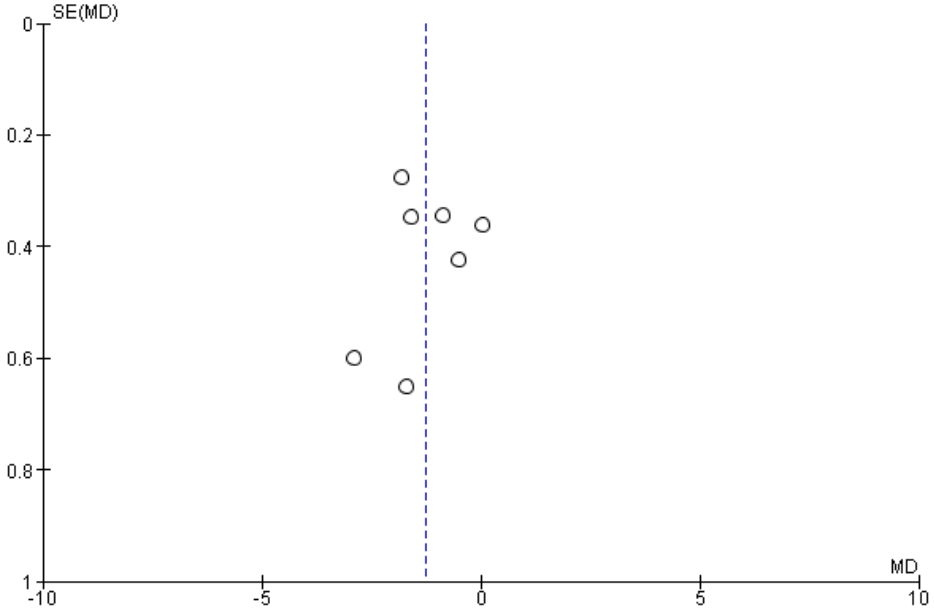
[6] The sample size is adequate (821 intervention arm, 842 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-1.2720 % (-1.9329, -0.6111)]. This body of evidence was not downgraded for imprecision.

[7] There were too few studies (n<10) to assess publication bias.

Forest Plot 4.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat



Funnel Plot 4.1: Effect of Weight Gain Prevention Interventions on Total % Body Fat



Egger's Test to Detect Publication Bias: Change in Total % Body Fat

Included Studies	P-value
All Studies Reporting Change in Total % Body Fat	**

** Too few studies (n<10) to assess

Evidence Set 5: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health/physiological outcomes (reduction in total cholesterol)?

- Summary of Change in Total Cholesterol Evidence
- GRADE Evidence Profile Table 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol
- GRADE Summary of Findings Table 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol
- Forest Plot 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol
- Funnel Plot 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol
- Egger's Test Results (for Publication Bias)

Summary of Change in Total Cholesterol Evidence

- 15 studies; 10,660 participants
- Statistically significant reduction (P=0.02) in total cholesterol level in the intervention group as compared to the control group [MD (95% CI) -0.06 mmol/L (-0.11, -0.01)]
- High statistical heterogeneity across studies [Chi^2=50.48, df=15 (P<0.0001), I^2=70%]

GRADE Evidence Profile Table 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol *

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in Total Cholesterol (mmol/L): Overall (Better indicated by lower values)											
15	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	none[7]	4,993	5,667	0.0582 lower (0.1053 to 0.0111 lower)	⊕⊕OO LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol

Outcome: Change in Total Cholesterol (mmol/L)	Compared to the control group, the mean reduction in total cholesterol level (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in Total Cholesterol	**0.0582 lower** (0.1053 to 0.0111 lower)	10,660 (15 studies[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6,7]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Total Cholesterol

[1] The 15 studies are:[65,67-69,72,75,78,79,82,84-87,89,90] Immediate post assessment for all but 6 studies; for these 6 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] and Khare[86] provide 9 month follow-up data post completion of 3 month interventions; Burke[72] presents 8 month follow-up data post completion of a 4 month intervention; Lawton[79] provides 3 month follow-up data post completion of a 9 month intervention; Sone[75] provides outcomes at 3 years post baseline assessment for an intervention of unspecified duration; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 9 studies (60%) were rated as unclear risk, 1 study (7%) was rated as high risk, and 5 studies (33%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (47%), allocation concealment (67%), and other sources of bias (93%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] The statistical heterogeneity is high and significant [Chi^2=50.48, df=15 (P<0.00001); I^2=70%] but the direction of the effect is fairly consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

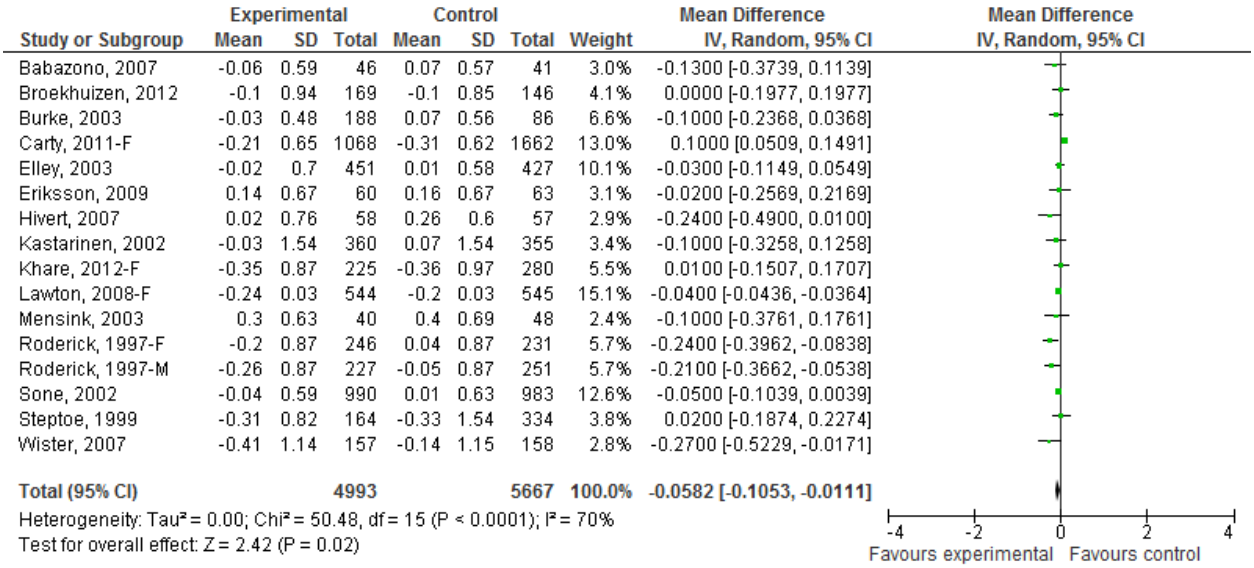
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 15 studies, baseline BMI ranged from 22.4 to 31.1; in 3 of the studies the baseline mean BMI of at least one study arm was <25; in 12 studies the baseline means were in the range for overweight/obese. Most studies (n=12) included mixed gender samples; 3 included only women. In 4 studies (33%) the participants had a high risk of CVD. In terms of type of intervention 2 were diet, 2 were exercise, 3 were diet plus exercise, and 8 were lifestyle. Control participants received usual care from their physicians or no intervention; in 5 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 10 studies and more than 12 months in 5 studies. Two studies were conducted in Canada, 2 in the US, 6 in European countries, 3 in Australia or New Zealand, and 2 in Japan. About one-third of the studies (n=4) were published in the last 5 years (2009-2012); the remaining 11 studies were published between 1997 and 2008.

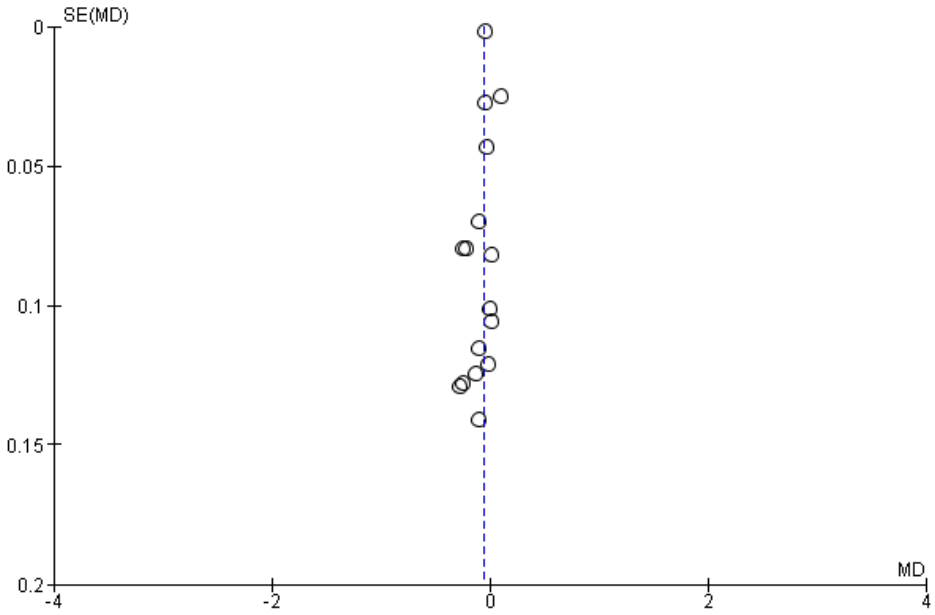
[6] The sample size is adequate (4,993 intervention arm, 5,667 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.0582 mmol/L (-0.1053, -0.0111)]. This body of evidence was not downgraded for imprecision.

[7] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (p=0.638). This body of evidence was not downgraded for suspected publication bias.

Forest Plot 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol



Funnel Plot 5.1: Effect of Weight Gain Prevention Interventions on Total Cholesterol



Egger's Test to Detect Publication Bias: Change in Total Cholesterol

Included Studies	P-value
All Studies Reporting Change in Total Cholesterol	0.638

Evidence Set 6: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health/physiological outcomes (reduction in low density lipoprotein cholesterol)?

