Appendix 15

NOTE: all text in italic is taken from the source documents as acknowledged.

Abbreviations

BEDD	Balanced energy-deficient diet
BMI	Body mass index
BP	Blood pressure
BT	Behavioural therapy
CAD	Coronary artery disease
CHD	Coronary heart disease
CI	Confidence interval
CON	Control
CRP	C-reactive protein
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DEXA	Dual-energy X-ray absorptiometry
DS-BPD	Duodenal switch-bileopancreatic diversion
EE	Energy expenditure
EWL	Excess weight loss
FEV	Forced expiratory volume
FFM	Fat-free mass
FPG	Fasting plasma glucose
FVC	Forced vital capacity
GBP	Gastric bypass
GI	Gastrointestinal
GP	General practitioner
GRP	Group
HP	High protein
HRQL	Health-related quality of life
ICAM	Intracellular adhesion molecule
IGT	Impaired glucose tolerance
IND	Individual treatment
INT	Intermittent
ITT	Intention to treat
KPWMP	Kaiser Permanente Weight Management Program
LAGB	Laparoscopic (adjustable) gastric banding
LB	Long bout
LED	Low-energy diet
LGBP	Laparoscopic Roux en Y gastric bypass
LGBY	Laparoscopic gastric bypass
LOCF	Last observation carried forward
LTPA	Leisure time physical activity
METS	Metabolic equivalent tasks
MI	Myocardial infarction
MP	Medium protein
NGT	Normal glucose tolerance
NIDDM	Non-insulin-dependent diabetes mellitus
NS	Not significant
OA	Osteoarthritis
OGTT	Oral glucose tolerance test
OR	Odds ratio
PEF	Peak expiratory flow
PS	Problem-solving
PSMF	Protein-sparing modified fast
RCT	Randomised controlled trial
RDA	Recommended daily allowance
ROC	Received operator characteristic

RP	Relapse prevention
RR	Relative risk
SB	Short bout
SBEQ	Short bout plus home treadmill
SBP	Systolic blood pressure
SBT	Standard behavioural therapy
SP	Standard protein
TAG	Triacylglycerol
TC	Total cholesterol
VLED	Very-low-energy diet
WC	Waist circumference
WHO	World Health Organization
WHR	Waist:hip ratio

Evidence tables

Comparison of guidelines included in the syntheses

COMPARISON OF SCOPE AND CONTENT	
Objective and Scope	
ACP (2005)	To provide recommendations based on a review of the evidence on pharmacological and surgical treatments of obesity To complement the guidelines on screening for obesity developed by the US Preventive Services Task Force
ACPM (2001)	To present a practice policy statement on weight management counselling of overweight adults
AGA (2002)	To provide gastroenterologists with a comprehensive evaluation of the important clinical issues in adult obesity, including prevalence, aetiology, physiology, pathophysiology, medical complications, metabolic and medical effects of weight loss, treatment options and treatment guidelines
BWH (2003)	To provide physicians with clear clinical pathways to identify and treat obesity
SINGAPORE MOH (2004)	To assist healthcare professionals who have a role in managing overweight or obese patients To provide current evidence-based clinical practice recommendations on various aspects of obesity management found across various medical disciplines To provide a framework to assist doctors in the management of overweight and obesity without restricting the physician's individual judgement To provide a review of the various medical, surgical, and ancillary intervention modalities in the management of obesity To aid primary care physicians in basic management of obesity and subsequent referrals to specialists for more resistant cases
USPSTF (2003)	To summarise the USPSTF recommendations on screening for obesity in adults based on the USPSTF's examination of evidence specific to obesity and overweight in adults To update the 1996 recommendations contained in the Guide to Clinical Preventive Services, Second Edition
Target Population	
ACP (2005)	USA Patients with a body mass index (BMI) ≥30 kg/m^2 Note: The target patient populations vary according to the intervention under consideration, since pharmacological and surgical trials have used different selection criteria with differing BMIs and comorbid conditions. This guideline does not apply to patients with BMIs <30 kg/m^2
ACPM (2001)	USA General adult population (Counselling/Prevention) Overweight and obese adults (Management)
AGA	USA

