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

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

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Abstract

Background: The purpose of this report is to synthesize evidence on behavioral interventions for preventing weight gain in normal weight adults.

Methods: We searched multiple databases from January 1980 to June 27, 2013, for trials in English or French. Study quality was assessed using the Cochrane Risk of Bias tool and GRADE.

Results: A total of 26 studies were included. Programs were successful in stabilizing weight and producing weight loss by the end of the interventions. Intervention participants lost 0.73 more kg (95% CI -0.93, -0.54, P<0.00001), lowered their BMI by 0.24 kg/m^2 more (95% CI -0.34, -0.15, P<0.00001), reduced their waist circumference by an additional 0.95 cm (95% CI -1.27, -0.63, P<0.00001) and lost 1.27% more total body fat (95% CI –1.93, -0.61, P=0.0002) compared to the control group. Small but not clinically meaningful effect sizes were found for secondary outcomes.

Interpretation: Behavioral interventions are associated with reductions in weight and other disease indicators in mixed weight adult populations but it is uncertain if these changes are clinically meaningful and if they are maintained over time.

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INTRODUCTION

Overweight and obesity, defined by a body mass index (BMI) of 25-29.9 kg/m^2, and ≥30 kg/m^2, are global problems with increasing prevalence in most countries.[1] Excess adiposity is related to considerable increase in morbidity[2-4] and premature mortality.[5,6]

The natural history of weight changes in adults has not been well studied but data were collected on Canadian adults through the National Population Health Survey and analyzed for changes in the time periods of 1996/1997 to 2004/2005. The overall change during eight years was average gain of 4 kg for men and 3.4 kg for women.[7] A large cohort study conducted in the United States found that non-obese adults gain, on average, 0.8 pounds (about 0.36 kg) per year.[8]

Several groups have produced guidelines related to overweight and obesity. The Australian[9], New Zealand[10], Scottish Intercollegiate Guidelines Network (SIGN)[11], and United States Preventive Services Task Force (USPSTF)[12] guidelines focused on treatment of overweight and/or obesity. The Obesity Canada Clinical Guidelines Expert Panel made recommendations for interventions for prevention of weight gain, but the underlying studies were graded as B or C (unclear whether benefits outweigh risks).[13] Similarly, the NICE recommendations about healthy lifestyle for weight gain prevention were based on cohort studies.[14]

Many guideline groups have identified a gap in knowledge of interventions that help people maintain normal weight. While prevention is ideal, is there high quality evidence that interventions in people of normal weight (BMI 18.5 kg/m^2 to 24.9 kg/m^2) prevent weight gain?

We aimed to identify interventions applicable to primary care settings aimed at preventing weight gain, particularly in normal weight adults. The key question for this review was: Do preventive interventions (behavioral) in normal weight adults lead to short-term or sustained

weight gain prevention, or improved health outcomes? Primary outcomes were weight, BMI, waist circumference, and % body fat; secondary outcomes included total and LDL cholesterol, blood pressure, fasting glucose, and incidence of type 2 diabetes (T2D). Secondary questions explored were: a) differences in efficacy between patient subgroups (e.g., age ≥65 years, sex, baseline cardiovascular risk status); b) adverse effects (e.g., labelling; disordered eating; psychological distress such as anxiety, depression and stigma; nutritional deficits; cost burden); c) differences in adverse effects between adult subgroups (e.g., age ≥65 years, sex, baseline cardiovascular risk status) and d) maintenance weight or health outcome changes.

A concurrent review to this one, studied a similar question but with different inclusion/exclusion criteria. Hutfless and colleagues included 11 trials and 11 observational studies and concluded that there may be effective strategies to prevent weight gain (low fat diets, eating fewer meals out of the home, consuming more fruits and vegetables, monitoring heart rate during exercise and participation in group lifestyle sessions with reminder text messages). [15]

METHODS

The protocol was registered with PROSPERO (# CRD42012002753) (www.crd.york.ac.uk/prospero/).

Search

We searched EMBASE, Medline, Cochrane Central Registry of Controlled Trials, and PsychINFO from January 1980 to June 27, 2013. Reference lists of primary studies included in this review and related systematic reviews were searched for relevant studies not captured by our search. The search strategy example for Medline-Ovid is provided in the online supplemental file (Table 3). In addition, a focused grey literature search of Canadian sources was done for recent

reports on obesity in Canada. All citations were uploaded to a web-based systematic review software program[16] for screening and data extraction.

Study Selection, Quality Assessment and Abstraction

Titles and abstracts of papers were reviewed in duplicate; articles marked for inclusion by either team member went on to full text screening, which was also done independently by two people. One team member completed full data abstraction and a second member verified all extracted data. All data were checked in a third round of verification prior to analysis. RCTs were assessed using Cochrane's Risk of Bias tool[17] and overall strength of the evidence was determined using GRADE.[18,19] The online supplemental file Table 1, summarizes the risk of bias ratings. At all levels, inter-rater conflicts were resolved through discussion.

Inclusion and Exclusion Criteria

Studies had to be randomized trials conducted in adults with a normal BMI (18-24.9 kg/m^2), reported in English or French. If there was no explicit statement about normal weight status we accepted studies when the baseline mean BMI minus one standard deviation (SD) fell below 25.

Trials limited to participants with cardiovascular disease or conditions which are predisposed to weight gain such as the metabolic syndrome, polycystic ovarian disease and pregnancy were excluded; as were studies focused on underweight adults or those with eating disorders.

Behavioural interventions had to centre on weight gain prevention and could include diet, exercise, diet plus exercise, or lifestyle strategies. Lifestyle strategies were typically referred to as such and usually included additional counseling, education or support and environmental changes in addition to diet and/or exercise. Pharmacological and surgical interventions were excluded.

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 hospital or 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 primary care setting were excluded.

Only studies that reported outcome data for at least 12 months post baseline assessment for one or more of the specified weight outcomes (weight, BMI, waist circumference, % body fat) were included. There were no timeframe or weight outcome requirements if a study reported data for any of the adverse effects of interest to this review. Secondary outcomes included total cholesterol (TC), low density lipoprotein (LDL), fasting glucose (FG), incidence of T2D, systolic blood pressure (SBP), and diastolic blood pressure (DBP).

Data Analysis

For meta-analyses, immediate post-treatment data (means, standard deviations) were utilized for continous outcomes while number of events data were utilized for binary outcomes (i.e., incidence of T2D). The DerSimonian and Laird random effects models with inverse variance method were 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.[20]

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.[21] For studies that provided neither SD nor 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. The units of measurement for total cholesterol, LDL 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 studies with more than one intervention arm (e.g., two diet + exercise arms, one using a clinic-based group and one using a correspondence course), we pooled data from the intervention groups to do a pair-wisecomparison with the control group. Alternatively, if the interventions were substantively different from each other (e.g., a low calorie diet group and a high intensity aerobic exerice group), we included the data for each intervention arm compared with the control group but split the sample size for the control group in half to avoid a unit-of-analysis error and double counting.[17]

We used Cochrane's Q (α=0.10) and the I^2 statistic to quantify heterogeneity, where $P<0.05$ indicated 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.[21] Sensitivity analyses were performed to evaluate statistical stability and effect on statistical heterogeneity. For the outcome of weight in kg, we did sensitivity analyses based on type of intervention (diet, exercise, diet + 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/no CVD risk or unselected population or not specified), and study risk of bias rating (high, unclear, low). One additional sensitivity analysis was performed based on baseline mean BMI (<25, ≥25) for the

outcome of BMI. Meta-analyses were performed using Review Manager version 5.1 software.[17] Publication bias for each outcome was assessed using the Egger's test.[22]

