

This is the author version of an article published in Obesity Reviews 2009;10(6)627-38 on behalf of IASO by Blackwell Publishing. The definitive version is available at www3.interscience.wiley.com.

Title:

Systematic Review of Long-term Lifestyle Interventions to Prevent Weight Gain and Morbidity in Adults.

Authors:

Tamara Brown^{1,5}, Alison Avenell², Laurel D. Edmunds³, Helen Moore^{4,5}, Vicki Whittaker⁵, Leah Avery⁵ and Carolyn Summerbell^{4,5} for the PROGRESS* team.

Institution:

¹Current address: School of Population, Community and Behavioural Sciences, University of Liverpool, Liverpool, UK.

²Health Services Research Unit, University of Aberdeen, Aberdeen, UK.

³Dept of Primary Health Care, University of Oxford, Oxford, UK.

⁴Current address: School of Medicine and Health, Durham University, Stockton on Tees, UK.

⁵School of Health and Social Care, University of Teesside, Middlesbrough, UK.

*This work was conducted as part of the PROGRESS (PREvent Obesity GRowing Economic Synthesis Study) which was funded by the National Preventative Research Initiative and the Universities of Aberdeen and Melbourne.

The PROGRESS group consists of the following applicants: Alison Avenell¹, Lorna Aucott², Flora Douglas², Alison Goode³, Kostas Mavromaras³, Mandy Ryan¹, Matt Sutton⁴, Edwin van Teijlingen² and Luke Vale^{1,5}.

¹ University of Aberdeen Health Services Research Unit (HSRU)

² University of Aberdeen Section for Population Health

³ University of Melbourne

⁴ University of Manchester

⁵ University of Aberdeen Health Economics Research Unit (HERU)

HERU and HSRU are core funded by the Chief Scientist's Office of the Scottish Government Health Directorates. AA was funded by a Career Scientist award from the Scottish Government Health Directorates.

Key Words:

Systematic Review, Prevention, Obesity, Adults

Running title:

Preventing Weight Gain in Adults.

Correspondence:

Tamara Brown, Population, Community and Behavioural Sciences, University of Liverpool, Liverpool, L69 3GB, United Kingdom. E-mail: t.brown@liverpool.ac.uk.

Conflict of interest:

No conflict of interest was declared.

1. Abstract

Objectives

To determine the effectiveness of long-term lifestyle interventions for the prevention of weight gain and morbidity in adults.

Methods

Prevention of weight gain is important in adults who are normal weight, overweight and obese. A systematic review of controlled trials of lifestyle interventions in adults with a body mass index of less than $35\text{kg}/\text{m}^2$ with at least two years follow-up was carried out.

Results

Eleven of 39 comparisons produced significant improvement in weight between groups at two years or longer with mean difference weight change ranging from -0.5 kg to 11.5 kg . Effective interventions included a 600kcal/day deficit/low-fat diet (with and without meal-replacements), low-calorie diet, Weight-Watchers diet, low-fat non-reducing diet, diet with behaviour therapy, diet with exercise, diet with exercise and behaviour therapy. Adding meal replacements to a low-fat diet (with and without exercise and behaviour therapy) produced significant improvement in weight. Head-to-head interventions failed to show significant effect on weight with the exception of a Mediterranean diet with behaviour therapy compared to low-fat diet. Diet with exercise and/or behaviour therapy demonstrated significant reduction in hypertension and improvement in risk of metabolic syndrome and diabetes compared to no treatment control.

Conclusions

Lifestyle interventions demonstrated significant improvement in weight, reduction in hypertension and reduction in risk of type 2 diabetes and the metabolic syndrome.

Word count: 213.

2. Introduction

Obesity and related disease present a public health crisis. Energy-dense diets and sedentary lifestyles are associated with obesity. Changing behaviours to reduce disease burden is recognised on a European and global scale through the EU Platform for Action on Diet, Physical Activity and Health¹ and the WHO global strategy on diet, physical activity and health². The UK government obesity strategy and £75m campaign³ is in response to the NICE obesity guidance⁴ and future predictions in the Foresight report⁵. Through the Change4Life campaign³ the UK Department of Health is providing £30m to help nine towns encourage healthy lifestyles⁶.

These initiatives are underpinned by evidence from interventions which focus on changing behaviours. An earlier review⁷ of obesity treatments recommended that a systematic review of interventions to prevent obesity should be undertaken.

This systematic review is the first phase of the National Prevention Research Initiative funded economic evaluation of obesity prevention for UK adults. The objective is to determine the effectiveness of interventions that focus on improving diet and activity behaviours in adults who are normal weight, overweight and obese, to prevent weight gain and morbidity in the long-term.

3. Methods

Included were randomised controlled trials (RCTs) and controlled before and after studies (CBAs) of a lifestyle interventions (diet, exercise, behaviour, environmental) in adults (18-65y) with body mass index (BMI) $<35\text{kg}/\text{m}^2$ reporting weight at least two years post randomisation. Data were also extracted for risk factors, morbidity and mortality. The amount and distribution of fat determines the risk of obesity-related diseases and in general the more overweight the greater the risk. Adults classified as pre-obese (BMI 25.0-29.9 kg/m^2) or obese class 1 (BMI 30.0-34.9 kg/m^2) are an important target group for the prevention of weight gain because they have an increased risk of elevated risk factors for disease and obesity-related morbidities; such as dyslipidaemia, hypertension, impaired glucose tolerance, metabolic and hormonal changes, which in turn contribute to cardiovascular disease, cancers, metabolic and endocrine diseases such as type 2 diabetes, and osteoarthritis.

Diets categorization included: 600kcal/day deficit/low-fat diet; low-calorie diet (LCD) (1000-1600 kcal/d); very low-calorie diet (VLCD) (<1000 kcal/d). Interventions were categorised as interventions with definite intention to lose weight (clearly targeted calorie reduction) and interventions with no definite intention to lose weight (no target for weight loss). No type of diet was excluded. If an intervention included two or more diets, the most stringent calorie restriction was used to classify the diet.

For exercise or behaviour therapy interventions study investigators had to give a detailed description of the components of the intervention and details of the theory underpinning the behavioural intervention.

Interventions targeting smoking cessation or salt reduction in addition to weight loss were not included. Studies were excluded in participants with eating disorders, pregnant women and severely mentally or physically

handicapped adults. Studies in non-white populations were included if the ethnic group and setting were relevant to the UK ethnic population.

The literature search involved four phases (see Appendix 1 for search strategies). Phase one: primary studies identified from two systematic reviews^{4,7}. Phase two: CAB Abstracts, CDSR, CINAHL, DARE, EMBASE, MEDLINE and PsycINFO were searched and systematic reviews were screened for primary studies. Phase three: CAB Abstracts, CCTR, CINAHL, EMBASE, MEDLINE and PsycINFO were searched for primary studies published between January 2005 - August 2006. Phase four: MEDLINE was searched for primary studies published between September 2006 - August 2007. A search of one database only was carried out in the final phase in order to identify any studies published since the main searches were performed in August 2006. No language restriction was applied. Only full reports from 1990 were considered. The International Journal of Obesity (January 2006 - August 2007) and Obesity were hand-searched online from January 2006 - September 2007 in order to identify studies which were not yet indexed on electronic databases.

Where results from studies could be quantitatively combined meta-analyses were undertaken. Data from RCTs and CBAs were analysed separately. Data synthesis (including handling of missing data) and quality assessment were based on those previously undertaken⁷. For continuous data a weighted mean difference (WMD) was calculated (weighted by the inverse of the variance of the effect estimate) and Mantel-Haenszel methods were applied for dichotomous data; both using a fixed effects approach and RevMan 4.2.5 software⁸. In the case of missing standard deviations (SDs) for changes in weight and risk factors, assumptions were made (irrespective of whether the changes were negative or positive). A linear regression was made of the SD of the mean change in weight on the absolute mean change for weight, for the studies which provided these data, and used to impute values for missing SDs:

- SD of weight change in kg = $5.915 + (0.283 \times \text{mean change in weight})$.

Similar linear regressions were attempted for risk factors. However, clear relationships were not found, so the means of reported SDs were used to impute values for missing SDs (see Appendix 14):

- SD for change in SBP = 12.7 mmHg
- SD for change in DBP = 8.3 mmHg
- SD for change in cholesterol = 1.08 mmol/l
- SD for change in LDL cholesterol = 0.74 mmol/l
- SD for change in HDL cholesterol = 0.29 mmol/l
- SD for change in triglycerides = 0.96 mmol/l.