(2002)	Overweight and obese adults
BWH (2003)	USA Women who are overweight or obese Women who are at risk of becoming overweight or obese
SINGAPORE MOH (2004)	Singapore Adults in Singapore who are obese or overweight, or who are at risk of obesity Note: Children and adolescents are also considered in this guideline; recommendations concerning these younger age groups are covered in a separate synthesis.
USPSTF (2003)	USA Adults seen in primary care settings
Intended Users	
ACP (2005)	Advanced Practice Nurses; Allied Health Personnel; Nurses; Physician Assistants; Physicians
ACPM (2001)	Advanced Practice Nurses; Allied Health Personnel; Dietitians; Nurses; Physical Therapists; Physician Assistants; Physicians
AGA (2002)	Physicians
BWH (2003)	Advanced Practice Nurses; Healthcare Providers; Physician Assistants; Physicians
SINGAPORE MOH (2004)	Advanced Practice Nurses; Allied Health Personnel; Dietitians; Nurses; Physician Assistants; Psychologists/Non-Physician Behavioural Health Clinicians; Public Health Departments; Respiratory Care Practitioners
USPSTF (2003)	Advanced Practice Nurses; Allied Health Personnel; Dietitians; Nurses; Physician Assistants; Physicians; Psychologists/Non-physician Behavioural Health Clinicians
Interventions and Practices Considered	
ACP (2005)	Counselling Dietary and physical activity counselling Management/Treatment Determination of weight loss and other therapeutic goals (for BMI ≥30 kg/m^2) Pharmacotherapy (drugs considered: sibutramine, orlistat, phentermine, diethylpropion, fluoxetine, bupropion) (for BMI ≥30 kg/m^2) Lifestyle modifications such as diet and exercise Surgery (for BMI ≥40 kg/m^2)
ACPM (2001)	Assessment and Preventive Counselling BMI Weight monitoring Dietary and physical activity counselling Management/Treatment Moderate physical activity Dietary interventions (e.g., energy-reduced or low-energy diet [LED]) Pharmacotherapy, such as sibutramine and orlistat (considered but not specifically recommended) Behaviour therapy Surgery (e.g., surgical gastroplasty and gastric bypass (GBP)

AGA (2002)	Assessment Medical evaluation, including a careful history, physical examination (including determination of BMI), and laboratory tests Assessment of weight loss readiness Management/Treatment Determination of therapeutic goals, considering patient readiness for obesity treatment and obesity-related health risk Dietary interventions (e.g., reduction of energy through strategies such as portion-controlled servings, pre-packaged prepared meals and liquid formula meal replacements) Physical activity at varying intensities Behaviour modification (e.g., self-monitoring activities, consultation with local professionals, group behaviour therapy) Pharmacotherapy (e.g., sibutramine hydrochloride [Meridia] and orlistat [Xenical]) Surgery Procedures primarily for gastric restriction (e.g., GBP and vertical banded gastroplasty) Procedures primarily for maldigestion/malabsorption (e.g., biliopancreatic diversion, biliopancreatic diversion with duodenal switch, distal GBP)
BWH (2003)	Assessment BMI Waist circumference Evaluation of risk factors and associated overweight and obesity health risks Identification of potential triggers (e.g., medications, injuries and/or medical conditions, smoking status, or behavioural, cultural, and economic issues that impact food choices or exercise options) Treatment/Management/Prevention Goal setting Dietary therapy (including changes in dietary composition and LED or very-low-energy diets [VLED}) Physical activity and exercise Behaviour therapy Pharmacotherapy (including, appetite suppressants [phentermine], serotonergic agonists [sibutramine], and fat malabsorption agents [orlistat]) Avoidance of medications that may contribute to weight gain Surgery (including GBP, vertical banded gastroplasty, and laparoscopic banding) Weight loss maintenance Referrals Psychiatric and nutrition referrals for binge eating or bulimia
SINGAPORE MOH (2004)	Assessment BMI Waist circumference Evaluation of risk factors for, and secondary causes of, obesity Screening for comorbid conditions Evaluation of patient motivation Management/Treatment Goal setting Dietary therapy (decrease in energy intake, macronutrient composition, meal size and distribution of food intake during day, LED and VLED) Physical activity and exercise Behaviour therapy Pharmacotherapy (e.g., orlistat, sibutramine, phentermine, mazindol, metformin) Non-prescription and off-label weight loss supplements Surgery (including, GBP, vertical banded gastroplasty, or laparoscopic banding) Weight loss maintenance Referrals Evaluation for depression and binge-eating disorders with referrals Note: Interventions for assessment and treatment of overweight and obesity in adolescents and children were also considered in this guideline. These