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RESULTS

Search Summary

We conducted four reviews, for obesity prevention in children, obesity treatment in children, obesity prevention in adults, and obesity treatment in adults. We believed some efficiency would be gained in the screening stage if we started with a comprehensive search strategy. Thus, the search and selection process for relevant literature occurred in stages. First, a comprehensive search including both adults and children located 30,196 unique citations of which 3,320 were for consideration for adult prevention (see supplemental file Figure 1a). The literature search was updated in June 2013 and added 1,778 citations for possible inclusion. We conducted hand-searches and reviewed reference lists of recent (published in 2012 and 2013) on topic systematic reviews to ensure that we had not missed 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 the adult prevention review (see supplemental file Figure 1b). All studies reported weight outcome data. Most (81%) of the studies were rated as having unclear or high risk of bias for the weight outcomes, primarily due to lack of information about or lack of procedures to ensure random sequence generation, allocation concealment and/or blinding of outcome assessment (see supplement file, Table 1). Due to the nature of behavioral interventions, there

was also high risk of bias for blinding of participants and personnel across all studies. The adults who volunteered or agreed to participate in these studies may have been more weight conscious than the general population and some may have been better motivated to lose weight.

Although this review focuses on the prevention of overweight and obesity, the population was not restricted to normal weight adults. A single study[23] 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 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;[24-27]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.[28-32]

None of the included studies specifically targeted or recruited seniors (≥ 65 years). Most studies (n=18) included mixed gender samples; seven targeted only women[31,33-38] and the analysis in one study was limited to male participants.[39] Few studies (n=4) were directed at participants at high risk for cardiovascular disease (i.e., screened/identified as high CVD risk and/or diagnosed with T2D, hypertension and/or dyslipidemia).[30,40-42] The intervention duration was ≤1 year in over two-thirds of the studies (n=18); in the remaining 8 studies the duration ranged from two years to up to 12 years, with half of these interventions (n=4) running for two years. Just over one-third of the studies (n=10) were done in European countries, with the remainder in the US (n=7), Australia and/or New Zealand (n=4) and Japan (n=2). Less than half of the studies (n=11) were

published in the last five years (2009-2012). The characteristics of the 26 included studies are reported in the online supplement file, Table 2.

Weight

We were unable to conclusively determine whether primary care-relevant interventions prevent weight gain or lead to improved health outcomes in normal weight adults. As noted above, the search found one study that included only normal weight adults that met the inclusion criteria.[23] The "Pound of Prevention" pilot study examined the effects of a 12 month, education and incentive-based lifestyle intervention 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). More intervention participants (82%) maintained their baseline weight or lost weight over the 12 month intervention compared with control group participants (56%). On average, intervention group participants lost 0.95 kg whereas control group participants lost 0.14 kg (P=0.0.3). Aside from weight, this study did not report any 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, as explained above. Twenty-five studies were found that met the expanded inclusion criteria. Therefore, the following analyses, based on subgroups of the 26 included RCTs, provide indirect evidence to address the review questions.

Nineteen RCTs of very low GRADE quality with a total of 48,460 participants provided data on weight that could be pooled. 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 mean BMIs were in the overweight/obese range. There was a statistically significant reduction in weight in the intervention group as compared with the control group [MD (95% CI) -0.73 kg (-0.93, -0.54)] (see Figure 1). Subanalysis by type of intervention found a reduction in weight in the intervention group as compared with the control group for diet [MD (95% CI) -0.51 kg (-0.65, -0.36)]; exercise [MD (95% CI) -0.88 kg (-1.44, -0.33)]; diet and exercise [MD (95% CI) -0.99 kg (-1.90, -0.08)]; and lifestyle interventions [MD (95% CI) -0.89 kg (-1.44, -0.34)] (see Table 1).

The test for subgroup differences found no significant results for duration of the intervention (> or <12 months) [Chi^2=3.07, df=1 (P=0.08), I^2=67%] or gender [Chi^2=1.34, df=1 (P=0.25), I^2=25%]. Weight loss interventions were effective for both those considered at high CVD risk [MD (95% CI) -0.88 kg (-1.45, -0.32)] and no or low CVD risk [MD (95% CI) -0.72 kg (-0.93, -0.52)]; and for those studies at unclear [MD (95% CI) -0.53 kg (-0.67, -0.40)] and low risk of bias [MD (95% CI) -1.22 kg (-2.16, -0.28)], but not for studies rated as high risk of bias [MD (95% CI) -1.20 kg (-3.04, 0.64)] (see Table 1).

BMI

Twenty RCTs of low GRADE quality with a total of 52,243 participants, whose baseline BMIs ranged from 22.4 to 33.2, were included. Most studies (n=14) included mixed gender samples. There was a statistically significant reduction in BMI in the intervention group as compared with the control group [MD (95% CI) -0.24 kg/m^2 (-0.34, -0.15)]. The test for subgroup differences was not significant [Chi^2=0.06, df=1 (P=0.81), I^2=0%] and, therefore, baseline mean BMI did not explain the variation across these studies (see Table 2).

When restricted to studies with a mean baseline BMI <25, the analysis included four RCTs of low GRADE quality. Baseline BMI ranged from 22.4 to 24.8 but all studies included some

overweight/obese adults. BMI was reduced more in the intervention group than the control [MD (95% CI) -0.27 kg/m^2 (-0.50, -0.05)]. This benefit was also observed in intervention groups in 16 RCTs with a baseline BMI ≥25 [MD (95% CI) -0.24 kg/m^2 (-0.36, -0.12)] (see Table 2).

Waist Circumference

Fifteen RCTs of very low GRADE quality with a total of 20,796 participants found a benefit of the intervention over the control group on waist circumference [MD (95% CI) -0.95 cm (-1.27, -0.63)] (see Table 2).

Percent Body Fat

Considering total % body fat, six RCTs of low GRADE quality that included 1,663 participants found that the intervention group had less body fat than the controls at the end of the interventions [MD (95% CI) -1.27 % (-1.93, -0.61)] (see Table 2) .

Secondary Outcomes

Pooled effect estimates for some secondary health outcomes were significant in favour of the interventions. At the post-intervention point, compared to the control group, intervention participants had reduced their total cholesterol by an additional 0.06 mmol/L (95% CI -0.11, -0.01), lowered their LDL level by an additional 0.06 mmol/L (95% CI -0.09, -0.03), and reduced their fasting glucose level by 0.04 mmol/L more (95% CI -0.08, -0.0016). These 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 T2D (see Tables 3 and 4).

Harms

No harms of interest to this review were reported. Only six studies mentioned adverse effects, half of which[27,30,32,36,38,43] 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.

Maintenance of weight or health outcomes

Only one study of a 9-month exercise intervention was available to address the question about the long-term benefits of weight gain prevention programs. There was a statistically significant increase ($P<0.00001$) 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 ($P=1.00$) 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.

Interpretation

To our knowledge, this is the first meta-analysis of prevention of obesity in adults. Gaining <0.5 kg over one year may not appear clinically meaningful[8] but this should be considered with regard to expected weight gain that typically occurs in adults (3-4 kg in 8 years)[7] and the associated obesity-related health problems.[2-6]

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[8] in control group participants. In this review we considered four measures of weight gain prevention: weight; BMI; waist circumference; and total % body fat. Across studies, interventions were successful in stabilizing weight and, in some cases, conferred 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. These results are consistent with the review by Hutfless et al.[15], although their inclusion/exclusion criteria and some outcomes differed.