In the case of fasting plasma glucose and HbA1c, two levels of SDs were used, to allow for the greater variability of such measures evident from the studies.

- If the initial fasting plasma glucose was <7 mmol/l, the SD for change in fasting plasma glucose was 1.35 mmol/l.
- If the initial fasting plasma glucose was ≥ 7 mmol/l, the SD for change in fasting plasma glucose was 3.77 mmol/l.
- If the initial HbA1c was $< 7\%$, the SD for change in HbA1c was 0.71%.

- If the initial HbA1c was $\geq 7\%$, the SD for change in HbA1c was 2.58%.

Results were described separately for individual studies where the change in outcome data between two time-points could not be calculated or the number of participants in each group was not reported.

4. Results

4.1 Literature search

Thirty-nine RCTs^{9-62;64} and one CBA⁶³ were included (Figure 1, Table 1). Twenty-four studies were US-based, four were based in Finland, three in The Netherlands, two in the UK^{27;28}, two in Canada, two in India, and one each in Germany, Italy and Australia. Eight were community studies and 32 were in secondary care. Twenty studies were 24-months in duration, 11 studies were between 30 and 36-months duration and nine studies ranged in duration from 38 to 97 months. Twenty studies recruited 200-2000 participants and five studies recruited over 2000 participants. In studies with less than 200 participants; sample size ranged from 16 to 180. The largest study was the Women's Health Initiative Dietary Modification Trial^{42;45;46;61;62} (WHIDMT) with nearly 49,000 women.

Twenty-five studies recruited men and women, 14 studies recruited women and one study recruited men. At least 29 studies recruited participants with risk factors for disease, history of disease or disease, such as hypertension, type 2 diabetes and breast cancer. Mean baseline BMI was $<30\text{kg/m}^2$ in 22 studies, unclear in two studies and $\geq 30\text{kg/m}^2$ in 16 studies. The majority of studies had a mean age between 40-60 years.

Twenty-four studies specifically intended participants to lose weight and 16 did not. Thirty-two studies included two comparisons groups only (Table 2). Forty studies provided 39 different comparisons. There were no long-term studies identified that compared an exercise intervention to control.

Reports of the 39 RCTs^{9-62;64} varied in quality with 12 clearly reporting allocation concealment, 10 applying an intention-to-treat analysis and two reporting effective blinding of outcome assessors (Table 3).

4.2 Study results (Table 4)

Studies with an intention to lose weight

Dietary interventions versus control

600 kcal/day deficit/low-fat diet versus control

Five studies assessed a 600 kcal/day deficit/low-fat diet^{21;22;24;30;33-34}. Three studies recruited people with hypertension or 'high normal' blood pressure, one study recruited patients with oesophageal cancer and one recruited participants with impaired glucose tolerance (IGT).

Weight

600 kcal/d deficit or low-fat diet was associated with non-significant weight changes at 24 and 30 months. However at 36 months, the Hypertension Prevention Trial²² (HPT) was associated with a significant WMD weight change of -3.49 kg (95% confidence interval (CI) -4.63 to -2.35 kg).

Two studies were not included in the meta-analyses. Kristal et al²⁴ reported a non-significant intervention effect on weight compared with control at 36 months (-1.4 kg). Ramachandran et al³⁰ reported a significant increase in weight from baseline at 24 and 30 months in the control group (approximately 0.8 and 0.95 kg respectively) and at 24 months only in the diet group (approximately 0.4 kg).

Risk factors

In the HPT²², blood pressure improved with diet at 36 months but did not reach statistical significance.

Clinical outcomes

Participants receiving diet in the Hypertension Optimal Treatment²¹ (HOT) study required significantly fewer antihypertensive medications. Nine percent of intervention and control groups required drug treatment for hypertension during the three years of the HPT²². Weight loss increased the likelihood a patient would be controlled on antihypertensive monotherapy in the Trial of Antihypertensive Interventions and Management (TAIM) study³³⁻³⁵.

In Ramachandran et al³⁰ the cumulative incidence of diabetes at three years was 55% in the control group and 39.3% in the diet group. Relative risk reduction was 28.5% compared with control.

Low-calorie diet (LCD) versus control

Weight

One study³⁸ was associated with a significant WMD weight change of -7.00 kg (95% CI -10.99 to -3.01 kg) at 24 months and -6.10 kg (95% CI -10.71 to -1.49 kg) at 36 months in 54 women treated for breast cancer. Wide CIs reflect the small sample size and there was nearly 40% dropout at 36 months.

Weight Watchers versus self-help

Weight

One study²⁰ of Weight Watchers was associated with a significant WMD weight change of -2.70 kg (95% CI -3.95 to -1.45 kg) at 24 months (423 adults, majority women, BMI 34 kg/m²).

Risk factors

Authors reported no significant difference between groups for risk factors or quality of life at 24 months.

600 kcal/day deficit/low-fat diet plus meal replacements versus control

Weight

One study⁶³ of a 600 kcal/day deficit/low-fat diet using meal replacements (Slimfast shakes twice daily for three months then once daily for 57 months) compared with a no-contact matched control group was associated with a WMD weight change of -11.49 kg (95% CI -12.98 to -10.00 kg) at two years.

Very low calorie diet (VLCD) using meal replacements (Cambridge diet) versus low-fat control

Weight

There was a non-significant weight change in favour of VLCD at 24 months amongst 16 obese Finnish adults with newly diagnosed type 2 diabetes³¹. Risk factor data were not assessed as there were significant baseline differences between groups.

Behavioural interventions versus control

Weight

Behaviour therapy delivered either by telephone or mail by trained nutritionists versus control showed no significant effect on weight at 24 months in US adults from a managed care organisation⁵⁴. Cost-effectiveness of telephone counselling was \$132/kg lost, with mail and usual care control achieving similar cost-efficiency of \$72/kg lost.

Diet and exercise versus control

Three RCTs^{18;19;26;28;59} assessed diet and exercise and all participants were at high risk of or had IGT. The types of diet and exercise interventions varied between studies (Table 1).

Weight

Diet and exercise was associated with significant WMD weight change at 24 months (-2.56 kg, 95% CI -3.34 to -1.77 kg).

Risk factors

There was an associated improvement in triglycerides in two studies^{26;28} (WMD -0.54 mmol/L, 95% CI -0.85 to -0.24 mmol/L) and fasting plasma glucose (FPG) in three studies^{18;19;26;28;59} (WMD -0.30 mmol/L, 95% CI -0.42 to -0.18 mmol/L) but not cholesterol, blood pressure or HbA1c.

Clinical outcomes

At four years the cumulative incidence of diabetes in the Finnish Diabetes Prevention Study (FDPS) was 11% (95% CI 6 to 15%) in the intervention group and 23% (95% CI 17 to 29%) in the control group (risk of diabetes reduced by 58%). At six years there was a 43% reduction in relative risk (RR)^{18;19}. Normal glucose tolerance was present in 50% of intervention participants and 29% of control participants after two years in the study by Mensink et al²⁶ (P<0.05). In the FDPS, at mean follow-up 3.9 years; 62.6% intervention participants and 71.2% control participants had metabolic syndrome (sex and age-adjusted odds ratio (OR) 0.62 (95% CI 0.40 to 0.95)⁵⁹.

Diet, exercise and behaviour therapy versus control

Five RCTs^{16;17;23;25;27;36;37} assessed diet, exercise and behaviour therapy. The types of diet and exercise interventions varied between studies (Table 1).

Weight

Diet and exercise and behaviour therapy was associated with significant WMD weight changes at 24 months (-2.47 kg, 95% CI -3.18 to -1.77 kg, two studies), 30 months (-2.04 kg, 95% CI -2.70 to -1.39 kg, two studies) and 54 months (-2.50 kg, 95% CI -3.59 to -1.41 kg, one study).

We were unable to meta-analyse the Diabetes Prevention Program^{16;17} (DPP) however the authors reported average weight loss at 2.8 years was 5.6 kg in the intensive low-fat diet, exercise and behavioural modification programme and 0.1 kg in the control group. Kuller et al²⁵ did not present participant numbers for the 30 and 42-month follow-up however the authors reported significant improvement in weight.