- Summary of Change in LDL-C Evidence
- GRADE Evidence Profile Table 6.1: Effect of Weight Gain Prevention Interventions on LDL-C
- GRADE Summary of Findings Table 6.1: Effect of Weight Gain Prevention Interventions on LDL-C
- Forest Plot 6.1: Effect of Weight Gain Prevention Interventions on LDL-C
- Funnel Plot 6.1: Effect of Weight Gain Prevention Interventions on LDL-C
- Egger's Test Results (for Publication Bias)

Summary of Change in LDL-C Evidence

- 11 studies; 5,635 participants
- Statistically significant reduction (P<0.0001) in LDL-C level in the intervention group as compared to the control group [MD (95% CI) -0.06 mmol/L (-0.09, -0.03)]
- Low statistical heterogeneity across studies [Chi^2=8.82, df=10 (P=0.55), I^2=0%]

GRADE Evidence Profile Table 6.1: Effect of Weight Gain Prevention Interventions on Change in LDL-C

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in LDL-C (mmol/L): Overall (Better indicated by lower values)											
11	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	none[7]	2,546	3,089	0.0635 lower (0.0945 to 0.0325 lower)	⊕⊕OO LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 6.1: Effect of Weight Gain Prevention Interventions on Change in LDL-C

Outcome: Change in LDL-C (mmol/L)	Compared to the control group, the mean reduction in LDL-C level (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in LDL-C	**0.0635 lower** (0.0945 to 0.0325 lower)	5,635 (11 studies[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6,7]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on LDL-C

[1] The 11 studies are:[65,67,68,71,72,78,82-86] Immediate post assessment for all but 5 studies; for these 5 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] and Khare[86] provide 9 month follow-up data post completion of 3 month interventions; Burke[72] presents 8 month follow-up data post completion of a 4 month intervention; Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 5 studies (45.5%) were rated as unclear risk, 1 study (9%) was rated as high risk, and 5 studies (45.5%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (37%), allocation concealment (55%), and other sources of bias (91%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that at least half of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] The statistical heterogeneity is low [Chi^2=8.82, df=10 (P=0.55); I^2=0%], the direction of the effect is fairly consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

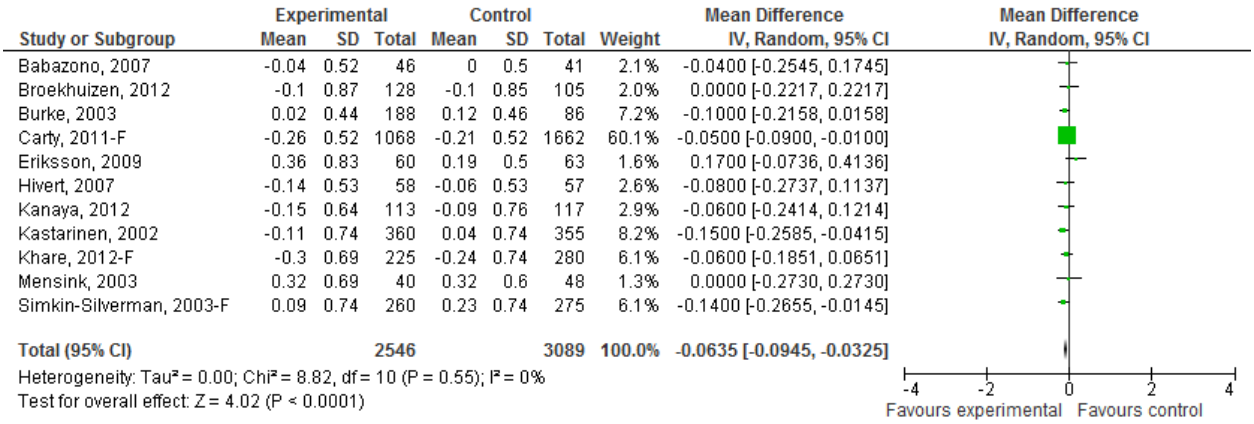
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 11 studies, baseline BMI ranged from 22.4 to 31.1; in 2 of the studies the baseline mean BMI of at least one study arm was <25; in 9 studies the baseline means were in the range for overweight/obese. Most studies (n=8) included mixed gender samples; 3 included only women. In 3 studies (27%) the participants had a high risk of CVD. In terms of type of intervention 1 was diet, 1 was exercise, 3 were diet plus exercise, and 6 were lifestyle. Control participants received usual care from their physicians or no intervention; in 4 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 6 studies and more than 12 months in 5 studies. One study was conducted in Canada, 4 in the US, 4 in European countries, 1 in Australia, and 1 in Japan. About half of the studies (n=5) were published in the last 5 years (2009-2012); the remaining 11 studies were published between 2002 and 2007.

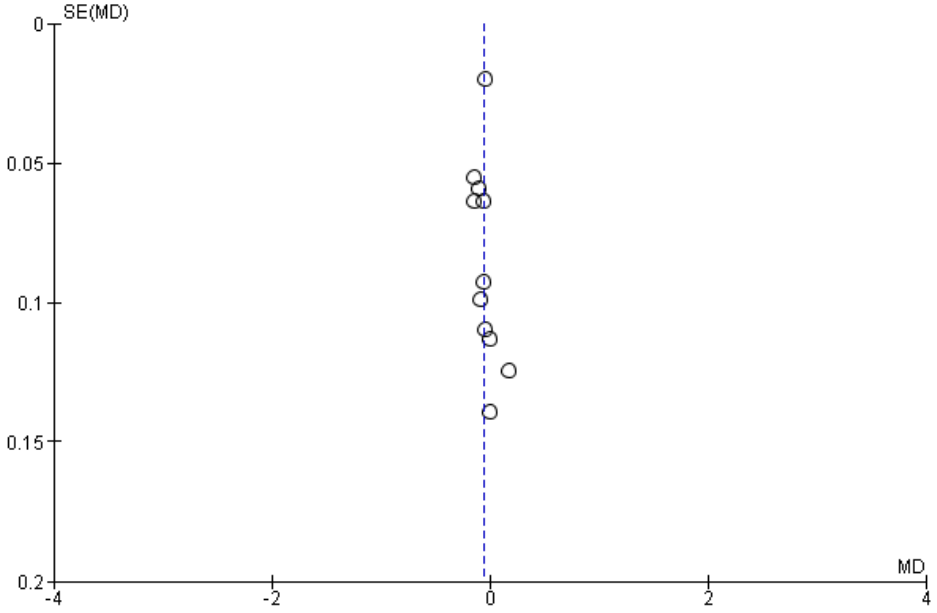
[6] The sample size is adequate (2,546 intervention arm, 3,089 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.0635 mmol/L (-0.0945, -0.0325)]. This body of evidence was not downgraded for imprecision.

[7] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (p=0.828). This body of evidence was not downgraded for suspected publication bias.

Forest Plot 6.1: Effect of Weight Gain Prevention Interventions on LDL-C



Funnel Plot 6.1: Effect of Weight Gain Prevention Interventions on LDL-C



Egger's Test to Detect Publication Bias: Change in LDL-C

Included Studies	P-value
All Studies Reporting Change in LDL-C	0.828

Evidence Set 7: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health/physiological outcomes (reduction in fasting glucose)?

- Summary of Change in Fasting Glucose Evidence
- GRADE Evidence Profile Table 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose
- GRADE Summary of Findings Table 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose
- Forest Plot 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose
- Funnel Plot 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose
- Egger's Test Results (for Publication Bias)

Summary of Change in Fasting Glucose Evidence

- 10 studies; 7,189 participants
- Statistically significant reduction (P=0.04) in fasting glucose level in the intervention group as compared to the control group [MD (95% CI) -0.04 mmol/L (-0.08, -0.0016)]
- Moderate statistical heterogeneity across studies [Chi^2=27.03, df=9 (P=0.001), I^2=67%]

GRADE Evidence Profile Table 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in Fasting Glucose (mmol/L): Overall (Better indicated by lower values)											
10	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	none[7]	3,399	3,790	0.0404 lower (0.0792 lower to 0.0016 lower)	⊕⊕OO LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose

Outcome: Change in Fasting Glucose (mmol/L)	Compared to the control group, the mean reduction in fasting glucose level (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in Fasting Glucose	**0.0404 lower** (0.0792 lower to 0.0016 lower)	7,189 (10 studies[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6,7]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Fasting Glucose

[1] The 10 studies are:[67,69,71,74,75,78-80,83,84] Immediate post assessment for all but 5 studies; for these 5 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Eriksson[84] provides 9 month follow-up data post completion of a 3 month intervention; Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Lawton[79] provides 3 month follow-up data post completion of a 9 month intervention; Sone[75] provides outcomes at 3 years post baseline assessment for an intervention of unspecified duration; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 2 studies (20%) were rated as unclear risk, 2 studies (20%) were rated as high risk, and 6 studies (60%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (30%), allocation concealment (40%), and other sources of bias (90%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. This body of evidence was not downgraded for serious study limitations.

[3] The statistical heterogeneity is moderate and significant [Chi^2=27.03, df=9 (P=0.001); I^2=67%], but the direction of the effect is fairly consistent across studies and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

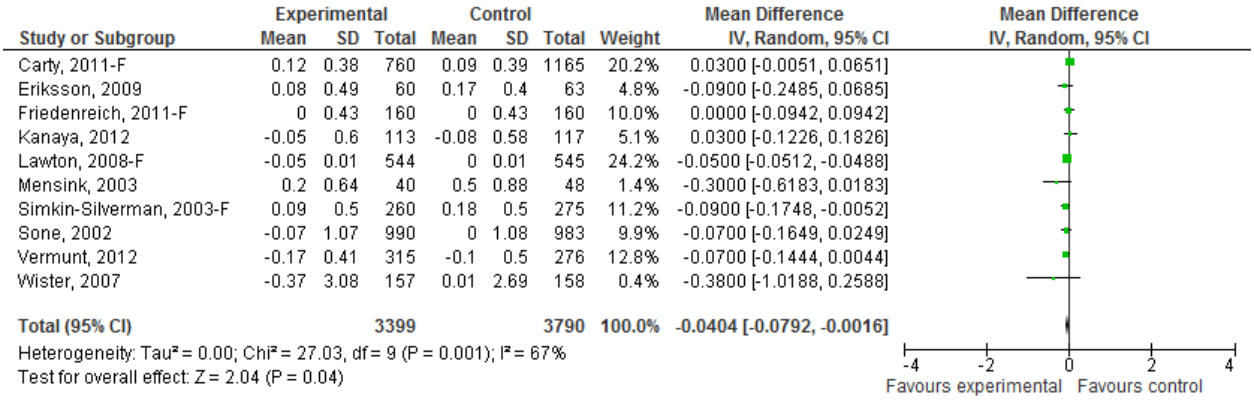
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 10 studies, baseline BMI ranged from 23.1 to 30.1; in 1 study the baseline mean BMI of at least one study arm was <25; in 9 studies the baseline means were in the range for overweight/obese. Just over half of the studies (n=6) included mixed gender samples; 4 included only women. In 1 study (10%) the participants had a high risk of CVD. In terms of type of intervention 1 was diet, 3 were exercise, 1 was diet plus exercise, and 5 were lifestyle. Control participants received usual care from their physicians or no intervention; in 4 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 5 studies and more than 12 months in 5 studies. Two studies were conducted in Canada, 3 in the US, 3 in European countries, 1 in New Zealand, and 1 in Japan. Half of the studies (n=5) were published in the last 5 years (2009-2012); the remaining 5 studies were published between 2002 and 2008.