For adults in an overweight or obese category, these changes do not represent clinically meaningful reductions in weight. However, this was not the goal of theses interventions, which was to prevent weight gain. With that goal, the benefits of these interventions could become apparent over time but long-term follow-up data are not available to draw such conclusions.

Sensitivity analyses performed on studies providing weight in kg and BMI data found no significant differences between any sub-groups. None of the specified categorizations (i.e., type of behavioral 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.

Most of the studies 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/or 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 behavioral interventions, there is a high risk of bias for blinding of participants and personnel across all studies.

As noted, only one pilot study addressed a normal weight population. All other data in this review is taken from studies with mixed weight populations, and thus constitutes only indirect evidence for primary prevention of adult overweight and obesity.

Results presented for the secondary health outcomes (total cholesterol, LDL, fasting glucose, blood pressure, incidence of T2D) should be considered with caution as we did not conduct a full systematic review for these components. To be included in this review studies had to report data for the primary outcome of weight; therefore any investigations of relevant interventions that examined the secondary outcomes but did not provide weight data were excluded. Finally, we restricted our search to papers in English or French, thus we may have missed the papers written in other languages.

Interpreting these results is challenging. People 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 serious 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 behaviorally-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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Figure 1: Meta-analysis of Weight Gain Prevention Interventions on Weight (kg)

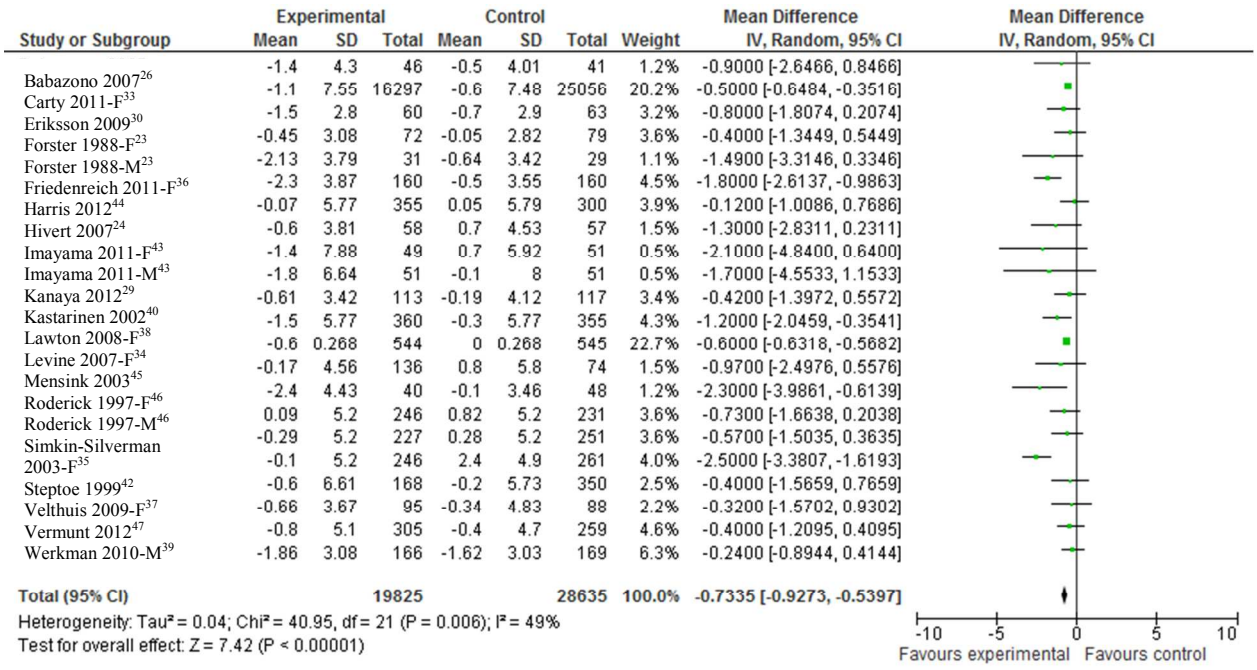

Table 1: Change in Weight (KG)

Group or Sub-group	Meta-analysis, Mean difference, weight in kg (95% CI)	Sub-group Differences	No. Participants	No. Studies	GRADE Rating*
Overall	-0.73 (-0.93 to -0.54)		48,460	19	Very Low
Type – Diet	-0.51 (-0.65 to -0.36)	P=0.25	42,308	2	Low
Type – Exercise	-0.88 (-1.44 to -0.33)		2,024	5	Low
Type – Diet + Exercise	-0.99 (-1.90 to -0.08)		748	4	Low
Type – Lifestyle	-0.89 (-1.44 to -0.34)		3,380	8	Low
Duration <= 12 Months	-0.61 (-0.70 to -0.51)	P=0.08	4,908	12	Low
Duration > 12 Months	-1.21 (-1.88 to -0.54)		43,552	7	Low
Gender – Male	-0.48 (-0.99 to 0.03)	P=0.25	975	4	Very Low
Gender – Female	-0.82 (-1.09 to -0.55)		44,390	9	Low
High CVD Risk	-0.88 (-1.45 to -0.32)	P=0.60	1,356	3	Low
No/Low CVD Risk	-0.72 (-0.93 to -0.52)		47,104	16	Very Low
High Risk Of Bias	-1.20 (-3.04 to 0.64)	P=0.29	652	2	Very Low
Unclear Risk of Bias	-0.53 (-0.67 to -0.40)		45,237	13	Very Low
Low Risk of Bias	-1.22 (-2.16 to -0.28)		2,571	4	Low

*Low=downgraded for risk of bias and indirectness
Very Low=downgraded for risk of bias, indirectness and reporting bias

Table 2: Changes in BMI, Waist Circumference, % Body Fat

Group or Sub-group	Meta-analyses: mean difference (95% CI)	Sub-group Differences	No. Participants	No. Studies	GRADE Rating*
Overall	-0.24 (-0.34 to -0.15)		52,243	20	Low
Baseline Mean BMI – Normal Weight (<25 kg/m^2)	-0.27 (-0.50 to -0.05)	P=0.81	5,152	4	Low
Baseline Mean BMI – Overweight/Obese (≥25 kg/m^2)	-0.24 (-0.36 to -0.12)		47,091	16	Low
Outcome: Waist Circumference (cm)					
Overall	-0.95 (-1.27 to -0.63)		20,796	15	Very Low
Outcome: Total % Body Fat					
Overall	-1.27 (-1.93 to -0.61)		1,663	6	Low

*Low=downgraded for risk of bias and indirectness
Very Low=downgraded for risk of bias, indirectness and reporting bias

Table 3: Changes in Total Cholesterol, LDL, Fasting Glucose and Blood Pressure

Outcome	Meta-analyses: mean difference (95% CI)	No. Participants	No. Studies	GRADE Rating*
Total Cholesterol (mmol/L)	-0.06 (-0.11 to -0.01)	10,660	15	Low
LDL (mmol/L)	-0.06 (-0.09 to -0.03)	5,635	11	Low
Fasting Glucose (mmol/L)	-0.04 (-0.08 to -0.0016)	7,189	10	Low
SBP (mmHg)	-0.31 (-0.84 to 0.22)	48,493	17	Very Low
DBP (mmHg)	-0.18 (-0.44 to 0.07)	47,945	15	Very Low

*Low=downgraded for risk of bias and indirectness
Very Low=downgraded for risk of bias, indirectness and imprecision