Risk factors

The benefit of significant weight loss was not consistently reflected in improved risk factors. Although Kuller et al²⁵ demonstrated significant weight loss and improvements in LDL-cholesterol there was no significant improvement in HDL-cholesterol, triglycerides, FPG or blood pressure at 54 months. The Trials of Hypertension Prevention phase II^{36;37} (TOHP II) study demonstrated significant weight loss and showed significant improvement in systolic but not diastolic blood pressure at 30 months.

Clinical outcomes

The DPP^{16;17} significantly reduced the risk of developing diabetes and the metabolic syndrome for up to three years in over 2000 obese adults with IGT at baseline.

In the DPP^{16;17} the crude incidence of diabetes was 11/100 in the control group and 4.8/100 in the lifestyle intervention. The incidence of diabetes was 58% lower (95% CI 48 to 66%) in the lifestyle intervention group than the control. The estimated cumulative incidence of diabetes at three years was 28.9% in the control and 14.4% in the lifestyle-intervention group. Incidence of metabolic syndrome was reduced 41% in the lifestyle intervention compared with control (P<0.001).

In TOHP II^{36;37}, the RR of developing hypertension for the weight loss group was 0.87 (p=0.06) at 48 months.

Adjuncts to diet

The addition of extra fruit and vegetables and exercise to a low-fat low-cholesterol diet was associated with a weight change of -6.10 kg compared with -2.1 kg in the low-fat low-cholesterol group at 36 months in mostly men with or at risk of coronary artery disease³². Authors reported significant improvement in cholesterol, triglycerides, fasting blood glucose and blood pressure.

The addition of exercise and behaviour therapy to diet was associated with a non-significant difference in weight loss between groups at 24 months in one study of obese adults with type 2 diabetes¹⁰. A significant improvement in total cholesterol was found at 24-months (-0.3 mmol/L (95% CI -0.6 to -0.1 mmol/L) but not for blood pressure.

The addition of meal replacements (Slimfast) to a low-fat diet for the initial three months was associated with a non-significant weight change at 27 months but a significant weight change at 51 months (-5.40 kg, 95% CI -8.97 to -1.83 kg)^{14;15;43}. There was significant improvement in HDL-cholesterol at 27 months (0.17 mmol/L, 95% CI 0.03 to 0.31 mmol/L) and SBP at 51 months (-12.0 mmHg, 95% CI -17.75 to -6.25 mmHg) but not other risk factors.

Women who received meal replacements (Slimfast) as part of low-fat diet, exercise and behaviour therapy provided in group sessions by a dietitian maintained the greatest weight loss at two years (WMD weight change -6.00 kg (95% CI -10.19 to -1.81 kg)⁹. However dropout was 65% at 24 months. The addition of meal replacements was associated with significant improvement in HDL-cholesterol (0.01 mmol/L, 95% CI 0.00 to 0.02 mmol/L) and glucose at 24 months (0.03 mmol/L, 95% CI 0.00 to 0.05 mmol/L) but not other risk factors.

The addition of pre-packaged food provision or financial incentives, or both combined and compared with a low-calorie diet, exercise and behaviour therapy intervention, did not significantly improve weight loss at 30 months in 200 overweight US adults in their late 30s²³.

Head-to-head comparisons

One study of higher energy expenditure (2500 kcal/wk) through exercise and increased social support plus small monetary incentives, compared with 1000 kcals/wk was associated with a non-significant weight change at 30 months⁵⁵. Both groups received low-fat diet and standard behaviour therapy.

There was no significant difference in weight between delivering behaviour therapy by telephone compared with mail in 1801 obese US adults from a managed care organisation at 24 months⁵⁴.

There was no significant difference in weight at 24 months between women who were seen by a dietitian in a group and women seen by a nurse or physician in a clinic. Both groups received low-fat diet including meal replacements, exercise and behaviour therapy⁹.

Glucose (0.03 mmol/L, 95% CI 0.01 to 0.05 mmol/L) and LDL-Cholesterol (0.02 mmol/L, 95% CI 0.01 to 0.03 mmol/L) were significantly improved in the nurse/physician group compared with the dietitian group at 24 months. There was significant difference in favour of lowered SBP for the dietitian group (-17.00 mmHg, 95% CI -27.91 to -6.09 mmHg). No other risk factor data was significantly different⁹.

4.3 Studies where the primary intention was not to lose weight

Dietary interventions versus control

Weight

A low-fat non-reducing diet was associated with a statistically significant weight change of -1.42 kg (95% CI -2.10 to -0.74 kg) at 24 months from two studies^{13;39; 40}. Both studies were in women of normal weight who had either survived breast cancer or were at risk of breast cancer.

Two other studies reported weight change. There was a significant reduction in weight in the intervention group compared with the control at 24-months (approximately -1.6 kg vs +1.5 kg respectively) in the feasibility trial for the Women's Intervention Nutrition Study⁴¹ (WINS-FT). In another study the intensive diet group increased mean weight by 2.09 kg and the routine diet group increased weight by 1.57 kg at a median of 51 months follow-up⁵⁷. There was a significant difference in the follow-up duration (median 58.6 months for intensive diet and 47.9 months for routine diet).

Clinical outcomes

There was no significant difference in the incidence of diabetes at 51 months in women of normal weight with a recent history of gestational diabetes⁵⁷, 6.1% for the intensive diet group and 7.3% for the routine diet group, an incidence rate of 0.83 (95% CI 0.47 to 1.48, $p=0.50$).

A low-fat non-reducing diet significantly reduced the area of mammographic density (a risk factor for cancer) compared with control at two years¹³.

Behavioural interventions versus control

Weight

Behaviour therapy versus control showed no significant effect on weight at 24 months (one study of 115 physically active Canadian undergraduates, mean age 20y, mean BMI 22.4 kg/m²)⁵⁰.

Risk factors

There were no significant differences between groups in total cholesterol or HDL-cholesterol, however there was a significant difference in favour of behaviour therapy for triglycerides at 24 months (-0.20 mmol/L, 95% CI -0.40 to 0.00 mmol/L)⁵⁰.

Diet and exercise versus control

Weight

Diet and exercise education – with or without financial incentives - did not prevent weight gain in 809 overweight but otherwise healthy adults in one community-based study (Pound of Prevention) at 24 and 36 months²⁹. For diet and exercise, diet and exercise with incentives, and control; weight change was +1.3 kg, +1.2 kg, +1.4 kg at two years and +1.6 kg, +1.5 kg, +1.8 kg at three years respectively.

Diet and behaviour versus control

Four studies^{42;45;46;52;58;60-62;64} ranged in size from 2079 participants to 48835 women. The Polyp Prevention Trial^{52;60} (PPT) recruited men and women with a recent large-bowel adenomatous polyp, two studies; Women's Healthy Eating and Living⁵⁸ (WHEL) and Women's Intervention Nutrition Study⁶⁴ (WINS) recruited women with previously treated or resected early stage breast cancer, and the Women's Health Initiative Dietary Modification Trial^{42;45;46;61;62} (WHIDMT) recruited postmenopausal women.

Weight

Diet and behaviour therapy was associated with a significant weight change of -1.01 kg (95% CI -1.34 to -0.68 kg, 2 studies) at 24 months, -1.77 kg (95% CI -1.94 to -1.59 kg, 3 studies) at 36 months (figure 2), -0.52 kg (95% CI -0.85 to -0.19 kg, 2 studies) at 48 months and -0.70 kg (95% CI -0.90 to -0.50 kg, one study) at 90 months. The difference in weight was not significant at 72 months. There was significant heterogeneity between the studies.

WINS⁶⁴ reported a difference between intervention and control (in favour of intervention) of -1.8 kg (95% CI -3.1 to 0.2 kg) at three years and -2.7 kg (95% CI -4.5 to -0.9 kg) at five years.

Risk factors

Despite significant weight loss, the PPT^{52;60} showed no significant difference between groups for cholesterol at 24, 36 and 48 months.

Clinical outcomes

Diet and behaviour therapy interventions did not significantly reduce incident cancers including colorectal, breast, endometrial or ovarian cancer⁶¹, risk of recurrent adenomas⁶⁰ or mortality from colorectal or breast cancer^{45;46} over 8 years. However interim results suggest that intervention women in WINS⁶⁴ had a 24% lower risk of relapse events than women in control at five years (HR 0.76, 95% CI 0.60, 0.98).