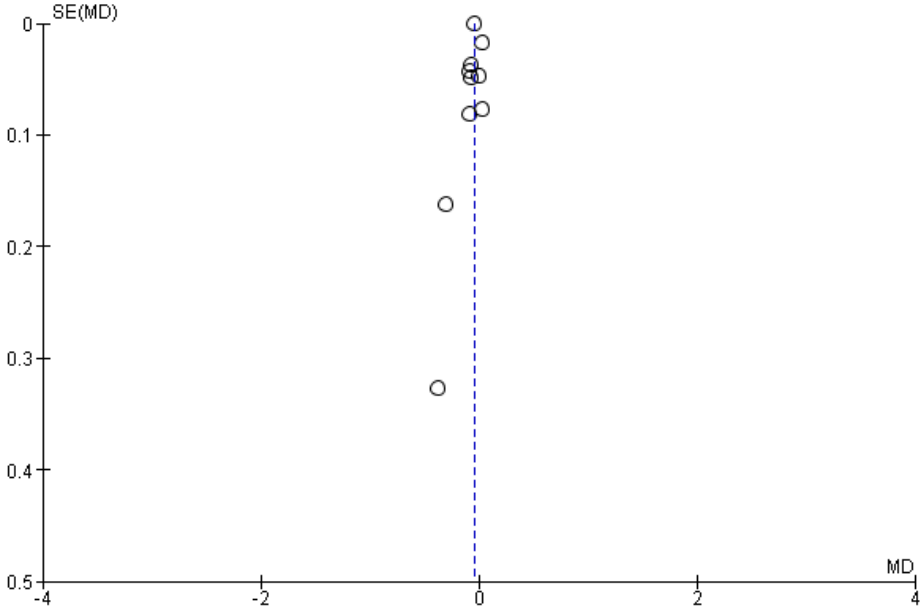
[6] The sample size is adequate (3,399 intervention arm, 3,790 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD=-0.0404 mmol/L (-0.0792, -0.0016)]. This body of evidence was not downgraded for imprecision.

[7] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (p=0.798). This body of evidence was not downgraded for suspected publication bias.

Forest Plot 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose



Funnel Plot 7.1: Effect of Weight Gain Prevention Interventions on Fasting Glucose



Egger's Test to Detect Publication Bias: Change in Fasting Glucose

Included Studies	P-value
All Studies Reporting Change in Fasting Glucose	0.798

Evidence Set 8: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health/physiological outcomes (reduction in incidence of Type 2 Diabetes)?

- Summary of T2D Incidence Evidence
- GRADE Evidence Profile Table 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D
- GRADE Summary of Findings Table 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D
- Forest Plot 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D
- Funnel Plot 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D
- Egger's Test Results (for Publication Bias)

Summary of T2D Incidence Evidence

- 2 studies; 46,537 participants
- No statistically significant difference (P=0.17) between the intervention and control groups on the outcome of diagnosis of new onset T2D [RR (95% CI) 0.95 (0.89, 1.02)]
- Low statistical heterogeneity across studies [Chi^2=0.38, df=1 (P=0.54), I^2=0%]
- Absolute Risk Reduction [ARR] = 0.34%
- NNT = 293

GRADE Evidence Profile Table 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D

Quality Assessment							No. of Participants		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	Relative (95% CI)	Absolute per Million (Range)		
T2D Incidence												
2	randomized trials[1]	serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	serious imprecision[6]	none[7]	1,344/18,715 (7.1814%)	2,085/27,822 (7.4941%)	RR 0.9544 (0.8934 to 1.0195)	3,417 fewer (from 7,989 fewer to 1,461 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D

Outcome: T2D Incidence	Illustrative Comparative Risks* (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk Number per Million Control	Corresponding Risk Number per Million Intervention			
All Studies Reporting T2D Incidence	**74,941**	**71,523** (66,952 to 76,402)	**RR 0.9544** (0.8934 to 1.0195)	46,537 (2 studies[1])	⨁⊖⊖⊖ **very low**[2,3,4,5,6,7]

*The assumed risk is the mean control group risk across studies. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Incidence of T2D

[1] The 2 studies are:[67,80] Immediate post assessment for one study but for the other study the data point closest to the immediate post and ≥12 months post baseline was selected (Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 1 study was rated as unclear risk and 1 study was rated as high risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (50%), allocation concealment (100%), incomplete reporting (100%), and other sources of bias (100%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that all of the information for this outcome is from studies at moderate and high risk of bias, this body of evidence was downgraded for serious study limitations.

[3] The statistical heterogeneity is low [Chi^2=0.38, df=1 (P=0.54); I^2=0%], the direction of the effect is consistent across studies, and the confidence intervals overlap. This body of evidence was not downgraded for inconsistency.

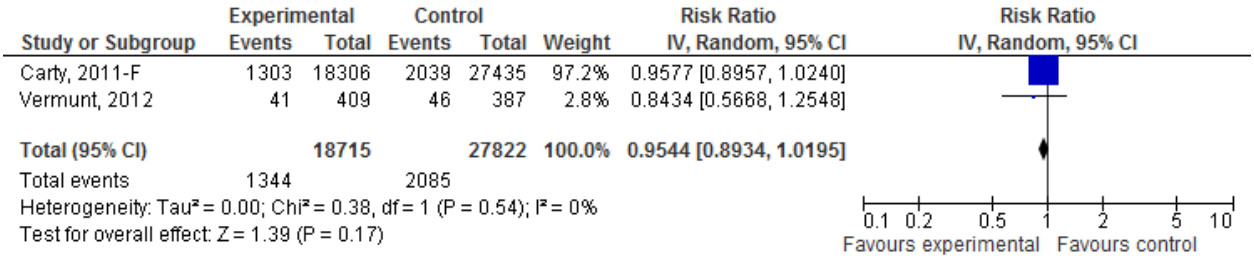
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 2 studies, baseline BMI ranged from 28.5 to 29.1; in both studies the baseline means were in the range for overweight/obese. One study included a mixed gender sample while the larger study included only women. In both studies the participants had low/unknown risk of CVD. In terms of type of intervention 1 was diet and 1 was lifestyle. Control participants received usual care from their physicians or no intervention as well as a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was more than 12 months in both studies. One study was conducted in the US and 1 in the Netherlands. Both were recently published studies (2011, 2012).

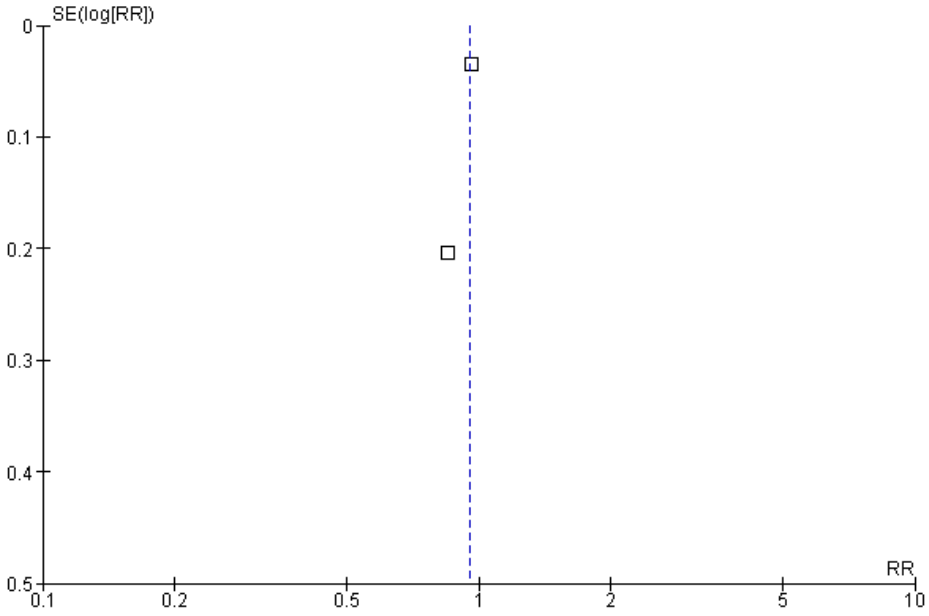
[6] The sample size is adequate (18,715 intervention arm, 27,822 control arm) and the number of events is sufficient (1,344 intervention arm, 2,085 control arm) but the pooled effect estimate is not precise with a confidence interval that includes the no effect value [RR=0.9544(0.8934, 1.0195)]. This body of evidence was downgraded for imprecision.

[7] There were too few studies (n<10) to assess publication bias.

Forest Plot 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D



Funnel Plot 8.1: Effect of Weight Gain Prevention Interventions on Incidence of T2D



Egger's Test to Detect Publication Bias: Incidence of T2D

Included Studies	P-value
All Studies Reporting Incidence of T2D	**

** Too few studies (n<10) to assess

Evidence Set 9: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health/physiological outcomes (reduction in systolic blood pressure)?