Table 4: Change in Type 2 Diabetes Incidence

Outcome	Relative Effect (95% CI)	Absolute Number per thousand (Range)	ARR	NNT	No. Participants	No. Studies	GRADE Rating*
T2D Incidence	RR 0.95 (0.89 to 1.02)	3 fewer (from 8 fewer to 2 more)	0.34%	293	46,537	2	Very Low

* Very Low=downgraded for risk of bias, indirectness and imprecision

Adult Obesity Prevention - Supplemental File

Figure 1 a: Initial Comprehensive Search Results

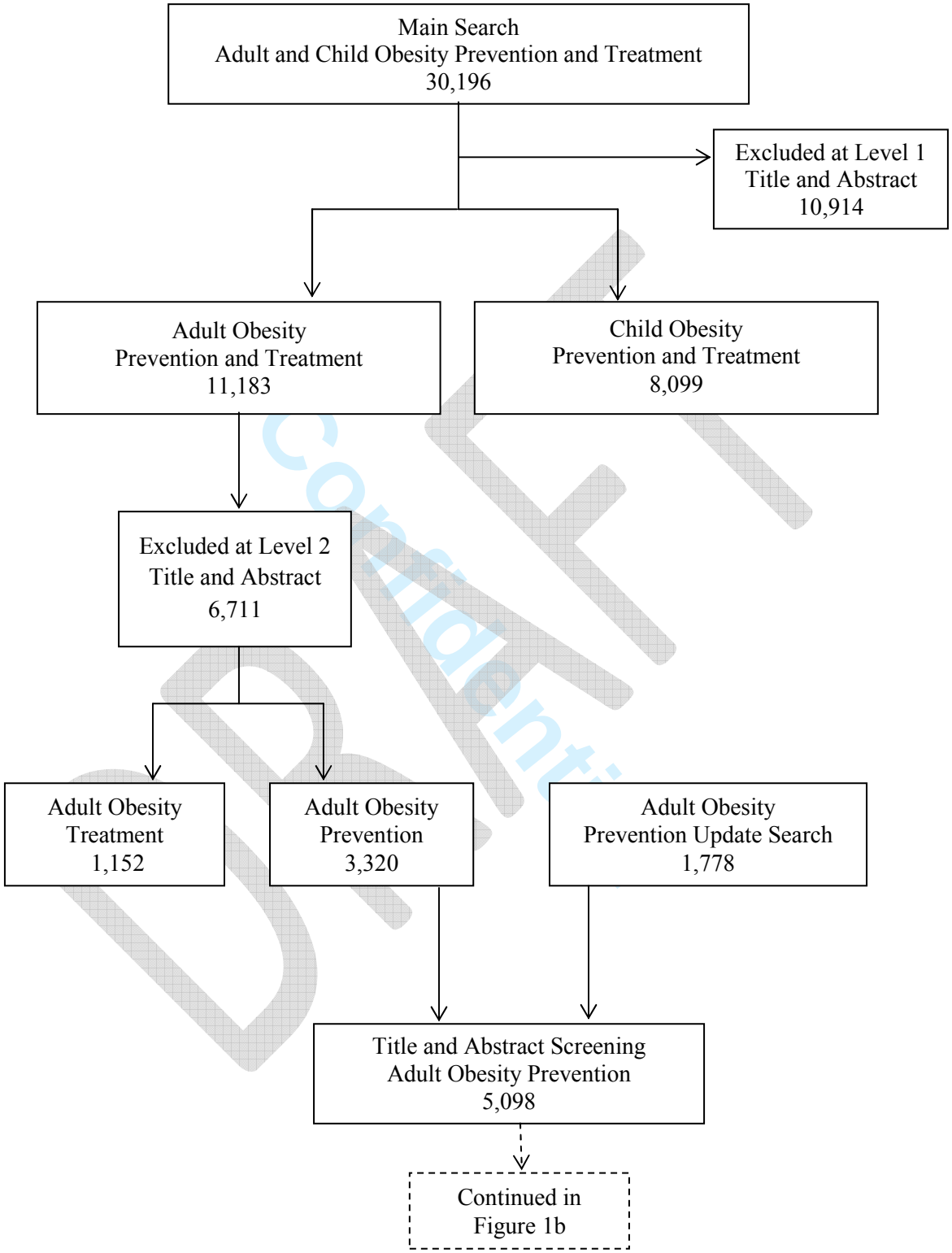

Figure 1b: Adult Overweight/Obesity Prevention Search Results

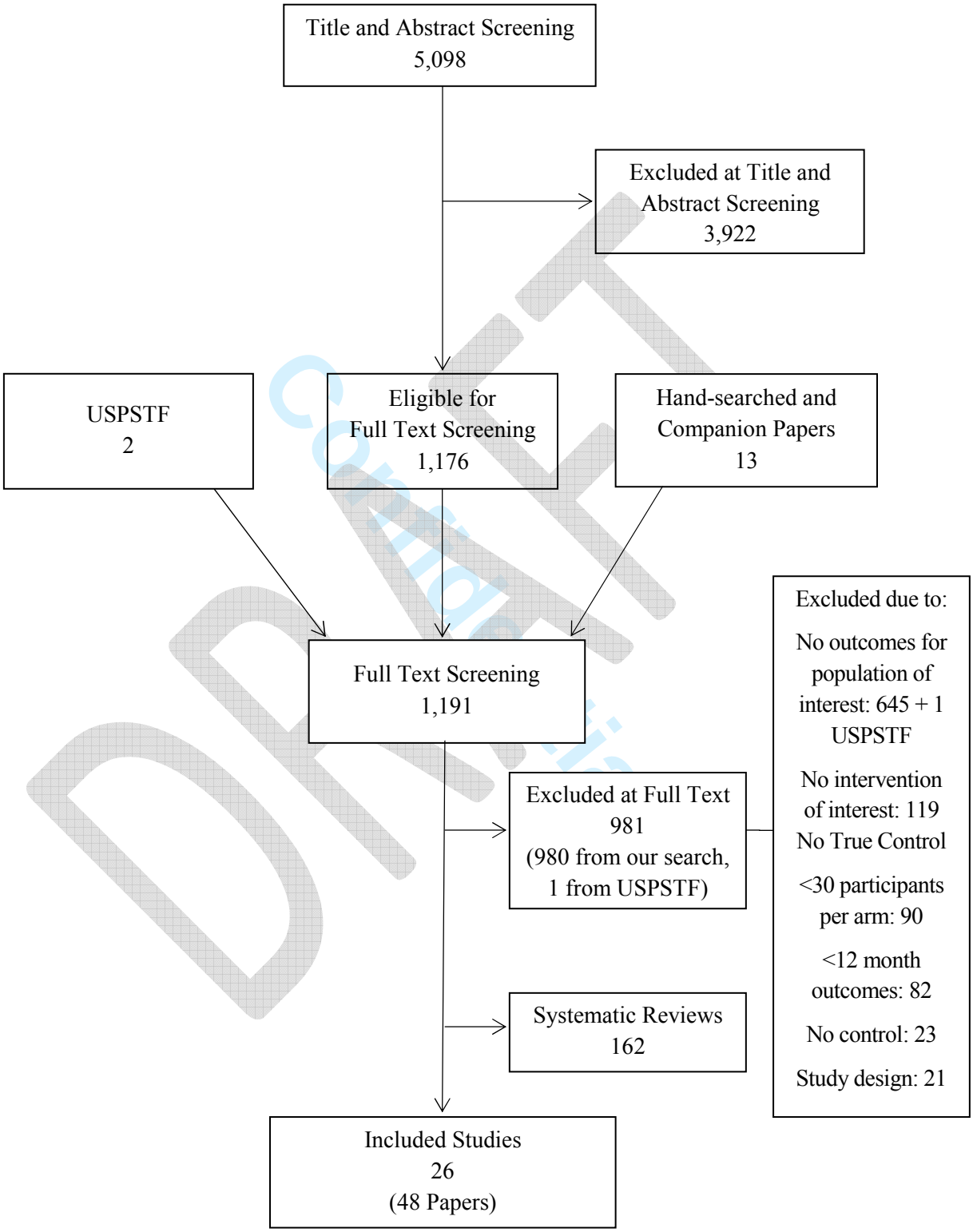

Table 1: Summary of Risk of Bias Assessment of Included RCTs Using Cochrane's Risk of Bias Tool[1]