The WHIDMT showed no significant difference in overall incidence of ovarian cancer (hazard ratio (HR) 0.83, 95% CI 0.60 to 1.14) and cancer of the endometrium (HR 1.11, 95% CI 0.88 to 1.40) at 8.1 years. However ovarian cancer risk was lower in the intervention group for the final four years (HR 0.60, 95% CI 0.38 to 0.96)⁶¹. HR for colorectal cancer was 1.08 (95% CI 0.90 to 1.29) and mortality from colorectal cancer was 1.26 (95% CI 0.85 to 1.85) over 8.1 years^{45;46}. HR for breast cancer was 0.91 (95% CI 0.83 to 1.01) and mortality from breast cancer was 0.77 (95% CI 0.48 to 1.22)^{45;46}. HR for confirmed breast cancer event was 0.96 (95% CI 0.80 to 1.14; P = 0.63) in the WHEL⁵⁸ study over 7.3 years.

Risk of recurrent adenomas was not significantly reduced in intervention participants of the PPT at four or eight years (RR 0.98, 95% CI 0.81 to 1.39 at 8y)⁶⁰.

The WHIDMT found no evidence for reducing diabetes risk after 8.1 years, HR 0.96 (95% CI 0.90 to 1.03)⁶².

Diet, exercise and behaviour therapy versus control

Weight

Diet and exercise and behaviour therapy (clinic-based or home-based) was associated with non-significant weight changes at 24 and at 36 months compared with control in 284 healthy women in their mid 30s⁵³.

Adjuncts to diet

Diet plus exercise versus diet

Two RCTs set in Finland were included^{11;12;49}. One study was community-based and recruited 90 men at risk of developing the metabolic syndrome (BMI 30-40 kg/m², waist circumference >100cm)^{11;12}. The other⁴⁹ recruited eighty-two women, mean age 40 years, mean BMI 34 kg/m². Both included studies had a VLCD of 8-12 weeks and had a mean weight loss of 13.1 to 14.3 kg prior to randomisation.

Weight

The addition of exercise to a low-fat diet was associated with a non-significant weight change at 29-33 months, irrespective of type (walking or resistance training) or amount (3.6 MJ/wk-8.4 MJ/wk) (figure 3). Men randomised to the walking group had 33% dropout compared with 13% dropout in the resistance training group^{11;12}.

Risk factors

The addition of exercise to a low-fat diet did not improve risk factors in women at 33 months⁴⁹.

Clinical outcomes

The OR for the occurrence of metabolic syndrome (from two months prior to randomisation, both groups combined) was 0.29 (95% CI 0.16 to 0.50).^{11;12}.

Other comparisons

A Mediterranean diet with behaviour therapy versus a standard low-fat diet was associated with significant weight change at 24 months (-2.80 kg, 95% CI -3.06 to -2.54 kg) in 180 sedentary Italian adults with metabolic syndrome⁴⁸. There were significant improvements in total cholesterol (-0.23mmol/L, 95% CI -0.26 to -0.20 mmol/L) and HDL-cholesterol (0.07 mmol/L, 95% CI 0.06 to 0.08 mmol/L), triglycerides (-0.21 mmol/L, 95% CI -0.23 to -0.29 mmol/L), glucose (-0.33 mmol/L, 95% CI -0.37 to -0.29 mmol/L) and blood pressure (SBP -3.00 mmHg, 95% CI -3.46 to -2.54 mmHg; DBP -2.00 mmHg, 95% CI -2.29 to -1.71 mmHg) at 24 months.

A low-fat non-reducing vegan diet compared with a low-fat non-reducing diet was associated with a non-significant weight change at 24 months in 62 overweight postmenopausal women⁵⁶. Participants offered group support for one year after the initial intervention (regardless of group) lost more weight at 24 months compared with participants not offered group support. Vegan supported participants lost significantly more weight than unsupported vegan participants at 24 months (-4.95 kg; 95% CI -7.50 to -2.40 kg) (figure 4).

There was no significant difference in weight between clinic-based diet, exercise and behaviour therapy and home-based diet, exercise and behaviour therapy at 24 and 36 months in 284 healthy normal weight women in their mid 30s⁵³.

There was no significant difference in BMI between supervised group-based higher-intensity exercise set in the community versus unsupervised individual higher-intensity home-based exercise⁵¹. There was no significant difference in BMI between unsupervised individual higher-intensity home-based exercise and unsupervised individual lower-intensity home-based exercise⁵¹. There were no significant differences between groups for risk factors.

There was no significant difference in weight between traditional structured exercise and behaviour therapy versus lifestyle physical activity and behaviour therapy at 24 months in 237 sedentary, overweight adults⁴⁷. Only triglycerides were significantly improved in participants in the traditional structured exercise group compared with lifestyle physical activity at 24 months (-0.18 mmol/L, 95% CI -0.33 to -0.03 mmol/L).

There was no significant difference in weight or risk factors between exercise to expend 8.4 MJ/wk versus 4.2 MJ/wk (both groups received diet) at 33 months in 82 obese premenopausal women⁴⁹.

There was no significant difference in weight between walking (5.2 MJ/wk) and resistance training (3.6 MJ/wk) at 31 months in 90 obese men^{11;12}.

Low-fat non-reducing diet and exercise with incentives compared with low-fat non-reducing diet and exercise without incentives did not prevent weight gain in 809 overweight but otherwise healthy adults in one community-based study at 24 and 36 months²⁹. Diet with exercise and incentives versus diet with exercise; weight change was +1.2 kg vs. +1.3 kg at two years and +1.5 kg vs. +1.6 kg at three years.

4.4 Deaths and clinical outcomes

Meta-analyses showed no significant difference between lifestyle interventions and control groups for deaths (figure 5), stroke, heart disease or cancer outcomes. Diet and behaviour therapy suggest reduced risk of breast cancer recurrence at five years⁶⁴ and ovarian cancer in the final four years of an eight year trial⁶¹.

Interim results suggest that intervention women in WINS⁶⁴ had a 24% lower risk of breast cancer recurrence than women in control at five years (HR 0.76, 95% CI 0.60 to 0.98). Ovarian cancer risk was lower in the intervention group for the final four years (HR 0.60, 95% CI 0.38 to 0.96) of the WHIDMT⁶¹.

There is evidence that lifestyle intervention can prevent diabetes and the metabolic syndrome. Two studies were terminated early^{16;17;30} due to unequivocal evidence of effectiveness of the lifestyle intervention in significantly reducing the risk of developing type 2 diabetes.

The DPP^{16;17} demonstrated that an intensive low-fat diet, exercise and psychological support intervention compared with control can prevent the metabolic syndrome at three years (OR 0.54, 95% CI 0.42 to 0.69). Combined data from the DPP^{16;17} and a study of Mediterranean diet and behaviour therapy versus standard low-fat diet⁴⁸ showed that these interventions can resolve cases of the metabolic syndrome for up to three years (RR 2.52, 95% CI 2.08 to 3.05). (In this case an RR of greater than 1 favours treatment as higher resolutions indicates a better outcome). In the FDPS⁵⁹, at mean follow-up 3.9 years; 62.6% intervention participants and 71.2% control participants had metabolic syndrome (sex and age-adjusted OR 0.62 (95% CI 0.40-0.95).

Three studies^{18;19;27;30;59} (diet versus control; diet and exercise versus control; diet, exercise and behaviour therapy versus control) showed a significant effect on the prevention of type 2 diabetes up to 6 years (RR 0.68, 95% CI 0.57 to 0.82). This result is consistent with the results from the DPP^{16;17} in which the incidence of diabetes was 58% lower (95% CI 48 to 66%) in the intensive lifestyle intervention group than the control. However the WHIDMT⁶² showed no evidence of reducing diabetes risk after 8.1 years.

5. Discussion

This systematic review captured a relatively large number of studies (40), capturing interventions aimed at preventing weight gain in adults who were normal weight, overweight and obese. In doing so it extends the evidence base beyond a recent review⁶⁵.

Eleven of 39 comparisons produced significant improvement in weight, of which eight compared an intervention to a non-treatment control. Eight intended to produce weight loss and produced greater weight loss than the three studies not intending weight loss (WMD weight change 2.0-11.5 kg versus 0.5-2.8 kg respectively). 600kcal/day deficit/low-fat diets with and without meal-replacements, low-calorie diets, Weight-Watchers, low-fat non-reducing diets; diets with behaviour therapy, exercise or exercise and behaviour therapy produced significant improvement in weight compared with control. Weight loss ranged from -0.5 kg to -11.5 kg. Adding meal replacements produced significant improvement in weight particularly long-term. Direct comparisons of interventions failed to show significant effect on weight with the exception Mediterranean diet and behaviour therapy compared with a low-fat diet.