- Summary of Change in SBP Evidence
- GRADE Evidence Profile Table 9.1: Effect of Weight Gain Prevention Interventions on SBP
- GRADE Summary of Findings Table 9.1: Effect of Weight Gain Prevention Interventions on SBP
- Forest Plot 9.1: Effect of Weight Gain Prevention Interventions on SBP
- Funnel Plot 9.1: Effect of Weight Gain Prevention Interventions on SBP
- Egger's Test Results (for Publication Bias)

Summary of Change in SBP Evidence

- 17 studies; 48,493 participants
- No statistically significant difference (P=0.25) between intervention and control group for the outcome of SBP [MD (95% CI) -0.31 mmHg (-0.84, 0.22)]
- High statistical heterogeneity across studies [Chi^2=71.04, df=16 (P<0.00001), I^2=77%]

GRADE Evidence Profile Table 9.1: Effect of Weight Gain Prevention Interventions on SBP

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in SBP (mmHg): Overall (Better indicated by lower values)											
17	randomized trials[1]	serious risk[2]	serious inconsistency[3]	serious indirectness[4,5]	serious imprecision[6]	none[7]	20,231	28,262	0.3126 lower (0.8427 lower to 0.2174 higher)	⊕OOO VERY LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 9.1: Effect of Weight Gain Prevention Interventions on SBP

Outcome: Change in SBP (mmHg)	Compared to the control group, the mean reduction in SBP (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in SBP	**0.3126 lower** (0.8427 lower to 0.2174 higher)	48,493 (17 studies[1])	⊕⊖⊖⊖ **very low**[2,3,4,5,6,7]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Change in SBP

[1] The 17 studies are:[65,67,68,71,72,75,76,79,82-90] Immediate post assessment for all but 8 studies; for these 8 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Sacerdote[88] presents 12 month follow-up data after a 15 minute educational intervention; Eriksson[84] and Khare[86] provide 9 month follow-up data post completion of 3 month interventions; Burke[72] presents 8 month follow-up data post completion of a 4 month intervention; Kanaya[83] provides 6 month follow-up data for a 6 month intervention; Lawton[79] provides 3 month follow-up data post completion of a 9 month intervention; Sone[75] provides outcomes at 3 years post baseline assessment for an intervention of unspecified duration; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 15 studies (88%) were rated as unclear risk and 2 studies (12%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (41%), allocation concealment (59%), blinding of outcome assessors (76%) and other sources of bias (88%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or

agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] The statistical heterogeneity is high and significant [Chi^2=71.04, df=16 (P<0.00001); I^2=77%] and the direction of the effect is not consistent across studies although the confidence intervals do overlap. This body of evidence was downgraded for inconsistency.

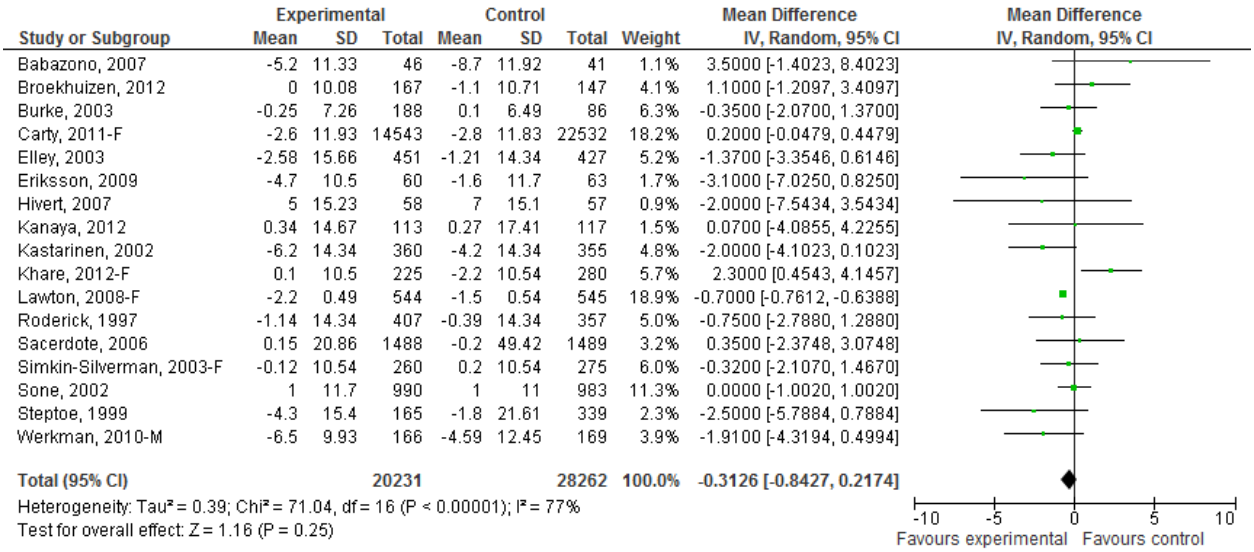
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 17 studies, baseline BMI ranged from 22.4 to 31.1; in 4 of the studies the baseline mean BMI of at least one study arm was <25; in 13 studies the baseline means were in the range for overweight/obese. Most studies (n=12) included mixed gender samples; 4 included only women and 1 included only men. In 4 studies (24%) the participants had a high risk of CVD. In terms of type of intervention 3 were diet, 3 were exercise, 3 were diet plus exercise, and 8 were lifestyle. Control participants received usual care from their physicians or no intervention; in 5 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 12 studies and more than 12 months in 5 studies. One study was conducted in Canada, 4 in the US, 7 in European countries, 3 in Australia or New Zealand, and 2 in Japan. About one-third of the studies (n=6) were published in the last 5 years (2009-2012); the remaining 11 studies were published between 1997 and 2008.

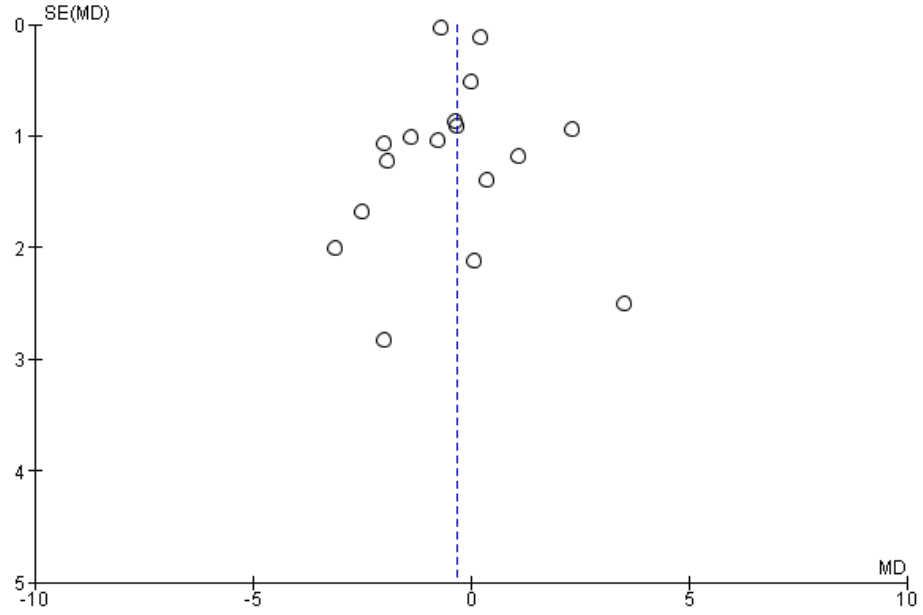
[6] The sample size is adequate (20,231 intervention arm, 28,262 control arm) but the pooled effect estimate is not precise with a confidence interval that includes the no effect value [MD -0.3126 mmHg (-0.8427, 0.2174)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[7] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (p=0.322). This body of evidence was not downgraded for suspected publication bias.

Forest Plot 9.1: Effect of Weight Gain Prevention Interventions on SBP



Funnel Plot 9.1: Effect of Weight Gain Prevention Interventions on SBP



Egger's Test to Detect Publication Bias: Change in SBP

Included Studies	P-value
All Studies Reporting Change in SBP	0.322

Evidence Set 10: Do primary care relevant prevention interventions (behavioural) in normal weight adults lead to improved health/physiological outcomes (reduction in diastolic blood pressure)?

- Summary of Change in DBP Evidence
- GRADE Evidence Profile Table 10.1: Effect of Weight Gain Prevention Interventions on DBP
- GRADE Summary of Findings Table 10.1: Effect of Weight Gain Prevention Interventions on DBP
- Forest Plot 10.1: Effect of Weight Gain Prevention Interventions on DBP
- Funnel Plot 10.1: Effect of Weight Gain Prevention Interventions on DBP
- Egger's Test Results (for Publication Bias)

Summary of Change in DBP Evidence

- 15 studies; 47,945 participants
- No statistically significant difference (P<0.00001) between intervention and control group for the outcome of DBP [MD (95% CI) -0.18 mmHg (-0.44, 0.07)]
- Moderate statistical heterogeneity across studies [Chi^2=40.65, df=14 (P=0.0002), I^2=66%]

GRADE Evidence Profile Table 10.1: Effect of Weight Gain Prevention Interventions on DBP

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in DBP (mmHg): Overall (Better indicated by lower values)											
15	randomized trials[1]	serious risk[2]	serious inconsistency[3]	serious indirectness[4,5]	serious imprecision[6]	none[7]	19,948	27,997	0.1849 lower (0.4417 lower to 0.0718 higher)	⊕OOO VERY LOW	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 10.1: Effect of Weight Gain Prevention Interventions on DBP

Outcome: Change in DBP (mmHg)	Compared to the control group, the mean reduction in DBP (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
All Studies Reporting Change in DBP	**0.1849 lower** (0.4417 lower to 0.0718 higher)	47,945 (15 studies[1])	⊕⊖⊖⊖ **very low**[2,3,4,5,6,7]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on DBP

[1] The 15 studies are:[65,67,68,71,72,75,76,79,84-90] Immediate post assessment for all but 7 studies; for these 7 studies the data point closest to the immediate post and/or ≥12 months post baseline was selected (Sacerdote[88] presents 12 month follow-up data after a 15 minute educational intervention; Eriksson[84] and Khare[86] provide 9 month follow-up data post completion of 3 month interventions; Burke[72] presents 8 month follow-up data post completion of a 4 month intervention; Lawton[79] provides 3 month follow-up data post completion of a 9 month intervention; Sone[75] provides outcomes at 3 years post baseline assessment for an intervention of unspecified duration; Carty[67] presents outcomes at 7.5 years post baseline assessment for an intervention that lasted for 8 to 12 years).