Study	Sequence Generation	Allocation Concealment	Blinding of Outcome Assessors			Incomplete Reporting			Selective Reporting	Other Bias	Overall Risk of Bias		
			OBJ	SUB	S-R	OBJ	SUB	S-R			OBJ	SUB	S-R
Babazono 2007[2]	U	U	L	U		L	L		L	H	U	U	
Broekhuizen 2012[3]	L	L	L	U		L	L		L	U	L	U	
Burke 2003[4]	L	U	L	U		H	H		L	U	U	U	
Carty 2011[5]	L	U	L	L		H	L		L	U	U	U	
Elley 2003[6]	U	U	L	U		L	L		L	U	U	U	
Eriksson 2009[7]	L	L	L	U	H	L	L	L	L	U	L	U	U
Forster 1988[8]	U	U		U			L		L	H		U	
Friedenreich 2011[9]	L	L	L	L		L	L		L	H	L	L	
Harris 2012[10]	L	U		L			L		L	L		L	
Hivert 2007[11]	L	L	L	U		L	L		L	U	L	U	
Imayama 2011[12]	L	U	L	L		L	L		L	H	U	U	
Kanaya 2012[13]	L	L	L	U		L	L		L	U	L	U	
Kastarinen 2002[14]	L	U	L	L		L	L		L	U	U	U	
Khare 2012[15]	U	U	L	U		H	H		L	H	U	U	
Lawton 2008[16]	L	L	L	L		L	L		L	U	L	L	
Levine 2007[17]	U	U		U			L		L	H		U	
Mensink 2003[18]	U	U	L	U		H	H		H	H	H	H	
Roderick 1997[19]	U	U	L	U		L	L		L	U	U	U	
Sacerdote 2006[20]	L	U		H			L		L	U		U	
Simkin-Silverman 2003[21]	L	L	L	L		L	L		L	L	L	L	
Sone 2002[22]	U	U	L	H		L	L		U	U	U	U	
Steptoe 1999[23]	U	U	L	U		H	H		L	L	U	U	
Velthuis 2009[24]	U	U	L	U		L	L		H	H	U	U	
Vermunt 2012[25]	H	H	L	U		H	H		L	H	H	H	
Werkman 2010[26]	U	L		H			L		L	H		U	
Wister 2007[27]	L	L	L	L	H	L	L	L	L	U	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 2: Characteristics of Included Studies

Study/Location	Babazano 2007[2] 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 130-150mmHg; DBP 85-99mmHg or HbA1c ≥5.6% Exclusion criteria: Persons with critical need for medical treatment
Participants	Sample n = 99 Intervention group n = 50; Control group n = 49 Age: Mean age Intervention (SD): 64.3 (7.1); Mean age Control (SD): 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[3] The Netherlands *Companion paper:* Broekhuizen[3]
Objective	This project evaluated the efficacy of an individualized tailored lifestyle intervention on lipids, systolic blood pressure, glucose, body mass index (BMI) and waist circumference in people with familial hypercholesterolemia (FH)
Methods	Design: RCT Selection: recruitment was 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 group n = 181; Control group n = 159 Age: Mean age Intervention (SD): 44.7 (12.9); Mean age Control (SD): 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[4] Australia *Companion papers:* Dzator,[28] Burke[29, 30]
Objective	The objective of this study was 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 age Overall (SD): 29.6 years in women (range 18-62); 31.4 years in men (range 20-61) Gender [Female n(%)]: 50% female 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[5] US *Companion papers*: Howard,[31, 32] Tinker,[33] Women's Health Initiative Study Group,[34] Hays[35]
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 were enrolled between 1993 and 1998 at 40 clinical centers throughout the United States Exclusion criteria: history of breast, colorectal, and other cancers except nonmelanoma 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 nonadherence; consumption of <600 kcal/day or >5000 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 age Overall (SD): 62.3 (6.9) Gender [Female n(%)]: 100% SES: college degree or higher Intervention: n=7,445 (38.3%); Control n=11,042 (37.9%) Loss to follow-up: Overall n=2027; Intervention n=727; Control n=1300
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 behavioral 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[6] 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 group n = 451; Control group n = 427 Age: Mean age Intervention (SD): 57.2 (10.8); Mean age Control (SD): 58.6 (11.5) Gender [Female n(%)]: Intervention n = 301 (67%); Control n = 281 (66%) Race/Ethnicity: Intervention: NR SES [lower SES]: 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 them using motivational interviewing techniques and give specific advice about exercise or community groups; quarterly newsletters from sports foundation about exercise initiatives in the community 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[7] Sweden *Companion paper*: Eriksson[36]
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 cardiovascular risk factor levels in the primary care setting
Methods	Design: RCT Selection: selected from the 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, type 2 diabetes, 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 group n = 71; Control group n = 74 Age: Mean age Intervention (SD): 57.7 (6.6); Mean age Control (SD): 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: standard care group given verbal and written information about healthy behaviours, including exercise and diet by the physician, a physiotherapist and a dietician at a group meeting following baseline exam Duration of intervention: 3 months Length of follow-up: 9 months

Study/Location	Forster 1988[8] US
Objective	The objective of this study was 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 cardiovascular 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: there was no lower weight limit for eligibility for the study
Participants	Sample: 219 Intervention n= NR ;Control n= NR Age: Mean age Overall (SD): 45.9 Gender [Female n(%)]: 71.0% overall 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 visit and a follow-up scheduled 1 year later Duration of intervention: 12 months