Interventions combining diet with additional elements compared to control were not always associated with greater weight loss. Both diet and exercise and diet, exercise and behaviour therapy produced similar weight changes, less than some of the diets alone and similar to that achieved by Weight Watchers²⁰. There was insufficient evidence to assess the benefit of adding exercise or behaviour therapy. There were no studies that assessed the effectiveness of adding behaviour therapy or exercise and behaviour therapy to a non-reducing diet. There did not appear to be any obvious pattern between intensity of contact or diet prescription and weight change.

The four meal replacement studies^{9;14;15;31;43;63} began with an intensive phase consisting of meal replacements 2-3 times daily for three months, then three studies continued to use meal replacements less often (in one study both groups received meal replacements for the maintenance period). Significant benefit to weight was demonstrated in the two studies that assessed the addition of meal replacements in the maintenance phase, although one of these was not a randomised study⁶³.

Risk factor data were limited; weight loss did not consistently improve risk factors, some risk factors improved independent of weight change. Another review including lifestyle interventions of at least two years duration found that weight loss of at least 5% baseline weight was not consistently associated with improvement in cardiovascular risk factors and benefits were specific to the intervention and occurred mainly in people with cardiovascular risk factors⁶⁶.

Few studies were powered to detect differences in morbidity and mortality or followed up for sufficient time. There was no significant difference between lifestyle interventions and control groups for deaths, stroke, heart disease or

cancer. Diet and behaviour therapy suggest reduced risk of breast cancer recurrence at five years⁶⁴ and ovarian cancer in the final four years of an eight year trial⁶¹. 600 kcal/day deficit/low-fat diets can reduce type 2 diabetes, improve blood pressure and reduce antihypertensive medication for up to three years. Diet and exercise reduce the risk of type 2 diabetes for up to six years and the metabolic syndrome at four years, compared to control. Diet with exercise and behaviour therapy can reduce the risk of type 2 diabetes, hypertension and the metabolic syndrome. The addition of exercise to diet can reduce the risk of metabolic syndrome in men. However a non-reducing diet and behaviour therapy did not reduce diabetes risk in nearly 49,000 women after 8.1 years⁶².

Research is required into whether effectiveness of interventions varies with baseline risk, age, gender, ethnic group and setting. WHIDMT⁶² suggests that relatively small amounts of weight loss without increase in physical activity, may account for why the intervention did not reduce the risk of diabetes compared with the FDPS^{18;19;59} and DPP^{16;17;44}. Participants in the FDPS and DPP were at higher risk of developing diabetes and had higher baseline BMI compared to the WHIDMT. In the DPP⁴⁴, lifestyle intervention was most effective in preventing diabetes in older participants (60-85y) perhaps due to greater weight loss and physical activity. Interim analysis of WINS⁶⁴ diet and behaviour intervention suggests significantly reduced risk of breast cancer recurrence in postmenopausal women, whereas the WHIDMT^{42;45;46;61;62} and WHEL⁵⁸ studies did not significantly reduce breast cancer morbidity. Women in the dietary intervention arm of WINS lost more weight than the other studies which may account for the lowered risk.

There was scant reporting of economic or quality of life data. The FDPS was used to assess whether a lifestyle intervention to prevent diabetes in adults with IGT is cost-effective in a Swedish setting⁶⁷. The model predicted that the intervention would be cost-saving, with an increase in estimated survival of 0.18 years. The predicted cost-effectiveness ratio was €2,363 per quality-adjusted life-year gained.

It was difficult to determine whether some studies were supposed to affect weight or not, or whether exercise or behaviour therapy were provided, and to classify types of diet. Classification of interventions was difficult because the information reported within the papers was insufficient; classification was often arrived at by a consensus process between reviewers. Where the calorie content of a diet was not clearly stated it was categorized as a '600 kcal/day deficit or low-fat diet' (where there was a definite intention to provide weight loss) or 'low-fat non-reducing diet' (where there was no definite intention to provide weight loss). For exercise or behaviour therapy interventions to be categorised as such, study investigators had to give a detailed description of the components of the intervention.

Studies were heterogeneous and the varied comparisons were underpinned by few studies making it difficult to generalise about effective interventions. There were inadequate data reported to include some studies in meta-analyses, in addition, it was necessary to calculate weight and risk factor change from absolute values or from graphs which meant that standard deviations needed imputing in 25% of studies. A minority of studies reported adequate allocation concealment, intention-to-treat analyses or blinding of outcome assessors. It was not possible to assess the differential effects of interventions according to demographic, socio-economic or cultural characteristics⁶⁸.

There is limited evidence for lifestyle interventions to prevent weight gain in healthy normal weight adults within the community. To widen the evidence-base requires review of uncontrolled interventions and synthesis of evidence from complex public health interventions with new methods to assess evidence.

These gaps in the evidence base and inadequacies relating to study design and reporting necessitate recommendations for future interventions to be longer-term and sufficiently powered to detect clinical outcomes. Adequate reporting of outcome data would enable all studies to be included in meta-analyses (where relevant to do so). Detailed reporting of interventions, participant characteristics, economic and quality-of-life data would improve the quality of future systematic reviews of lifestyle intervention.

Conclusion

Diet, alone and with the addition of exercise and/or behaviour therapy demonstrated significant weight loss and improvement in metabolic syndrome and diabetes compared to no treatment control for at least two years.

Word count: 5848.

Reference List

- (1) EU members. EU Platform on Diet, Physical Activity and Health, 15th March 2005, Diet, Physical Activity and Health - A European platform for action. 2005. Ref Type: Report
- (2) World Health Organization. Global strategy on diet, physical activity and health. 2004. Ref Type: Report
- (3) Department of Health. Change4Life: The healthy living revolution starts here. (WWW document). URL <http://www.dh.gov.uk/en/index.htm>[accessed December 08].
- (4) National Institute for Health and Clinical Excellence (NICE). Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children. Clinical guideline. CG43. National Institute for Health and Clinical Excellence (NICE): London, 2006. Ref Type: Report
- (5) Government Office for Science. 'Tackling Obesity: Future Choices – Project Report'. Department for Innovation, Universities and Skills: London, 2007. [WWW document]. URL http://www.foresight.gov.uk/Obesity/obesity_final/17.pdf (accessed December 08).
- (6) Department of Health. £30m healthy towns kick start Change4life. (WWW document). URL:http://www.dh.gov.uk/en/News/Recentstories/DH_090107 (accessed December 08).
- (7) Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, Smith WCS, Jung RT, Campbell MK, Grant AM.. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technology Assessment* 2004; 8(21).
- (8) Deeks JJ, Higgins JPT, Altman DG, editors. Analysing and presenting results. In: Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions* 4.2.6 [updated September 2006]; Section 8. In: *The Cochrane Library*, Issue 4, 2006. Chichester, UK: John Wiley & Sons, Ltd.
- (9) Ashley JM, Sachiko T St Jeor, Perumean-Chaney S, Schrage J, Bovee V. Meal replacements in weight intervention. *Obesity Research* 2001; 9 (suppl 4):312s-320s.
- (10) Blonk MC, Jacobs MAJM, Biesheuvel EHE, Weeda-Mannak WL, Heine RJ. Influences of weight loss in type 2 diabetic patients: Little long-term benefit from group behaviour therapy and exercising training. *Diabetic Medicine* 1994; 11:449-457.
- (11) Borg P, Kukkonen-Harjula K, Fogelholm M, Pasanen M. Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: a randomized trial. *International Journal of Obesity and Related Metabolic Disorders* 2002; 26(5):676-683.
- (12) Kukkonen-Harjula KT, Borg PT, Nenonen AM, Fogelholm MG. Effects of a weight maintenance program with or without exercise on the metabolic syndrome: a randomized trial in obese men. *Preventive Medicine* 2005; 41(3-4):784-790.
- (13) Boyd NF, Greenberg C, Lockwood G, Little L, Martin L, Byng J, Yaffe M, Trichler D. Effects at two years of a low-fat, high carbohydrate diet on radiologic features of the breast: results from a randomized trial. *Journal of the National Cancer Institute* 1997; 89(7):488-496.
- (14) Ditschuneit HH, Flechtner-Mors M, Johnson TD, Adler G. Metabolic and weight-loss effects of long-term dietary intervention in obese patients. *American Journal Clinical Nutrition* 1999; 69(2):198-204.
- (15) Flechtner-Mors M, Ditschuneit HH, Johnson TD, Suchard MA, Adler G. Metabolic and weight-loss effects of long-term dietary intervention in obese patients: four year results. *Obesity Research* 2000; 8(5):399-402.
- (16) Orchard TJ, Temprosa M, Goldberg R, Haffner S, Ratner R, Marcovina S, Fowler S, for the Diabetes Prevention Program Research Group. The effect of metformin and intensive lifestyle intervention on the

metabolic syndrome: the Diabetes Prevention Program randomized trial. *Annals of Internal Medicine* 2005; 142(8):611-619.