[2] Using Cochrane's Risk of Bias tool, for this outcome 13 studies (87%) were rated as unclear risk and 2 studies (13%) were rated as low risk. Across studies, there was a lack of certainty (unclear ratings) or a high risk of bias associated with sequence generation (47%), allocation concealment (67%), blinding of outcome assessors (73%) and other sources of bias (87%; i.e., industry funding, imbalance in baseline characteristics and/or selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel across all studies. Furthermore, the adults who volunteered or agreed to participate in these studies may be more weight conscious than the general population and some may have been interested in losing weight. Given that most of the information for this outcome is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] The statistical heterogeneity is moderate and significant [Chi^2=40.65, df=14 (P=0.0002); I^2=66%] and the direction of the effect is not consistent across studies although the confidence intervals do overlap. This body of evidence was downgraded for inconsistency.

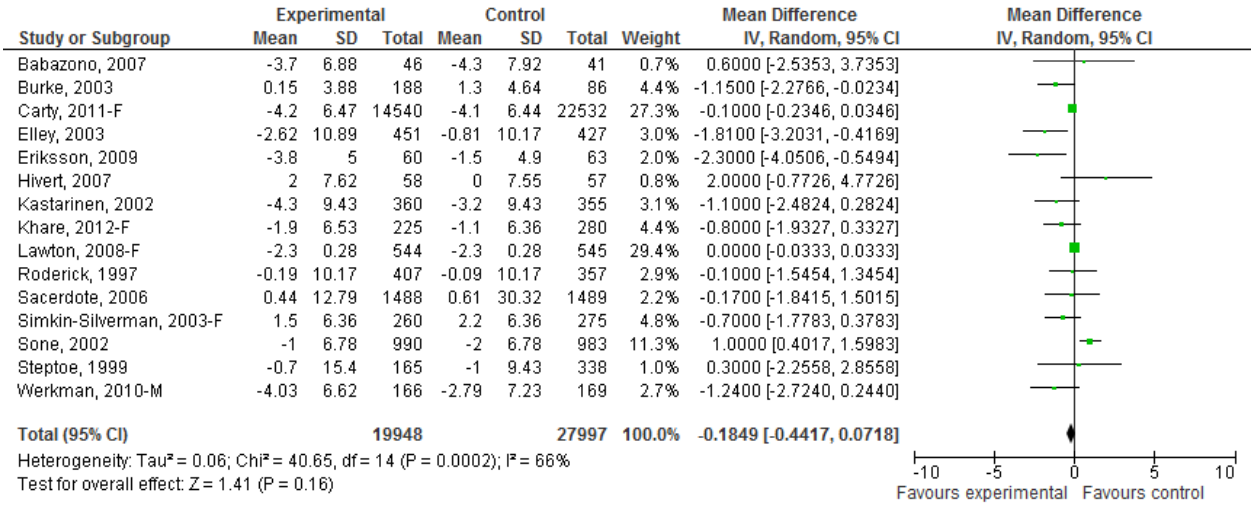
[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] Across the 15 studies, baseline BMI ranged from 22.4 to 31.1; in 4 of the studies the baseline mean BMI of at least one study arm was <25; in 11 studies the baseline means were in the range for overweight/obese. Two-thirds of the studies (n=10) included mixed gender samples; 4 included only women and 1 included only men. In 3 studies (20%) the participants had a high risk of CVD. In terms of type of intervention 3 were diet, 2 were exercise, 3 were diet plus exercise, and 7 were lifestyle. Control participants received usual care from their physicians or no intervention; in 5 of these studies control participants received a minimal component (e.g., printed materials on healthy lifestyles). Intervention duration was 12 months or less in 10 studies and more than 12 months in 5 studies. One study was conducted in Canada, 3 in the US, 6 in European countries, 3 in Australia or New Zealand, and 2 in Japan. About one-quarter of the studies (n=4) were published in the last 5 years (2009-2012); the remaining 11 studies were published between 1997 and 2008.

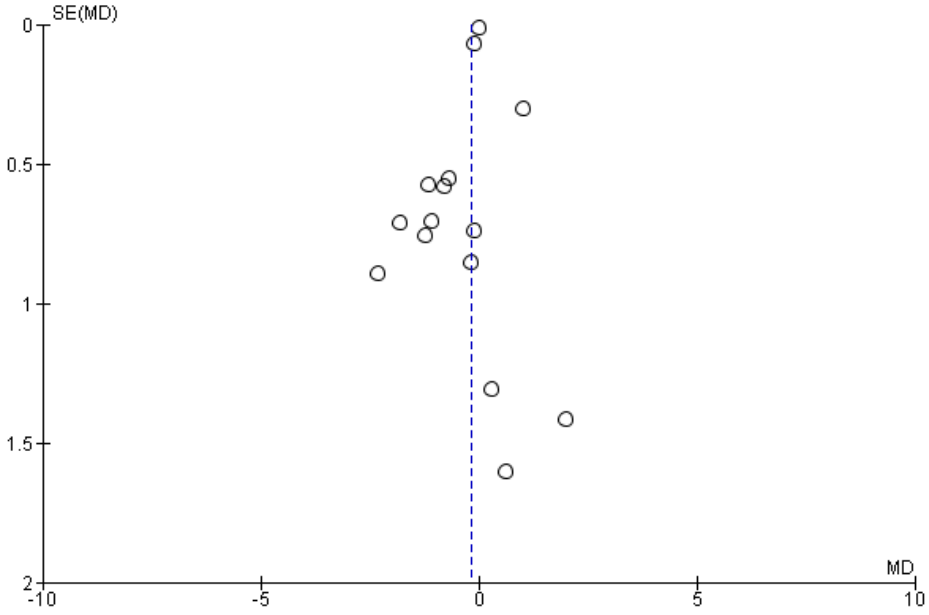
[6] The sample size is adequate (19,948 intervention arm, 27,997 control arm) but the pooled effect estimate is not precise with a confidence interval that includes the no effect value [MD -0.1849 mmHg (-0.4417, 0.0718)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[7] The funnel plot for these studies and this outcome is roughly symmetrical. The Egger's test was conducted to detect publication bias; results were not significant (P=0.156). This body of evidence was not downgraded for suspected publication bias.

Forest Plot 10.1: Effect of Weight Gain Prevention Interventions on DBP



Funnel Plot 10.1: Effect of Weight Gain Prevention Interventions on DBP



Egger's Test to Detect Publication Bias: Change in DBP

Included Studies	P-value
All Studies Reporting Change in DBP	0.156

Evidence Set 11: How well is weight gain prevented or health outcomes maintained after an intervention is completed (at follow-up)?

- Summary of Weight Gain Prevention and Change in Health Outcomes at Follow-Up Evidence
- GRADE Evidence Profile Table 11.1: Effect of Weight Gain Prevention Interventions on Weight and Health Outcomes at Follow-up
- GRADE Summary of Findings Table 11.1: Effect of Weight Gain Prevention Interventions on Weight and Health Outcomes at Follow-up
- Forest Plot 11.1: Effect of Weight Gain Prevention Interventions on Weight (kg) at Follow-up
- Forest Plot 11.2: Effect of Weight Gain Prevention Interventions on Waist Circumference (cm) at Follow-up
- Forest Plot 11.3: Effect of Weight Gain Prevention Interventions on Total Cholesterol (mmol/L) at Follow-up
- Forest Plot 11.4: Effect of Weight Gain Prevention Interventions on Fasting Glucose (mmol/L) at Follow-up
- Forest Plot 11.5: Effect of Weight Gain Prevention Interventions on SBP (mmHg) at Follow-up

Summary of Weight Gain Prevention and Change in Health Outcomes at Follow-Up Evidence

- 1 study; 1,089 participants
- Statistically significant increase (P<0.00001) in weight in the intervention group as compared to the control group from the immediate post assessment to follow-up 12 to 15 months later [MD (95% CI) 0.20 kg (0.17, 0.23)]
- No statistically significant difference (P=1.00) in waist circumference in the intervention group as compared to the control group from the immediate post assessment to follow-up 12 to 15 months later [MD (95% CI) 0.00 cm (-0.03, 0.03)]
- Statistically significant increase (P<0.00001) in total cholesterol level in the intervention group as compared to the control group from the immediate post assessment to follow-up 12 to 15 months later [MD (95% CI) 0.03 mmol/L (0.027, 0.033)]
- Statistically significant increase (P<0.00001) in fasting glucose level in the intervention group as compared to the control group from the immediate post assessment to follow-up 12 to 15 months later [MD (95% CI) 0.04 mmol/L (0.038, 0.042)]
- Statistically significant increase (P<0.00001) in SBP in the intervention group as compared to the control group from the immediate post assessment to follow-up 12 to 15 months later [MD (95% CI) 0.90 mmHg (0.84, 0.96)]

GRADE Evidence Profile Table 11.1: Effect of Weight Gain Prevention Interventions on Weight and Health Outcomes at Follow-up

Quality Assessment							No. of Participants		Effect	Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention	Control	Mean Difference (95% CI)		
Change in Weight (kg) at Follow-up (15 months) (Better indicated by lower values)											
1	randomized trial[1]	no serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[6]	none[7]	544	545	0.2000 higher (0.1682 to 0.2318 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in Waist Circumference (cm) at Follow-up (15 months) (Better indicated by lower values)											
1	randomized trial[1]	no serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	serious imprecision[8]	none[7]	544	545	0.0000 higher (0.0315 lower to 0.0315 higher)	⊕⊕OO LOW	CRITICAL
Change in Total Cholesterol (mmol/L) at Follow-up (15 months) (Better indicated by lower values)											
1	randomized trial[1]	no serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[9]	none[7]	544	545	0.0300 higher (0.0267 to 0.0333 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in Fasting Glucose (mmol/L) at Follow-up (15 months) (Better indicated by lower values)											
1	randomized trial[1]	no serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[10]	none[7]	544	545	0.0400 higher (0.0376 to 0.0424 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in SBP (mmHg) at Follow-up (15 months) (Better indicated by lower values)											
1	randomized trial[1]	no serious risk[2]	no serious inconsistency[3]	serious indirectness[4,5]	no serious imprecision[11]	none[7]	544	545	0.9000 higher (0.8412 to 0.9588 higher)	⊕⊕⊕O MODERATE	CRITICAL

* Footnotes appear after the Summary of Findings Table

GRADE Summary of Findings Table 11.1: Effect of Weight Gain Prevention Interventions on Weight and Health Outcomes at Follow-up