	Length of follow-up: immediate post

Study/Location	Friedenreich 2011[9] Canada *Companion papers*: Friedenreich[37-39]
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: women recruited through targeted mailings to participants in the Alberta Breast Screening Program, posters and brochures distributed to family physicians and media campaigns between May 2003 and June 2006 Inclusion criteria: age 50-74 years; postmenopausal; no previous cancer diagnosis; no major comorbidities; acceptable baseline fitness test; sedentary (<90 min of weekly exercise or, if between 90 and 120 min, having a VO2max level <34 kg-1min-1); able to do unrestricted physical activity; normal blood lipid and hormone levels, BMI between 22 and 40 kg/m2; nonsmoker; <14 drinks per week of alcohol; no medications or exogenous hormones that might influence estrogen metabolism and not currently or planning to undertake a weight loss program
Participants	Sample: 320 Intervention n=160 ; Control n=160 Age: Mean age Intervention (SD): 61.2 (5.4); Mean age Control: 60.6 (5.7) Gender [Female n(%)]: 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 on 5 days per week for 1 year; at least three sessions per week were facility based with on-site exercise trainers and remaining sessions were home based; prescription ramped up over the first 3 months starting with three 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 were 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[10] 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: participants who had attended the practice in the previous 12 months and were either aged 40-55 years with a recorded diagnosis of hypertension and/or hyperlipidaemia or were aged 56-64 with or without recorded risk factors
Participants	Sample: n= 699 Intervention group n = 384; Control group n = 315 Ages: 40-55 years Intervention group: 96 (25.0%); Control: 78 (24.8%); Ages: 56-64 Intervention group: 288 (75.0%); Control: 237 (75.2%) Gender [Female n(%)]: Intervention: 232 (60.4); Control: 169 (53.7) Race/Ethnicity: Intervention: NR SES [post-secondary education]: Intervention: 18.8; Control: 30.2 Loss to follow-up: Intervention n = 29; Control n = 15
Intervention	Intervention: brief intervention, which included an initial visit with a dietician or exercise physiologist for an assessment and individual goal setting, followed by attendance at a group education program "CHANGE for HIPS" which comprised 4 1.5 hours sessions over the first 3 months and a further two follow-up sessions at 6 and 9 months focused on education, physical activity (20-30 minutes of 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[11] 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); having left parental home for <2 years; BMI between 18-30 kg/m2 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 age Intervention (SD): 19.9 (0.2); Mean age Control (SD): 19.5 (0.2) Gender [Female n(%)]: Intervention n=47 (81.0%); Control n=47 (82.4%) Loss to follow-up: Overall 19; Intervention 10; Control 9
Intervention	Intervention: small group interactive educational/behavioural seminars of 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[12] US *Companion paper:* McTiernan[40]
Objective	The purpose of this study was 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 to a trial specifically focused on obesity prevention]; recruited between 2001 and 2004 through gastroenterology practices, media placements, flyers, a study website and referrals Inclusion criteria: 40 to 75 years old; colonoscopy within the previous 3 years; engaged in < 90 minutes/ week of moderate-to-vigorous intensity exercise during the previous 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 a maximal exercise tolerance test; normal complete blood count and blood chemistries; and no contraindications for colon biopsy.
Participants	Sample: 202 Intervention n=100 ;Control n=102 Age: Mean age Intervention (SD): women 54.4 (7.1) range 43-73; men 56.2 (6.7) range 40-69; Mean age Control (SD): women 53.7 (5.6) range 42-65; men 56.6 (7.6) range 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 6; Control 2

Intervention	Intervention: goal of 60 minutes/day, 6 days/week of moderate-to vigorous intensity aerobic exercise performed at facilities and at home, with gradual increase over first 12 weeks; participants required to exercise 3 times/week at one of four facilities under supervision of exercise specialists, provided with Polar (Polar Electro Inc., Lake Success, NY) heart rate monitors and advised to exercise at 60%-85% of their maximal heart rate on their baseline VO2max test; participants also asked to exercise at home or at exercise facilities 3 days/week with same instructions for exercise duration and intensity Control: asked not to change their exercise or diet habits during the trial Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Kanaya 2012[13] USA
Objective	A community-based, translational lifestyle program to reduce diabetes risk in lower–socioeconomic status (SES) 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 between 106 and 160 milligrams per deciliter who had a moderate to high diabetes risk appraisal score; aged 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 group n = 119; control group n = 119 Age: Mean age Intervention (SD): 58 (16); Mean age Control (SD): 55 (17) Gender [Female n(%)]: 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: a 6-month active intervention phase and a 6-month maintenance phase; trained health department counselors provided education and skills training to modify diet and physical activity through primarily telephone-based 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[14] 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: Eligible subjects were 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 group n = 360; Control group n = 355 Age: Mean age Intervention (SD): 54.4 (10.1); Mean age Control (SD): 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: the core of the actual intervention consisted of four visits by participants to local public health nurses during the first year of the follow-up (1, 3, 6 and 9 months after randomization), and of three visits during the second year (15, 18 and 21 months after the randomization); participants systematically instructed to change their health behaviour primarily on the basis of their individual situation; a 2-h group session concentrates mainly on advice targeting reduction of salt intake and overweight was organized for the intervention group in every health care centre at 6 and 18 months Control: instructed to visit their 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[15] USA *Companion paper:* Khare[41]
Objective	Aimed at reducing 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 who were enrolled in the Illinois Breast and Cervical Cancer Program (IBCCP)
Participants	Sample n= 833 Intervention group n = 418; Control group n = 415 Age: Mean age Overall (SD): 52.5 (7.0); Mean age Intervention (SD): 52.4 (7.0); Mean age Control (SD): 52.5 (6.9) Gender [Female n(%)]: 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, a 12-week lifestyle intervention, and 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[16] 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 their general practitioner to a previous observational study of postmenopausal women between 1999 and 2002 from 10 primary care practices in Wellington; the remainder of the participants were recruited from 13 primary care practices in 2004-5, including two Maori health clinics; general practitioners at participating practices were asked to identify women in the age group from their practice register, excluding patients deemed inappropriate for participation in a physical activity trial and then sent letters to those identified as suitable, inviting them to participate in a lifestyle study. Inclusion criteria: women between 40-74; physically inactive, as determined by a one question screening tool

	Exclusion criteria: women with a medical condition that might be adversely affected by increasing their physical activity, as determined by the physical activity readiness questionnaire (PAR-Q) and subsequent assessment by their own general practitioner
Participants	Sample: 1089 Intervention n=544 ; Control n=545 Age: Mean age Intervention (SD): 59.1 (6.8) ; Mean age Control: 58.7 (6.9) Gender [Female n(%)]: 100% SES [lower socioeconomic status]: Intervention: 87 (16%), Control: 75 (14%) Loss to follow-up: 7% at 12 months and 11% at 24 months
Intervention	Intervention: primary care nurse briefly counsels (7-13 minutes) patients using motivational interviewing techniques to increase physical activity among those who are physically inactive (recommended goal was moderate intensity physical activity such as brisk walking, with a goal of achieving 30 minutes five days a week; follow-up was extended to include telephone calls over a nine month period (average of five calls, each lasting 15 minutes) with an added 30 minute visit with the primary care nurse at six months Control: usual care from primary care practice Duration of intervention: 9 months Length of follow-up: 3 months and 15 months

Study/Location	Levine 2007[17] US
Objective	To evaluate the efficacy of two interventions relative to a control group in preventing weight gain among normal or overweight women and to identify demographic, behavioral, 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 and 44 years of age; good health according to a self-report questionnaire; BMI between 21 and 30 Exclusion criteria: pregnant; had been pregnant or participated in a weight loss program in the past year; were receiving treatment for a psychiatric disorder; had taken a medication affecting body weight during the past 3 months; or were planning to relocate within the next 36 months. In addition, women who were unable to engage in moderate physical activity or make modest changes in dietary intake were excluded
Participants	Sample: 284 Intervention 1 (clinic) n=97; Intervention 2 (correspondence) n=94; Control n=93

	Age: Mean age Intervention 1 (SD): 36.4 (5.7); Mean age Intervention 2 (SD): 35.0 (6.1); Mean age Control: 35.4 (5.3) Gender [Female n(%)]: 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-month period. Sessions led by trained nutritionists and behavioral interventionists and held biweekly for first 2 months and bimonthly for next 22 months Intervention 2 (correspondence): 15 lessons by mail over 24-month period. The lessons were identical in content to the Clinic group and contained a brief homework assignment to be completed by the participant and returned by mail; participants asked to weigh themselves and report their weight on their returned assignment 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 and 12 months