- (17) Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England Journal of Medicine* 2002; 346(6):393-403.
- (18) Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rasta M, Salminen V, Aunola S, Cepaitis Z, Moltchanov V, Hakumaki M, Mannelin M, Martikkala V, Sundvall J, Uusitupa M, for the Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine* 2001; 344(18):1343-1350.
- (19) Lindstrom J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemio K, Hämäläinen H, Harkonen P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Mannelin M, Paturi M, Sundvall J, Valle TT, Uusitupa M, Tuomilehto J, on behalf of the Finnish Diabetes Prevention Study Group. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *The Lancet* 2006; 368(9548):1673-1679.
- (20) Heshka S, Anderson JW, Atkinson RL, Greenway FL, Hill JO, Phinney SD, Kolotkin RL, Miller-Kovach K, Pi-Sunyer FX. Weight loss with self-help compared with a structured commercial program. *Journal of the American Medical Association (JAMA)* 2003; 289(14):1792-1798.
- (21) Jones DW, Miller ME, Wofford MR, Anderson DC, Cameron ME, Willoughby DL, Adair CT, King NS. The effect of weight loss intervention on hypertensive medication requirements in the Hypertension Optimal Treatment (HOT) study. *American Journal of Hypertension* 1999; 12(pt 1-2):1175-1180.
- (22) Hypertension Prevention Trial Research Group. The Hypertension Prevention Trial: three-year effects of dietary changes on blood pressure. *Archives of Internal Medicine* 1990; 150(1):153-162.
- (23) Jeffery RW, Wing RR. Long-term effects of interventions for weight loss using food provision and monetary incentives. *Journal of Consulting and Clinical Psychology* 1995; 63(5):793-796.
- (24) Kristal AR, Blount PL, Schenk JM, Sanchez CA, Rabinovitch PS, Odze RD, Standley J, Vaughan TL, Reid BJ. Low-fat, high fruit and vegetable diets and weight loss do not affect biomarkers of cellular proliferation in Barrett esophagus. *Cancer Epidemiology, Biomarkers & Prevention* 2005; 14(10):2377-2383.
- (25) Kuller LH, Simkin-Silverman LR, Wing RR, Meilahn EN, Ives DG. Women's Healthy Lifestyle Project: A randomized clinical trial: results at 54 months. *Circulation* 2001; 103(1):32-37.
- (26) Mensink M, Blaak EE, Corpeleijn E, Saris WM, de Bruin TW, Feskens EJ. Lifestyle intervention according to general recommendations to improve glucose tolerance. *Obesity Research* 2003; 11(12):1588-1596.
- (27) Oldroyd JC, Unwin NC, White M, Mathers JC, Alberti KGMM. Randomised controlled trial evaluating lifestyle interventions in people with impaired glucose tolerance. *Diabetes Research and Clinical Practice* 2006; 72(2):117-127.
- (28) Page RC, Harnden KE, Cook JT, Turner RC. Can lifestyles of subjects with impaired glucose tolerance be changed? A feasibility study. *Diabetic Medicine* 1992; 9(6):562-566.
- (29) Jeffery RW, French SA. Preventing weight gain in adults: the Pound of Prevention study. *American Journal of Public Health* 1999; 89(5):747-751.
- (30) Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. Indian Diabetes Prevention Program (IDPP). The Indian Diabetes Program shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006; 49(2):289-297.

- (31) Simonen P, Gylling H, Howard AN, Miettinen TA. Introducing a new component of the metabolic syndrome: low cholesterol absorption. *American Journal Clinical Nutrition* 2000; 72(1):82-88.
- (32) Singh RB, Rastogi V, Rastogi SS, Niaz MA, Beegom R. Effect of diet and moderate exercise on central obesity and associated disturbances, myocardial infarction and mortality in patients with and without coronary artery disease. *Journal of the American College of Nutrition* 1996; 15(6):592-601.
- (33) Davis BR, Blaufox MD, Oberman A, Wassertheil-Smoller S, Zimbaldi N, Cutler JA, Kirchner K, Langford HG. Reduction in long-term antihypertensive medication requirements. Effects of weight reduction by dietary intervention in overweight persons with mild hypertension. *Archives of Internal Medicine* 1993; 153(15):1773-1782.
- (34) Davis BR, Oberman A, Blaufox MD, Wassertheil-Smoller S, Hawkins CM, Cutler JA, Zimbaldi N, Langford HG. Effect of antihypertensive therapy on weight loss. The Trial of Antihypertensive Interventions and Management Research Group. *Hypertension* 1992; 19(4):393-399.
- (35) Davis BR, Oberman A, Blaufox MD, Wassertheil-Smoller S, Zimbaldi N, Kirchner K, Wylie Rosett J, Langford HG. Lack of effectiveness of low-sodium/high-potassium diet in reducing antihypertensive medication requirements in overweight persons with mild hypertension. *American Journal of Hypertension* 1994; 7(10 (pt1)):926-932.
- (36) Trials of Hypertension Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, Phase II. *Archives of Internal Medicine* 1997; 157(6):657-667.
- (37) Stevens VJ, Obarzanek E, Cook NR, Lee I-M, Appel LJ, Smith West D, Milas NC, Mattfeldt-Beman M, Belden L, Bragg C, Millstone M, Raczynski J, Brewer A, Singh B, Cohen J, for the Trials of Hypertension Prevention Research Group. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, Phase II. *Annals of Internal Medicine* 2001; 134(1):1-11.
- (38) de Waard FD, Ramlau R, Mulders Y, Vries TD, Waveren SV. A feasibility study on weight reduction in obese postmenopausal breast cancer patients. *European Journal of Cancer Prevention* 1993; 2(3):233-238.
- (39) Sheppard L, Kristal AR, Kushi LH. Weight loss in women participating in a randomized trial of low-fat diets. *American Journal Clinical Nutrition* 1991; 54(5):821-828.
- (40) Insull W, Henderson MM, Prentice RL, Thompson DJ, Clifford C, Goldman S, Gorbach S, Moskowitz M, Thompson R, Woods M. Results of a randomized feasibility study of a low-fat diet. *Archives of Internal Medicine* 1990; 150(2):421-427.
- (41) Chlebowski RT, Blackburn GL, Buzzard IM, Rose DP, Martino S, Khandekar JD, York RM, Jeffery RW, Elashoff RM, Wynder EL. Adherence to a dietary fat intake reduction program in postmenopausal women receiving therapy for early breast cancer. The Woman's Intervention Nutrition Study. *Journal of Clinical Oncology* 1993; 11:2072-2080.
- (42) Howard BV, Manson JE, Stefanick ML, Beresford SA, Frank G, Jones B, Rodabough RJ, Snetselaar L, Thomson C, Tinker L, Vitolins M, Prentice R. Low-fat dietary pattern and weight change over 7 years: the Woman's Health Initiative Dietary Modification Trial. *Journal of the American Medical Association (JAMA)* 2006; 295(1):39-49.
- (43) Ditschuneit HH, Flechtner-Mors M. Value of structured meals for weight management: risk factors and long-term weight maintenance. *Obesity Research* 2001; 9[suppl 1]: 284s-289s.
- (44) Diabetes Prevention Program Research Group, [Prepared by Crandall J, Schade D, Ma Y, Fujimoto WY, Barrett-Connor E, Fowler S, Dagogo-Jack S, Andres, R.] The influence of age on the effects of lifestyle

modification and metformin in prevention of diabetes. *J Gerontol A Biol Sci Med Sci* 2006; 61(10):1075-1081.