Outcome	Compared to the control group, the mean (95% CI) in the intervention groups was	No. of Participants (Studies)	Quality of the Evidence (GRADE)
Change in Weight (kg) at Follow-up (15 months)	**0.2000 higher** (0.1682 to 0.2318 higher)	1,089 (1 study[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,6,7]
Change in Waist Circumference (cm) at Follow-up (15 months)	**0.0000 even** (0.0315 lower to 0.0315 higher)	1,089 (1 study[1])	⊕⊕⊖⊖ **low**[2,3,4,5,7,8]
Change in Total Cholesterol (mmol/L) at Follow-up (15 months)	**0.0300 higher** (0.0267 to 0.0333 higher)	1,089 (1 study[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,7,9]
Change in Fasting Glucose (mmol/L) at Follow-up (15 months)	**0.0400 higher** (0.0376 to 0.0424 higher)	1,089 (1 study[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,7,10]
Change in SBP (mmHg) at Follow-up (15 months)	**0.9000 higher** (0.8412 to 0.9588 higher)	1,089 (1 study[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,7,11]

Footnotes for GRADE Evidence Profile and Summary of Findings Tables for Effect of Weight Gain Prevention Interventions on Weight and Health Outcomes at Follow-up

[1] Single study; Lawton provides 15 month follow-up data post completion of a 9 month intervention.[79]

[2] Using Cochrane's Risk of Bias tool, for this outcome the study was rated as low risk. Low risk ratings were applied to sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome reporting, and selective reporting; an unclear rating was applied to other sources of bias (i.e., potential selection bias). Due to the nature of behavioural interventions, there is a high risk of bias for blinding of participants and personnel. Furthermore, the women who volunteered or agreed to participate in this study may be more weight conscious than the general population and some may have been interested in losing weight. This body of evidence was not downgraded for study limitations.

[3] Inconsistency cannot be assessed with a single study.

[4] This body of evidence was downgraded because the population was not restricted to normal weight adults. Although study samples had to include at least some normal weight adults, as long as the inclusion rule was satisfied (must apply to at least one study arm, baseline mean BMI <25, or baseline mean BMI >25 but minus one SD <25, or n or % normal weight participants specified) the samples could also include overweight and obese adults.

[5] The baseline BMI of the all-female sample was 29.2 and the participants had low/unknown risk of CVD. Participants received a 9 month exercise focused intervention or usual care. The study was conducted in New Zealand and was published in 2008.

[6] The sample size is adequate (544 intervention arm, 545 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD 0.2006 kg (0.1682, 0.2318)]. This body of evidence was not downgraded for imprecision.

[7] There were too few studies (n<10) to assess publication bias.

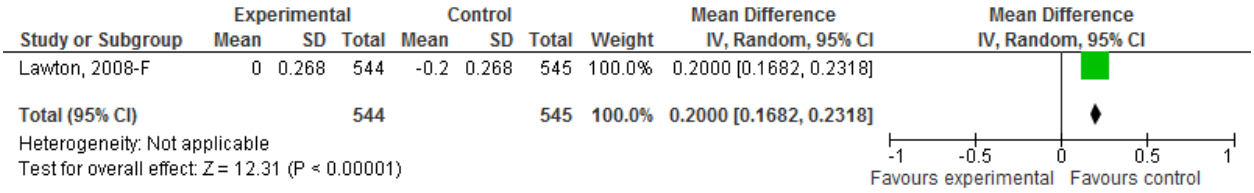
[8] The sample size is adequate (544 intervention arm, 545 control arm) but the pooled effect estimate is not precise with a confidence interval that includes the no effect value [MD 0.0000 cm (-0.0315, 0.0315)]. This body of evidence was downgraded for imprecision.

[9] The sample size is adequate (544 intervention arm, 545 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD 0.0300 mmol/L(0.0267, 0.0333)]. This body of evidence was not downgraded for imprecision.

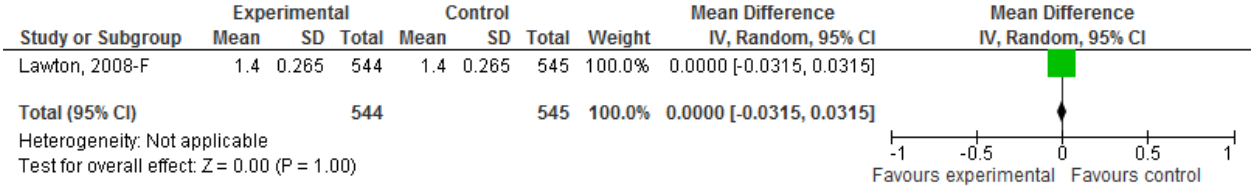
[10] The sample size is adequate (544 intervention arm, 545 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD 0.0400 mmol/L(0.0376, 0.0424)]. This body of evidence was not downgraded for imprecision.

[11] The sample size is adequate (544 intervention arm, 545 control arm) and the pooled effect estimate is precise with a narrow confidence interval [MD 0.9000 mmHg(0.8412, 0.9588)]. This body of evidence was not downgraded for imprecision.

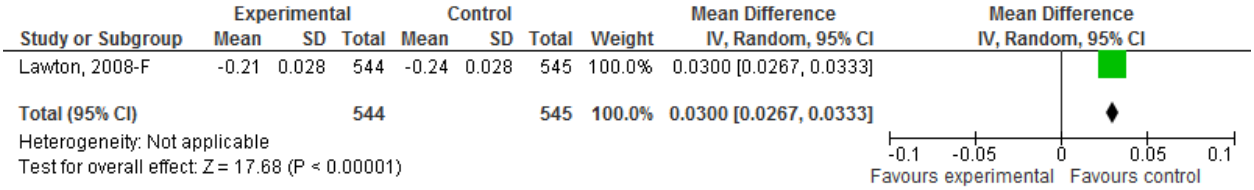
Forest Plot 11.1: Effect of Weight Gain Prevention Interventions on Weight (kg) at Follow-up



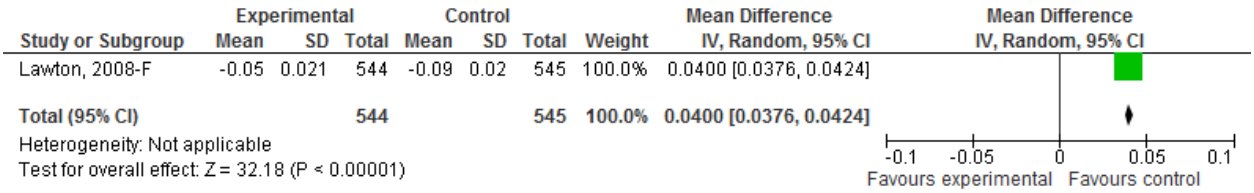
Forest Plot 11.2: Effect of Weight Gain Prevention Interventions on Waist Circumference (cm) at Follow-up



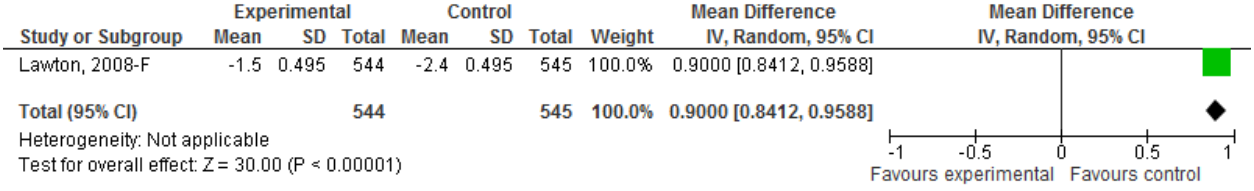
Forest Plot 11.3: Effect of Weight Gain Prevention Interventions on Total Cholesterol (mmol/L) at Follow-up



Forest Plot 11.4: Effect of Weight Gain Prevention Interventions on Fasting Glucose (mmol/L) at Follow-up



Forest Plot 11.5: Effect of Weight Gain Prevention Interventions on SBP (mmHg) at Follow-up



Appendices

- Appendix 1: Search Strategies
- Appendix 2: Acknowledgements

Appendix 1: Search Strategies for Key Questions (KQ) and Contextual Questions (CQ)

Medline - OVID (KQ)
Last Run: April 19 2013
1. Obesity/dh, th, dt, rh
2. Obesity, Morbid/dt, dh, th, rh or Obesity, Abdominal/dt, dh, th, rh
3. Overweight/dh, dt, th, rh
4. "Behavior-Therapy"/
5. Cognitive Therapy/
6. Counseling/
7. Directive Counseling/
8. counsel?ing.ti,ab.
9. Anti-Obesity Agents/
10. orlistat.ti,ab.
11. xenical.ti,ab.
12. sibutramine.ti,ab.
13. meridia.ti,ab.
14. metformin/
15. metformin.ti,ab.
16. glucophage.ti,ab.
17. Diet, Reducing/
18. Diet, Fat-Restricted/
19. Caloric Restriction/
20. Diet Therapy/
21. (diet$ adj counsel$).ti,ab.
22. (diet$ adj education$).ti,ab.
23. (nutrition$ adj counsel$).ti,ab.
24. (nutrition$ adj education$).ti,ab.
25. (nutrition$ adj intervention$).ti,ab.
26. (diet$ adj (modif$ or therapy or intervention$ or strateg$)).ti,ab.
27. ((diet or dieting or slim$) adj (club$ or organi?ation$)).ti,ab.
28. (weightwatcher$ or weight watcher$).ti,ab.
29. Exercise/
30. Exercise Therapy/
31. Motor Activity/
32. Physical Fitness/
33. physical activity.ti,ab.
34. (exercise adj3 (program$ or intervention$)).ti,ab.
35. or/4-34
36. Obesity/
37. Obesity, Morbid/ or Obesity, Abdominal/
38. Overweight/
39. Weight Loss/
40. obes$.ti.
41. overweight.ti.