Study/Location	Mensink 2003[18] 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: subjects with high risk of glucose intolerance, i.e., those of age > 40 years and a family history of diabetes or a BMI ≥25 kg/m2 selected from an existing cohort and invited to undergo a first oral glucose-tolerance test (OGTT) Exclusion criteria: overt or previously diagnosed diabetes (not gestational diabetes); medication use known to interfere with glucose tolerance; participation in regular vigorous exercise or an intensive weight reduction program during the previous year; presence of any (chronic) disease that hampered participation in a lifestyle intervention program; improbability of 5-year survival
Participants	Sample: 114 Intervention: n= 55; Control n = 59 Age: Mean age Intervention (SD): 55.6 (0.9); Mean age Control (SD): 57.8 (1.0) Gender [Female n(%)]: 50 (44%) Loss to follow-up: Intervention n= 14; Control n= 11

Intervention	Intervention: consisted of a dietary and physical activity component, with visits scheduled at regular intervals throughout the study Control: received oral and written information about the beneficial effects of a healthy diet, weight loss, and increased physical activity; however, no individual advice or programs were provided and visits were only for the annual measurements Duration of intervention: 2 years Length of follow-up: immediate post

Study/Location	Roderick 1997[19] 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: eight practices from the Medical Research Centre's (MRC's) general practice research framework (GPRF) were selected in pairs with one pair from each of four geographical areas - Yorkshire, Midlands, south-east England and South Wales Inclusion: ages 35-59 attending surgery who did not have contra-indications, i.e known causes of secondary hyperlipidaemia, sever psychiatric illness, pregnancy, terminal illness or those already attending a coronary heart disease health promotion clinic
Participants	Sample n= 956 Intervention group n = 473; Control group n = 483 Age: Mean age Intervention (SD): 47.2 years; Mean age Control (SD): 47.4 years 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, based on negotiated changed, which aimed for food substitution (i.e nurse and patient negotiated and agreed up to 5 changes) after review of the type, quantity and frequency of key foods consumed; specially designed dietary sheets were given out according to whether weight loss was required; all foods were classified as 'to eat plentifully', 'in moderation' or 'on special occasions only'; patients who were overweight (BMI over 25 kg/m2) were given special advice, including a self-monitoring chart and a choice of a calorie-restricted diet Control: standard health education from the leaflets Guides to Healthy Eating, Giving up smoking, Look After Your Heart, Heart Disease, and Exercise, Why Bother? Duration of intervention: 12 months Length of follow-up: immediate post

Study/Location	Sacerdote 2006[20] 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 were selected through their professional organizations as those most motivated in the trial. All patients aged 18–65 years attending the wards of 33 selected GPs (in the cities of Torino and Asti, Italy) Inclusion: patients aged 18–65 years attending the wards of 33 selected GPs (in the cities of Torino and Asti, Italy) were eligible if they were not obese [body mass index, (BMI) , 30] or affected by chronic or severe diseases. Only patients who visited their GP for reasons unrelated to gastrointestinal problems, and without dietary restrictions, were enrolled
Participants	Sample n= 3179 Intervention group n = 1592; Control group n = 1587 Age: Mean age Intervention (SD): 44.7 (12.6); Mean age Control (SD): 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: at first visit to the intervention group the GP administered a 15-min personalized nutritional intervention, based on a brochure about diet and health that summarized the 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[21] US *Companion papers:* Simkin-Silverman,[42] Salamone,[43] Klem,[44] Kuller,[45] Park[46]
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 ages 44-50 years; premenopausal by self-report; not taking hormone replacement therapy; BMI 20-34 kg/m2, fasting total cholesterol 140-260 mg/dl, fasting LDL-c 80-160 mg/dl, fasting glucose levels < 140 mg/dl and diastolic blood pressure < 95 mm Hg Exclusion criteria: Women taking lipid-lowering medication, antihypertensive

	medication, insulin, thyroid medication, or psychotropic medications
Participants	Sample: 535 Intervention n= 260; Control n= 275 Age: Mean age Overall (SD): ages 44 to 50 Gender [Female n(%)]: 100% Loss to follow-up: Overall ; Intervention n=14 ; Control n= 12
Intervention	Intervention: 5-year behavioral dietary and physical activity program conducted in 2 phases during the 5 years trial Phase 1 (weeks 1-20): 15 group meetings, presentation, handouts, homework assignments, low-fat/reduced-calorie meal plan, suggested increase in physical activity expenditure (activity prescription) for 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 control group Duration of intervention: 54 months Length of follow-up: immediate post

Study/Location	Sone 2002[22] Japan
Objective	To determine whether long-term lifestyle intervention can improve glycemic control and prevent complications in patients with type 2 diabetes.
Methods	Design: RCT Selection: patients previously diagnosed with type 2 diabetes with HbA1c levels >6.5% from all over Japan were recruited from 59 institutes specializing in diabetes care
Participants	Sample: 2205 Intervention n=1105 ;Control n=1100 Age: Mean age Intervention (SD): 59.4 (7.5); Mean age Control (SD): 59.4 (7.4) Gender [Female n(%)]: Intervention n=495; Control n=505 SES [college degree or higher]: Intervention: 240; Control: 238 Unemployed: Intervention 681; Control 353 Co-morbidities: Diabetes Loss to follow-up: Overall loss 232; Intervention 115; Control 117
Intervention	Intervention: lifestyle modification program with intensive lifestyle management at each outpatient visit and telephone counseling sessions by trained nurse educators at

	least once every 2 weeks Control: regular conventional care Duration of intervention: not specified Length of follow-up: 36 months post initiation

Study/Location	Steptoe 1999[23] UK
Objective	To measure the effect of behaviourally oriented counseling in general practice on healthy behaviour and biological risk factors in patients at increased 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 cardiovascular risk factors: regular cigarette smoking (>1 cigarette/day), high serum cholesterol concentration (6.59.0 mmol/l), combined high BMI (2535) and low physical activity (<12 episodes of vigorous or moderate exercise for at least 20 minutes in the 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 group n =316; Control group n = 567 Age: Mean age Overall (SD): 46.7 (0.4 SE) Gender [Female n(%)]: n=477 (54.0%) Loss to follow-up: Overall n = 365; Intervention n = 148; Control n = 217
Intervention	Intervention: invited for three counseling sessions if they had two risk factors and for two counseling sessions if only one risk factor; counseling sessions scheduled to last ≤20 minutes, and between sessions the nurse contacted the 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[24] The Netherlands *Companion paper:* Monninkhof[47]
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 in Utrecht and surroundings in the Netherlands Inclusion criteria: post-menopausal women; 50-69 years old; sedentary (<2 hours/week in moderate sport recreational activities and not adherent to the International Physical Activity Recommendation); non-smokers for ≥12 months; not abusing alcohol or drugs; not planning a strict diet; not experiencing diabetes mellitus or other endocrine related diseases or any disease/disorder (locomotor, optical, neurological, mental) that might impede participation in exercise program; BMI 22-40 kg/m2; fluent in Dutch language; had last menses ≥12 months ago; not used hormone replacement or oral contraceptives in the past 6 months; not diagnosed with breast cancer; not diagnosed with other cancers in the past 5 years; not currently using cortico steroids or beta-blockers
Participants	Sample: 189 Intervention n=96 ; Control n=93 Age: Mean age Intervention (SD): 58.9 (4.6); Mean age Control: 58.4 (4.2) Gender [Female n(%)]: 100% Loss to follow-up: Overall n=6; Intervention n=1; Control n=5
Intervention	Intervention: one-year moderate to vigorous exercise program, which included 2 supervised group sessions of 1 hour/week and an additional 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[25] The Netherlands *Companion paper:* Vermunt[48]
Objective	To determine the effectiveness of a 2.5-year lifestyle intervention for Type 2 diabetes prevention in Dutch general practice compared with usual care
Methods	Design: RCT Selection: recruited by 48 general practitioners from 14 general practices in Eindhoven and surroundings Inclusion criteria: Age between ≥40 and ≤70 and a score of ≥13 point on a Dutch translation of the Finnish FINDRISC
Participants	Sample: n= 1065 Intervention n = 479 and Control n = 446