- (45) Prentice RL, Caan B, Chlebowski RT, Patterson R, Kuller LH, Ockene JK, Margolis KL, Limacher MC, Manson JE, Parker LM, Paskett E, Phillips L, Robbins J, Rossouw JE, Sarto GE, Shikany JM, Stefanick ML, Thomson CA, Van Horn L, Vitolins MZ, Wactawski-Wende J, Wallace RB, Wassertheil-Smoller S, Whitlock E, Yano K, Adams-Campbell L, Anderson GL, Assaf AR, Beresford SAA, Black HR, Brunner RL, Brzyski RG, Ford L, Gass M, Hays J, Heber D, Heiss G, Hendrix SL, Hsia J, Hubbell FA, Jackson RD, Johnson KC, Kotchen JM, LaCroix AZ, Lane DS, Langer RD, Lasser NL, Henderson MM. Low-fat dietary pattern and risk of invasive breast cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *Journal of the American Medical Association (JAMA)* 2006; 295: 629-642.
- (46) Beresford SA, Johnson KC, Ritenbaugh C, Lasser NL, Snetselaar LG, Black HR, Anderson GL, Assaf AR, Bassford T, Bowen D, Brunner RL, Brzyski RG, Caan B, Chlebowski RT, Gass M, Harrigan RC, Hays J, Heber D, Heiss G, Hendrix SL, Howard BV, Hsia J, Hubbell FA, Jackson RD, Kotchen JM, Kuller LH, LaCroix AZ, Lane DS, Langer RD, Lewis CE, Manson JE, Margolis KL, Mossavar-Rahmani Y, Ockene JK, Parker LM, Perri MG, Phillips L, Prentice RL, Robbins J, Rossouw JE, Sarto GE, Stefanick ML, Van Horn L, Vitolins MZ, Wactawski-Wende J, Wallace RB, Whitlock E. Low-fat dietary pattern and risk of colorectal cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *Journal of the American Medical Association (JAMA)* 2006; 295: 643-654.
- (47) Dunn AL, Marcus BH, Kampert JB, Garcia ME, Kohl H, Blair SN. Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: A randomized trial. *Journal of the American Medical Association (JAMA)* 1999; 281[4]: 327-334.
- (48) Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiento M, D'Andrea F, Giugliano D. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *Journal of the American Medical Association (JAMA)* 2004; 292:1440-1446.
- (49) Fogelholm M, Kukkonen-Harjula K, Nenonen A, Pasanen M. Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. *Archives of Internal Medicine* 2000;160[14]: 2177-2184.
- (50) Hivert M-F, Langlois M-F, Berard P, Cuerrier J-P, Carpentier C. Prevention of weight gain in young adults through a seminar-based intervention program. *International Journal of Obesity* 2007;31:1262-1269.
- (51) King AC, Haskell WL, Young DR, Oka RK, Stefanick ML. Long-term effects of varying intensities and formats of physical activity on participation rates, fitness, and lipoproteins in men and women aged 50 to 65 years. *Circulation* 1995; 91: 2596-2604.
- (52) Lanza E, Schatzkin A, Daston C, Corle D, Freedman L, Ballard-Barbash R, Caan B, Lance P, Marshall J, Iber F, Shike M, Weissfeld J, Slattery M, Paskett E, Mateski D, Albert P and the PPT Study Group. Implementation of a 4-y, highfiber, high-fruit-and-vegetable, low-fat dietary intervention: results of dietary changes in the Polyp Prevention Trial. *American Journal of Clinical Nutrition* 2001;74: 387-401.
- (53) Levine MD, Klem ML, Kalarchian MA, Wing RR, Weissfeld L, Qin L, Marcus MD. Weight gain prevention among women. *Obesity* 2007; 15(5):1267-1277.
- (54) Sherwood NE, Jeffery RW, Pronk NP, Boucher JL, Hanson A, Boyle R, Brelje K, Hase K, Chen V. Mail and phone interventions for weight loss in a managed-care setting: weigh-to-be 2-year outcomes. *International Journal of Obesity* 2006; 30(10):1565-1573.
- (55) Tate DF, Jeffery RW, Sherwood NE, Wing RR. Long-term weight losses associated with prescription of higher physical activity goals. Are higher levels of physical activity protective against weight regain? *American Journal Clinical Nutrition* 2007; 85(4):954-959.

- (56) Turner-McGrievy GM, Barnard ND, Scialli AR. A Two-Year Randomized Weight Loss Trial Comparing a Vegan Diet to a More Moderate Low-Fat Diet. *Obesity* 2007;15[9]: 2276-2281.
- (57) Wein P, Beischer N, Harris C, Permezel M. A trial of simple versus intensified dietary modification for prevention of progression to diabetes mellitus in women with impaired glucose tolerance. *Aust N Z J Obstet Gynaecol* 1999;39:162-166.
- (58) Pierce JP, Natarajan L, Caan BJ, Parker BA, Greenberg ER, Flatt SW, Rock CL, Kealey S, Al-Delaimy WK, Bardwell WA, Carlson RW, Emond JA, Faerber S, Gold EB, Hajek RA, Hollenbach K, Jones LA, Karanja N, Madlensky L, Marshall J, Newman VA, Ritenbaugh C, Thomson CA, Wasserman L, Stefanick ML. Influence of a diet very high in vegetables, fruit and fiber and low in fat on prognosis following treatment for breast cancer. The Women's Health Eating and Living (WHEL) Randomized Trial. *Journal of the American Medical Association (JAMA)* 2007;298[3]: 289-298.
- (59) Ilanne-Parikka P, Eriksson JG, Lindstrom J, Peltonen M, Aunola S, Hamalainen H, Keinänen-Kiukaanniemi S, Laakso M, Valle TT, Lahtela J, Uusitupa M, Tuomilehto J, on behalf of the Finnish Diabetes Prevention Study Group. Effect of lifestyle intervention on the occurrence of metabolic syndrome and its components in the Finnish Diabetes Prevention Study. *Diabetes Care* 2008; 31(4):805-807.
- (60) Lanza E, Binbing Y, Murphy G, Albert PS, Caan B, Marshall J.R, Lance P, Paskett ED, Weissfeld J, Slattery M, Burt R, Iber F, Shike M, Kikendall JW, Brewer BK, Schatzkin A, the Polyp Prevention Trial Study Group The Polyp Prevention Trial - Continued Follow-up Study: No Effect of a Low-Fat, High-Fiber, High-Fruit, and -Vegetable Diet on Adenoma Recurrence Eight Years after Randomization. *Cancer Epidemiology, Biomarkers & Prevention* 2007;16[9]:1745-1752.
- (61) Prentice RL, Thomson CA, Caan B, Hubbell FA, Anderson GL, Beresford SA, Pettinger M, Lane DS, Lessin L, Yasmeen S, Singh B, Khandekar J, Shikany JM, Satterfield S, Chlebowski RT. Low-fat dietary pattern and cancer incidence in the Women's Health Initiative Dietary Modification Randomized Controlled Trial. *Journal of the National Cancer Institute* 2007; 99(20):1534-1543.
- (62) Tinker LF, Bonds DE, Margolis KL, Manson JE, Howard BV, Larson J, Perri MG, Beresford SAA, Robinson JG, Rodríguez B, Safford MM, Wenger NK, Stevens VJ, Parker LM. Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: the Women's Health Initiative randomized controlled dietary modification trial. *Archives of Internal Medicine* 2008; 168(14):1500-1511.
- (63) Quinn Rothacker D. Five-year self-management of weight using meal replacements: comparison with matched controls in rural Wisconsin. *Nutrition* 2000; 15(5):344-348.
- (64) Chlebowski RT, Blackburn GL, Thomson CA, Nixon DW, Shapiro A, Hoy MK, Goodman MT, Giuliano AE, Karanja N, McAndrew P, Hudis C, Butler J, Merkel D, Kristal A, Caan B, Michaelson R, Vinciguerra V, Del Prete S, Winkler M, Hall R, Simon M, Winters BL, Elashoff RM. Dietary Fat Reduction and Breast Cancer Outcome: Interim Efficacy Results from the Women's Intervention Nutrition Study. *Journal of the National Cancer Institute* 2006; 98[24]:1767-1776.
- (65) Lemmens VE, Oenema A, Klepp KI, Henriksen HB, Brug J. A systematic review of the evidence regarding efficacy of obesity prevention interventions among adults. *Obesity Reviews* 2008; 9(5):446-455.
- (66) Douketis JD, Macie C, Thabane L, Williamson DF. Systematic review of long-term weight loss studies in obese adults: clinical significance and applicability to clinical practice. *International Journal of Obesity* 2005; 29(10):1153-1167.
- (67) Lindgren P, Lindstrom J, Tuomilehto J, Uusitupa M, Peltonen M, Jonsson B, de Faire U, Hellénus M-L, and The DPS Study Group. Lifestyle intervention to prevent diabetes in men and women with impaired glucose tolerance is cost-effective. *International Journal of Technology Assessment in Health Care* 2007; 23(2):177-183.