42. weight.ti.
43. or/36-42
44. 35 and 43
45. (weight loss adj (intervention$ or program$ or trial$)).ti,ab.
46. (weight reduc$ adj (intervention$ or program$ or trial$)).ti,ab.
47. (weight management adj (intervention$ or program$ or trial$)).ti,ab.
48. (weight control adj (intervention$ or program$ or trial$)).ti,ab.
49. (36 or 37 or 38) and 39
50. 1 or 2 or 3 or 44 or 45 or 46 or 47 or 48 or 49
51. limit 50 to (clinical trial or controlled clinical trial or meta analysis or randomized controlled trial)
52. clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/
53. Meta-Analysis as Topic/
54. (control$ adj3 trial$).ti,ab.
55. random$.ti,ab.
56. clinical trial$.ti,ab.
57. 52 or 53 or 54 or 55 or 56
58. 50 and 57
59. 51 or 58
60. limit 59 to "all child (0 to 18 years)"
61. limit 59 to "all adult (19 plus years)"
62. 60 not 61
63. 59 not 62
64. limit 63 to animals
65. limit 63 to humans
66. 64 not 65
67. 63 not 66
68. limit 67 to (english or french)
69. limit 68 to ed=20100801-20130419
70. (harm or harms or harmful or harmed).ti,ab.
71. (risky behavior$ or risky behaviour$).ti,ab.
72. weight cycling.ti,ab.
73. (adverse effects or mortality or toxicity).fs.
74. Mortality/
75. Morbidity/
76. death/
77. Athletic injuries/
78. Malnutrition/
79. nutritional defici$.ti,ab.
80. Arrhythmias, Cardiac/
81. Arrhythmia$.ti,ab.
82. Bone Density/
83. (bone mass adj3 loss).ti,ab.
84. Bone Resorption/
85. (death or deaths).ti,ab.
86. suicide/
87. Suicide, Attempted/

88. suicid$.ti,ab.
89. or/70-88
90. 50 and 89
91. limit 90 to ed=20100801-20130419
92. or/9-16
93. 50 and 92
94. limit 93 to ed=20100801-20130419
95. case-control studies/ or cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/
96. case control$.ti,ab.
97. cohort.ti,ab.
98. longitudinal.ti,ab.
99. (follow-up or followup).ti,ab.
100. prospective$.ti,ab.
101. (comparison group$ or control group$).ti,ab.
102. observational.ti,ab.
103. retrospective studies/
104. retrospective$.ti,ab.
105. database$.ti,ab.
106. nonrandomi$.ti,ab.
107. population$.ti,ab.
108. or/95-107
109. 91 or 94
110. 108 and 109
111. limit 110 to "all child (0 to 18 years)"
112. limit 110 to "all adult (19 plus years)"
113. 111 not 112
114. 110 not 113
115. limit 114 to animals
116. limit 114 to humans
117. 115 not 116
118. 114 not 117
119. limit 118 to (english or french)
120. 69 or 119
121. exp *bariatric surgery/
122. limit 120 to ed=20100801-20130419
123. 122 not 121

EMBASE - OVID (KQ)

Last Run: April 19 2013

1. obesity/dm, dt, pc, rh, si, th [Disease Management, Drug Therapy, Prevention, Rehabilitation, Side Effect, Therapy]
2. diabetic obesity/dm, dt, pc, rh, si, th
3. abdominal obesity/dm, dt, pc, rh, si, th
4. morbid obesity/dm, dt, pc, rh, si, th
5. exp psychotherapy/
6. exp counseling/

7. counsel?ing.ti,ab.
8. antiobesity agent/
9. orlistat.ti,ab.
10. sibutramine.ti,ab.
11. meridia.ti,ab.
12. metformin/
13. metformin.ti,ab.
14. glucophage.ti,ab.
15. exp diet therapy/
16. (diet$ adj counsel$).ti,ab.
17. (diet$ adj education$).ti,ab.
18. (nutrition$ adj counsel$).ti,ab.
19. (nutrition$ adj education$).ti,ab.
20. (nutrition$ adj intervention$).ti,ab.
21. (diet$ adj (modif$ or therapy or intervention$ or strateg$)).ti,ab.
22. ((diet or dieting or slim$) adj (club$ or organi?ation$)).ti,ab.
23. (weightwatcher$ or weight watcher$).ti,ab.
24. exp exercise/
25. exp kinesiotherapy/
26. motor activity/
27. fitness/
28. (exercise adj3 (program$ or intervention$)).ti,ab.
29. physical activity.ti,ab.
30. or/5-29
31. obesity/
32. diabetic obesity/
33. abdominal obesity/
34. morbid obesity/
35. weight reduction/
36. obes$.ti.
37. overweight.ti.
38. weight.ti.
39. or/31-38
40. 30 and 39
41. (weight loss adj (intervention$ or program$ or trial$)).ti,ab.
42. (weight reduc$ adj (intervention$ or program$ or trial$)).ti,ab.
43. (weight management adj (intervention$ or program$ or trial$)).ti,ab.
44. (weight control adj (intervention$ or program$ or trial$)).ti,ab.
45. 31 or 32 or 33 or 34
46. 35 and 45
47. 1 or 2 or 3 or 4 or 40 or 41 or 42 or 43 or 44 or 46
48. limit 47 to (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study or phase 1 clinical trial or phase 2 clinical trial or phase 3 clinical trial or phase 4 clinical trial)
49. limit 47 to (meta analysis or "systematic review")
50. meta analysis/
51. controlled study/ or exp controlled clinical trial/ or exp "controlled clinical trial (topic)"/

52. (control* adj3 trial*).ti,ab.
53. random*.ti,ab.
54. clinical trial*.ti,ab.
55. 50 or 51 or 52 or 53 or 54
56. 47 and 55
57. 48 or 49 or 56
58. limit 57 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)
59. limit 57 to (adult <18 to 64 years> or aged <65+ years>)
60. 58 not 59
61. 57 not 60
62. limit 61 to animals
63. limit 61 to humans
64. 62 not 63
65. 61 not 64
66. limit 65 to (english or french)
67. limit 66 to yr="2010 -Current"
68. (harm or harms or harmful or harmed).ti,ab.
69. (risky behavior* or risky behaviour*).ti,ab.
70. weight cycling.ti,ab.
71. (ae or to or si).mp. or co.fs. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
72. exp mortality/
73. exp morbidity/
74. death/
75. sport injury/
76. exp malnutrition/
77. nutritional defici*.ti,ab.
78. exp heart arrhythmia/
79. Arrhythmia*.ti,ab.
80. bone density/
81. (bone mass adj3 loss).ti,ab.
82. bone resorption.ti,ab.
83. (death or deaths).ti,ab.
84. (disordered eating or eating disorders*).ti,ab.
85. suicide/
86. suicide attempt/
87. suicid*.ti,ab.
88. or/68-87
89. 47 and 88
90. exp case control study/ or pretest posttest control group design/
91. cohort analysis/
92. longitudinal study/
93. follow up/
94. prospective study/
95. observational study/

96. retrospective study/
97. case-control*.ti,ab.
98. cohort.ti,ab.
99. longitudinal.ti,ab.
100. (follow-up or followup).ti,ab.
101. prospective$.ti,ab.
102. (comparison group* or control group*).ti,ab.
103. observational.ti,ab.
104. retrospective*.ti,ab.
105. database*.ti,ab.
106. nonrandom*.ti,ab.
107. population*.ti,ab.
108. or/90-107
109. 89 and 108
110. limit 109 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)
111. limit 109 to (adult <18 to 64 years> or aged <65+ years>)
112. 110 not 111
113. 109 not 112
114. limit 113 to animals
115. limit 113 to humans
116. 114 not 115
117. 113 not 116
118. limit 117 to (english or french)
119. limit 118 to yr="2010 -Current"
120. 67 or 119
121. exp *bariatric surgery/
122. 120 not 121
123. (pediatric* or paediatric* or child* or adolescent? or youth? or teenager? or teen?).ti,ab,jn.
124. 122 not 123

Cochrane Central Register of Controlled Trials - OVID (KQ)
Last Run: April 19 2013
1. Obesity/dh, th, dt, rh
2. Obesity, Morbid/dt, dh, th, rh or Obesity, Abdominal/dt, dh, th, rh
3. Overweight/dh, dt, th, rh
4. "Behavior-Therapy"/
5. Cognitive Therapy/
6. Counseling/
7. Directive Counseling/
8. counsel?ing.ti,ab.
9. Anti-Obesity Agents/
10. orlistat.ti,ab.
11. xenical.ti,ab.
12. sibutramine.ti,ab.
13. meridia.ti,ab.

14. metformin/
15. metformin.ti,ab.
16. glucophage.ti,ab.
17. Diet, Reducing/
18. Diet, Fat-Restricted/
19. Caloric Restriction/
20. Diet Therapy/
21. (diet$ adj counsel$).ti,ab.
22. (diet$ adj education$).ti,ab.
23. (nutrition$ adj counsel$).ti,ab.
24. (nutrition$ adj education$).ti,ab.
25. (nutrition$ adj intervention$).ti,ab.
26. (diet$ adj (modif$ or therapy or intervention$ or strateg$)).ti,ab.
27. ((diet or dieting or slim$) adj (club$ or organi?ation$)).ti,ab.
28. (weightwatcher$ or weight watcher$).ti,ab.
29. Exercise/
30. Exercise Therapy/
31. Motor Activity/
32. Physical Fitness/
33. physical activity.ti,ab.
34. (exercise adj3 (program$ or intervention$)).ti,ab.
35. or/4-34
36. Obesity/
37. Obesity, Morbid/ or Obesity, Abdominal/
38. Overweight/
39. Weight Loss/
40. obes$.ti.
41. overweight.ti.
42. weight.ti.
43. or/36-42
44. 35 and 43
45. (weight loss adj (intervention$ or program$ or trial$)).ti,ab.
46. (weight reduc$ adj (intervention$ or program$ or trial$)).ti,ab.
47. (weight management adj (intervention$ or program$ or trial$)).ti,ab.
48. (weight control adj (intervention$ or program$ or trial$)).ti,ab.
49. (36 or 37 or 38) and 39
50. 1 or 2 or 3 or 44 or 45 or 46 or 47 or 48 or 49
51. limit 50 to yr="2010 -Current"

PsycINFO – OVID (KQ)
Last Run: April 19 2013
1. exp overweight/
2. exp Obesity/
3. obes*.ti.
4. weight control/ or weight loss/
5. overweight.ti.