	Age: Range ≥ 40 years and ≤70 years Loss to follow-up: Intervention n = 70; Control n = 59
Intervention	Intervention: 11 consultations of 20 min were scheduled over 2.5 years alternately with the nurse practitioner and the general practitioner; five group meetings were organized by to provide more detailed information on diet and exercise; also included a 1-h consultation with a dietician, in which a 3-day food record was discussed Control: oral and written information on T2M and healthy lifestyle provided Duration of intervention: 2.5 years Length of follow-up: immediate post

Study/Location	Werkman 2010[26] 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 in the WAAG-Study from September 2003 to mid March 2004 Inclusion criteria: recent retirees (date of retirement <= 6 months before or after baseline); 55-65 years; not undergoing medical treatments that might affect body composition.
Participants	Sample: 415 Intervention n=174 ;Control n=178 Characteristics: Age: Mean age Intervention (SD): 59.5 (2.5); Mean age Control 59.4 (2.3) Gender [Female n(%)]: 0% SES [% low education level]: Intervention: 25%; Control: 23% Loss to follow-up: Intervention n=27; Control n=24
Intervention	Intervention: five program modules during the one year intervention period; newsletters every 2-3 months that contained study information, information about diet and physical activity and encouragements to use the modules Control: provided with 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 and had access to the general information about the study design only.

	Duration of intervention: 12 months Length of follow-up: immediate post and 12 months

Study/Location	Wister 2007[27] Canada
Objective	The objective of this study was to test the efficacy of a low intensity lifestyle intervention aimed at reducing the risk of cardiovascular disease 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: The 3 eligibility criteria were age 45–64 years, residence in the Fraser Health region and cardiovascular risk profile according to the literature for primary and secondary prevention
Participants	Sample: 611 Intervention 1 (Primary Prevention group) n= 157; Control 1 (Primary Prevention group) n= 158; Intervention 2 (Secondary Prevention group) n= 153; Control 2 (Secondary Prevention group) n= 143 Age: Mean age Intervention 1 (SD): 55.8 (5.5); Mean age Control 1 (SD): 55.1 (5.2); Mean age Intervention 2 (SD): 56.6 (5.1) ; Mean age Control 2 (SD): 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: The intervention consisted of a 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

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Table 3 - Search Strategy Medline-OVID

Most Recent Search: June 27 2013
1. (suicide adj prevent*).tw.
2. Weight Reduction Programs/
3. exp obesity/pc
4. Overweight/pc
5. weight maintenance.tw.
6. weight management.tw.
7. Diet, Reducing/
8. Diet, Fat-Restricted/
9. Caloric Restriction/
10. Diet Therapy/
11. (diet* adj counsel*).ti,ab.
12. (diet* adj education*).ti,ab.
13. (nutrition* adj (counsel* or education* or intervention)).ti,ab.
14. (diet$ adj (modi*$ or therapy or intervention* or strateg* or healthy)).ti,ab.
15. ((diet or dieting or slim$) adj (club$ or organi?ation$)).ti,ab.
16. ((healthy living or healthy lifestyle) adj (program* or intervention? or group or club or strategy)).tw.
17. (weightwatcher* or weight watcher* or commerical weightloss or commerical weight loss or Jenny Craig).tw.
18. exp *Exercise/
19. Exercise Therapy/
20. Motor Activity/
21. Physical Fitness/
22. physical activity.ti,ab.
23. (exercise adj3 (program* or intervention* or strategy or club?)).ti,ab.
24. Fitness Centers/
25. health promotion/ or preventive health services/
26. Primary Prevention/
27. 25 or 26
28. exp *obesity/
29. *overweight/
30. *Weight Gain/
31. 28 or 29 or 30
32. 27 and 31
33. 2 or 3 or 4 or 5 or 6
34. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
35. 27 and 34
36. exp obesity/
37. overweight/
38. weight gain/
39. Weight Loss/
40. (weight or bmi or body mass index or waist circumference or obese or obesity).ti.
41. 36 or 37 or 38 or 39 or 40
42. 35 and 41
43. 32 or 33 or 42

44. animals/ not humans/
45. 43 not 44
46. limit 45 to "all child (0 to 18 years)"
47. limit 45 to "all adult (19 plus years)"
48. 46 not 47
49. 45 not 48
50. limit 49 to (english or french)
51. limit 50 to (case reports or comment or editorial or in vitro or letter or news or newspaper article or webcasts)
52. 50 not 51
53. limit 52 to ed=20120426-20130527
54. meta-analysis/
55. exp meta-analysis as topic/
56. (meta analy* or metaanaly* or met analy* or metanaly*).tw.
57. review literature as topic/
58. (collaborative research or collaborative review* or collaborative overview*).tw.
59. (integrative research or integrative review* or intergrative overview*).tw.
60. (quantitative adj3 (research or review* or overview*)).tw.
61. (research integration or research overview*).tw.
62. (systematic* adj3 (review* or overview*)).tw.
63. (methodologic* adj3 (review* or overview*)).tw.
64. exp technology assessment biomedical/
65. (hta or thas or technology assessment*).tw.
66. ((hand adj2 search*) or (manual* adj search*)).tw.
67. ((electronic adj database*) or (bibliographic* adj database*)).tw.
68. ((data adj2 abstract*) or (data adj2 extract*)).tw.
69. (analys* adj3 (pool or pooled or pooling)).tw.
70. mantel haenszel.tw.
71. (cohrane or pubmed or pub med or medline or embase or psycinfo or psyclit or psychinfo or psychlit or cinahl or science citation index).ab.
72. or/54-71
73. limit 53 to "review"
74. 53 and 72
75. 73 not 74
76. 53 not 75
77. (weight or BMI or waist circumference or waist to hip ratio).mp.
78. Lifestyle.ti.
79. *Life Style/
80. 78 or 79
81. 77 and 80
82. 27 and 81
83. (prevent or prevention or primary care).tw.
84. 81 and 83
85. 82 or 84
86. limit 85 to (english or french)

87. limit 86 to (case reports or comment or editorial or in vitro or letter or news or newspaper article or webcasts)
88. 86 not 87
89. animals/ not humans/
90. 88 not 89
91. limit 90 to "all child (0 to 18 years)"
92. limit 90 to "all adult (19 plus years)"
93. 91 not 92
94. 90 not 93
95. limit 94 to "review"
96. 72 and 94
97. 95 not 96
98. 94 not 97
99. 98 not 76
100. limit 99 to yr="1980 -Current"
101. 76 or 100

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	title page (pg1)
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract (pg 2)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table 3, Supplemental file
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Included in every results subsection, 11-14
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7-8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8, also in Flow diagram, supplemental file
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Supplemental file
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supplemental file, Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 1, tables 1-4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 1, tables 1-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	In each section under results (11-14)
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Tables 1-4
DISCUSSION			

PRISMA 2009 Checklist

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14-16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14-16
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

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