- (68) Ogilvie D, Fayter D, Petticrew M, Sowden A, Thomas S, Whitehead M, Worthy G. The harvest plot: A method for synthesising evidence about the differential effects of interventions. *BMC Medical Research Methodology* 2008;8[8].

APPENDIX 1. Search strategies.

FIGURES.

FIGURE 1. Flow diagram for locating primary studies of controlled trials for systematic review.

FIGURE 2. Diet and behaviour therapy versus control at 36 months. No intention to lose weight.

FIGURE 3. Diet and exercise versus diet at 29/33 months. No intention to lose weight.

FIGURE 4. Low-fat vegan diet versus low-fat NCEP diet at 24-months. No intention to lose weight.

FIGURE 5. Overall deaths.

TABLES.

TABLE 1 Table of included studies.

TABLE 2 Overview of included studies.

TABLE 3 Table of quality assessment of RCTs.

TABLE 4 Table of weight results from meta-analyses.

APPENDIX 1 Search strategies.

A. Search strategy to identify systematic reviews in MEDLINE and EMBASE and adapted for other databases.

1. Obesity/
2. Overweight/
3. weight gain/
4. weight loss/
5. obesity.ti,ab.
6. obese.ti,ab.
7. (los\$ adj1 weight).ti,ab.
8. (gain\$ adj1 weight).ti,ab.
9. (overweight or over weight or over-weight).ti,ab.
10. (change\$ adj1 weight).ti,ab.
11. (weight adj1 maint\$).ti,ab.
12. (weight adj1 reduc\$).ti,ab.
13. (weight adj1 control).ti,ab.
14. ((bmi or body mass index) adj2 (gain or loss or change)).ti,ab.
15. ((bmi or body mass index) adj2 (maint\$ or reduc\$)).ti,ab.
16. (prevent\$ adj1 (weight gain or obesity)).ti,ab.
17. or/1-16
18. exp meta analysis/
19. metaanalys:.ti,ab.
20. meta-analys:.ti,ab.
21. meta analys:.ti,ab.
22. cochrane.ti,ab,sh.
23. (synthes: adj3 (quantitative: or literature: or research or studies or data)).ti,ab.
24. pooled analys:.ti,ab.
25. ((data adj2 pool:) and studies).ti,ab.
26. ((review: or overview:) adj10 (systematic: or methodologic: or quantitativ: or research: or literature: or studies: or trial: or effective:)).ti,ab.
27. or/18-26
28. (retrospective: adj2 review:).ti,ab,sh.
29. (case: adj2 review:).ti,ab,sh.
30. (patient: adj 2 review:).ti,ab,sh.
31. (patient: adj2 chart:).ti,ab,sh.
32. (peer: adj2 review:).ti,ab,sh.
33. (chart: adj2 review:).ti,ab,sh.
34. (case: adj2 report:).ti,ab,sh.
35. or/28-34
36. 35 not (35 and 27)
37. 27 not 36
38. editorial.pt.
39. letter.pt.
40. or/38-39
41. 37 not 40
42. exp animal/
43. exp human/
44. 42 not (42 and 43)
45. 41 not 44
46. 17 and 45
47. limit 46 to (adolescent <13 to 17 years> or aged <65+ years> or child or embryo or infant or preschool child <1 to 6 years> or school child <7 to 12 years>)
48. 46 not 47
49. limit 48 to yr="1990 - 2006"
50. Obesity/
51. Overweight/

52. weight gain/
 53. weight loss/
 54. obesity.ti,ab.
 55. obese.ti,ab.
 56. (los\$ adj1 weight).ti,ab.
 57. (gain\$ adj1 weight).ti,ab.
 58. (overweight or over weight or over-weight).ti,ab.
 59. (change\$ adj1 weight).ti,ab.
 60. (weight adj1 maint\$).ti,ab.
 61. (weight adj1 reduc\$).ti,ab.
 62. (weight adj1 control).ti,ab.
 63. ((bmi or body mass index) adj2 (gain or loss or change)).ti,ab.
 64. ((bmi or body mass index) adj2 (maint\$ or reduc\$)).ti,ab.
 65. (prevent\$ adj1 (weight gain or obesity)).ti,ab.
 66. or/50-65
 67. exp meta analysis/
 68. metaanalys:.ti,ab.
 69. meta-analys:.ti,ab.
 70. meta analys:.ti,ab.
 71. cochrane.ti,ab,sh.
 72. (synthes: adj3 (quantitative: or literature: or research or studies or data)).ti,ab.
 73. pooled analys:.ti,ab.
 74. ((data adj2 pool:) and studies).ti,ab.
 75. ((review: or overview:) adj10 (systematic: or methodologic: or quantitativ: or research: or literature: or studies: or trial: or effective:)).ti,ab.
 76. or/67-75
 77. (retrospective: adj2 review:).ti,ab,sh.
 78. (case: adj2 review:).ti,ab,sh.
 79. (patient: adj 2 review:).ti,ab,sh.
 80. (patient: adj2 chart:).ti,ab,sh.
 81. (peer: adj2 review:).ti,ab,sh.
 82. (chart: adj2 review:).ti,ab,sh.
 83. (case: adj2 report:).ti,ab,sh.
 84. or/77-83
 85. 84 not (84 and 76)
 86. 76 not 85
 87. editorial.pt.
 88. letter.pt.
 89. or/87-88
 90. 86 not 89
 91. exp animal/
 92. exp human/
 93. 91 not (91 and 92)
 94. 90 not 93
 95. 66 and 94
 96. limit 95 to ("all infant (birth to 23 months)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)" or "aged (80 and over)")
 97. 95 not 96
 98. limit 97 to yr="1990 - 2006"
 99. 49 or 98
 100. remove duplicates from 99

B. Search strategy to identify primary studies in MEDLINE and adapted for other databases.

1. Obesity/
2. Overweight/
3. weight gain/
4. weight loss/
5. obesity.ti,ab.
6. obese.ti,ab.
7. (los\$ adj1 weight).ti,ab.
8. (gain\$ adj1 weight).ti,ab.
9. (overweight or over weight or over-weight).ti,ab.
10. (change\$ adj1 weight).ti,ab.
11. (weight adj1 maint\$).ti,ab.
12. (weight adj1 reduc\$).ti,ab.
13. (weight adj1 control).ti,ab.
14. ((bmi or body mass index) adj2 (gain or loss or change)).ti,ab.
15. ((bmi or body mass index) adj2 (maint\$ or reduc\$)).ti,ab.
16. (prevent\$ adj1 (weight gain or obesity)).ti,ab.
17. or/1-16
18. randomized controlled trial.pt.
19. controlled clinical trial.pt.
20. randomized controlled trials/
21. random allocation/
22. double blind method/
23. single blind method/
24. controlled clinical trials/
25. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).ti,ab.
26. placebos/
27. placebo\$.ti,ab.
28. research design/
29. control groups/
30. (control\$ adj3 before adj2 after adj3 (stud\$ or trial\$ or design\$)).ti,ab.
31. (matched communities or matched populations).ti,ab.
32. comparison group\$.ti,ab.
33. matched pairs.ti,ab.
34. (quasiexperimental or quasi experimental).ti,ab.
35. nonrandomi?ed.ti,ab.
36. (control\$ adj (group\$ or trial\$)).ti,ab.
37. randomi?ed.ti,ab.
38. intervention studies/
39. evaluation studies/
40. (pretest or pre test or (posttest or post test)).ti,ab.
41. or/18-40
42. 17 and 41
43. animal/ not human/
44. 42 not 43
45. limit 44 to ("all infant (birth to 23 months)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "aged (80 and over)")
46. 44 not 45
47. limit 46 to yr="2005 - 2006"
48. pregnancy/
49. 47 not 48
50. editorial.pt.
51. letter.pt.
52. 50 or 51
53. 49 not 52
54. eating disorders/
55. 53 not 54