6. weight.ti.
7. or/1-6
8. behavior modification/ or exp behavior therapy/
9. exp *psychotherapy/ or exp cognitive behavior therapy/
10. counseling/ or group counseling/ or peer counseling/
11. counsel?ing.ti,ab.
12. exp appetite depressing drugs/
13. orlistat.ti,ab.
14. xenical.ti,ab.
15. sibutramine.ti,ab.
16. meridia.ti,ab.
17. metformin.ti,ab.
18. glucophage.ti,ab.
19. diets/ or dietary restraint/
20. diet therapy.mp.
21. (diet* adj counsel*).ti,ab.
22. (diet* adj education*).ti,ab.
23. (nutrition* adj counsel*).ti,ab.
24. (nutrition* adj education*).ti,ab.
25. (nutrition* adj intervention*).ti,ab.
26. (diet* adj (modif* or therapy or intervention* or strateg*)).ti,ab.
27. ((diet* or dieting or slim* or weight loss) adj (club* or organi?ation*)).ti,ab.
28. physical activity/ or exp exercise/ or active living/ or activity level/ or exp health behavior/ or exp locomotion/ or physical fitness/
29. physical activity.ti,ab.
30. (exercise adj3 (program* or intervention*)).ti,ab.
31. exercise.ti.
32. or/8-31
33. (weight loss adj (intervention* or program* or trial*)).ti,ab.
34. (weight reduc* adj (intervention* or program* or trial*)).ti,ab.
35. (weight management adj (intervention* or program* or trial*)).ti,ab.
36. (weight control adj (intervention* or program* or trial*)).ti,ab.
37. 7 and 32
38. 1 or 2 or 3 or 5 or 6
39. 4 and 38
40. 33 or 34 or 35 or 36 or 37 or 39
41. meta analysis/
42. clinical trials/
43. (control* adj3 trial*).ti,ab.
44. random*.ti,ab.
45. clinical trial*.ti,ab.
46. 41 or 42 or 43 or 44 or 45
47. 40 and 46
48. limit 47 to (100 childhood or 120 neonatal or 140 infancy or 160 preschool age or 180 school age or 200 adolescence)

49. limit 47 to ("300 adulthood " or 320 young adulthood or 340 thirties or 360 middle age or "380 aged " or "390 very old ")
50. 48 not 49
51. 47 not 50
52. limit 51 to animal
53. limit 51 to human
54. 52 not 53
55. 51 not 54
56. limit 55 to (english or french)
57. limit 56 to up=20100801-20130419
58. exp "side effects (treatment)"/
59. (harm or harms or harmful or harmed).ti,ab.
60. (risky behavior* or risky behaviour*).ti,ab.
61. (adverse effects or adverse events or mortality or toxicity).ti,ab.
62. morbidity/
63. weight cycling.ti,ab.
64. disordered eating.ti,ab.
65. injuries/
66. athletic injur*.ti,ab.
67. exp nutritional deficiencies/
68. nutritional defici*.ti,ab.
69. "arrhythmias (heart)"/
70. Arrhythmia*.ti,ab.
71. osteoporosis/
72. (bone mass adj3 loss).ti,ab.
73. bone resorption.mp.
74. (death or deaths).ti,ab.
75. suicide/ or attempted suicide/
76. suicid*.ti,ab.
77. or/58-76
78. 40 and 77
79. case-control studies.mp.
80. case-control.ti,ab.
81. (cohort or longitudinal or follow-up or followup or prospective*).ti,ab.
82. (comparison group* or control group*).ti,ab.
83. observational.ti,ab.
84. retrospective*.ti,ab.
85. database*.ti,ab.
86. nonrandom*.ti,ab.
87. population*.ti,ab.
88. or/79-87
89. 78 and 88
90. limit 89 to (100 childhood or 120 neonatal or 140 infancy or 160 preschool age or 180 school age or 200 adolescence)
91. limit 89 to ("300 adulthood " or 320 young adulthood or 340 thirties or 360 middle age or "380 aged " or "390 very old ")

92. 90 not 91
93. 89 not 92
94. animals/ not humans/
95. 93 not 94
96. limit 95 to (english or french)
97. limit 96 to up=20100801-20130419
98. 57 or 97

Medline - OVID (CQ)

August 16, 2013
1. exp continental population groups/
2. exp Ethnic Groups/
3. indians, north american/ or inuits/
4. first nations.tw.
5. (aboriginal? and canada).tw.
6. native canadians.tw.
7. (immigran* or new canadians).tw.
8. ((African or Asian or Indo or Columbian or Spanish or Chinese) adj2 Canadian?).mp.
9. Rural Population/
10. (rural adj (population? or area? or region?)).tw.
11. Rural Health/ or Rural Health Services/
12. Healthcare Disparities/
13. Social Class/
14. poverty/
15. socioeconomic.tw.
16. Socioeconomic Factors/
17. (poor or disadvantaged or poverty or social status).tw.
18. exp homeless persons/ or vulnerable populations/
19. exp "Costs and Cost Analysis"/
20. (cost or costs).tw.
21. *"patient acceptance of health care"/ or *patient compliance/ or *patient participation/ or patient satisfaction/ or patient preference/ or *treatment refusal/
22. (women? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
23. (consumer? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
24. (patient? adj3 (acceptance or perference? or satisfaction or experience?)).tw.
25. willingness to pay.tw.
26. ((conjoint or contingent) adj3 (valuation or analysis)).tw.
27. exp Canada/
28. (Canada or Canadian or Ontario or British Columbia or Alberta or Saskatchewan or Manitoba or Quebec or Nova Scotia or Prince Edward Island or Newfoundland or New Brunswick or Yukon or Northwest Territories or Nunavut).tw.
29. (meta anal* or metaanal*).ti,ab.
30. meta-analysis.pt,ti,ab,sh.
31. (meta anal$ or metaanal$).ti,ab,sh.
32. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ti.
33. ((methodol$ or systematic$ or quantitativ$) adj3 (review$ or overview$ or survey$)).ab.

34. ((pool$ or combined or combining) adj (data or trials or studies or results)).ti,ab.
35. (medline or embase or cochrane or pubmed or pub med).ti,ab.
36. or/33-35
37. review.pt,sh.
38. 36 and 37
39. or/30-32
40. 38 or 39
41. "Process Assessment (Health Care)"/ or Quality Indicators, Health Care/ or Quality Assurance, Health Care/
42. Benchmarking/
43. (performance adj2 (indicators or measures)).tw.
44. or/41-43
45. or/1-28
46. 44 or 45
47. 40 and 46
48. Weight Reduction Programs/
49. exp obesity/pc
50. Overweight/pc
51. weight maintenance.tw.
52. weight management.tw.
53. exp *obesity/
54. *overweight/
55. *Weight Gain/
56. exp obesity/
57. overweight/
58. weight gain/
59. Weight Loss/
60. (weight or bmi or body mass index or waist circumference or obese or obesity).ti.
61. or/48-60
62. 47 and 61
63. limit 62 to yr="2007 -Current"
64. limit 63 to (english or french)
65. 29 or 30 or 31 or 32 or 33 or 34
66. 46 and 61 and 65
67. limit 66 to yr="2007 -Current"
68. limit 67 to (english or french)
69. (Canada or Canadian or Ontario or British Columbia or Alberta or Saskatchewan or Manitoba or Quebec or Nova Scotia or Prince Edward Island or Newfoundland or New Brunswick or Yukon or Northwest Territories or Nunavut).ti.
70. 53 or 54 or 55 or 60
71. 69 and 70
72. limit 71 to yr="2007 -Current"
73. limit 72 to (english or french)
74. weight gain/de
75. molecular weight.ti.
76. 74 or 75

77. (Meta-analysis or review).pt. or systematic review.ti.
78. 64 and 77
79. 73 or 78
80. 79 not 76
81. limit 80 to ed=20121017-20130816

EMBASE – OVID (CQ)
August 16, 2013
1. meta analysis/
2. systematic review/
3. (systematic* adj3 (review* or overview*)).tw.
4. exp "ethnic and racial groups"/
5. first nations.tw.
6. (aboriginal? and canada).tw.
7. native canadians.tw.
8. (immigran* or new canadians).tw.
9. ((African or Asian or Indo or Columbian or Spanish or Chinese) adj2 Canadian).mp.
10. rural health care/
11. rural population/
12. (rural adj (population? or area? or region?)).tw.
13. exp economic evaluation/
14. cost.tw.
15. or/13-14
16. exp patient attitude/
17. (women? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
18. (consumer? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
19. (patient? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
20. willingness to pay.tw.
21. ((conjoint or contingent) adj3 (valuation or analysis)).tw.
22. or/16-21
23. ((process or performance or outcome) adj2 (measure? or indicator?)).tw.
24. performance measurement system/
25. or/23-24
26. exp socioeconomics/
27. exp social status/
28. (poor or disadvantaged or poverty or social status).tw.
29. health care disparity/
30. miscellaneous named groups/ or lowest income group/ or medically underserved/ or vulnerable population/
31. or/4-12
32. or/26-30
33. 15 or 22 or 25 or 31 or 32
34. exp Canada/
35. (Canada or Canadian or Ontario or British Columbia or Alberta or Saskatchewan or Manitoba or Quebec or Nova Scotia or Prince Edward Island or Newfoundland or New Brunswick or Yukon or Northwest Territories or Nunavut).tw.

36. or/34-35
37. *obesity/
38. *diabetic obesity/
39. *abdominal obesity/
40. *morbid obesity/
41. *weight reduction/
42. obes$.ti.
43. overweight.ti.
44. weight.ti.
45. or/37-44
46. (weight loss adj (intervention$ or program$ or trial$)).ti,ab.
47. (weight reduc$ adj (intervention$ or program$ or trial$)).ti,ab.
48. (weight management adj (intervention$ or program$ or trial$)).ti,ab.
49. (weight control adj (intervention$ or program$ or trial$)).ti,ab.
50. 37 or 38 or 39 or 40
51. 41 and 50
52. 33 and 45
53. 1 or 2 or 3
54. 15 or 22 or 25 or 31 or 32 or 36
55. 53 and 54
56. 45 or 51
57. 55 and 56
58. limit 57 to yr="2007 -Current"
59. limit 58 to (english or french)
60. (Canada or Canadian or Ontario or British Columbia or Alberta or Saskatchewan or Manitoba or Quebec or Nova Scotia or Prince Edward Island or Newfoundland or New Brunswick or Yukon or Northwest Territories or Nunavut).ti.
61. 56 and 60
62. limit 61 to yr="2007 -Current"
63. limit 62 to (english or french)
64. 59 or 63
65. limit 64 to em="201237-201332"

Appendix 2: Acknowledgements

We would like to thank the following reviewers and staff members for their advice and work on this review:

John Garcia PhD	Associate Professor & Interim Director School of Public Health and Health Systems Faculty of Applied Health Sciences University of Waterloo	Full Draft Reviewer
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