	interventions are addressed in a separate synthesis.
USPSTF (2003)	Assessment/Screening BMI Waist circumference Management *Combined counselling and behavioural interventions including*: Low-, moderate- and high-intensity counselling Nutritional education Behavioural strategies including the 5-A framework (Assess, Advise, Agree, Assist and Arrange) Note: Treatment interventions such as medications (orlistat and sibutramine) and surgery (GBP, vertical banded gastroplasty and adjustable gastric banding) were considered.

1.1 Measures other than BMI

Dasgupta 1999

Country	India
Setting	Outpatient clinic
Aim or objective	To assess the correlation between waist circumference and waist:hip ratio (WHR) and BMI. Also to assess if a simple measurement such as waist circumference (WC) can be used as an independent indicator for detecting health risk and management
Adults or children	Assumed to be adults
No. of participants	1000. 500 male (M) and 500 female (F)
Prevalence	Only 7% of the males and 16% of the females had BMI ≥25 kg/m^2
Included participants	Mean age 47 years M and 46 years F. People attending clinics
Excluded participants	People with disease such as ascites, Cushings or oedema
Self-referred or not	Nor reported (N/R)
Definitions	Defined as low WC <80 for men, <72 cm for women. Low BMI <25 kg/m^2
Reference standard	BMI
Source of funding	N/R
Results	About 50% of both males and females had WHR above the desirable range (0.80 for females and 0.95 for males). About 99% of females with WC ≥72 cm had either BMI ≥25 kg/m^2 or high WHR ≥0.80 or both. Similarly, 99% of males with WC ≥80 cm had either high BMI ≥25 kg/m^2 or high WHR ≥0.90 or both.

For men with WC ≥80 cm and women with WC ≥72 cm

	M	F
Total	293	**355**
With low WHR	224	**223**
	44.8%	**44.5%**
With high WHR	69	**132**
With high WHR but BMI <25 kg/m^2	66	**126**
	13.2%	**25.2%**
With high WHR and high BMI ≥25 kg/m^2	**3**	**6**
	0.6%	**1.2%**

WC showed a high specificity (98.4% in men and 99.4% in women) and a high sensitivity (98.5% in men and 95.9% in women).

Authors' conclusions	WC is simple to assess and can be used as an independent measure to identify those at risk from either increased body weight or central fat distribution or both.
Quality and notes	– Lack of reporting of methods. Not sure if population is

generalisable.

Gill 2003	
Country	Australia
Setting	Community
Aim or objective	To determine the proportion of a representative population sample of adults who have a BMI classified as normal or underweight, but who also have a WC or WHR that indicates obesity
Adults or children	Adults
No. of participants	2523
Prevalence	Overall prevalence of overweight by BMI over 25 kg/m^2 was 35.2%. For BMI over 30 kg/m^2, prevalence of obesity was 28.5%.
Included participants	Randomly recruited participants. Age range 18 to >60 years.
Excluded participants	…
Self-referred or not	N/R
Definitions	Defined as Action level 1. Low WC <95 cm for men, <80 cm for women. Low BMI <25 kg/m^2 Defined as Action level 2. Low WC <100 cm for men, <90 cm for women. Low BMI <30 kg/m^2
Reference standard	BMI
Source of funding	None reported, but collaboration between Health Services and universities
Results	Among women with a normal BMI, 19.0% had a high WC (≥80 cm) and 8.5% had a high WHR (>0.85). Among males with a normal BMI, 3.4% had a high WC (≥95 cm) and 0.1% had a high WHR (>1.0)
Authors' conclusions	The authors concluded that BMI, WHR and WC all have a role in the identification of those who are obese or overweight
Quality and notes	+ No blinding

Goodman-Gruen 1996	
Country	USA
Setting	Community
Aim or objective	To describe sex differences in obesity and body fat distribution using commonly used assessment methods in men and women age 65–96 years.
Adults or children	Adults
No. of participants	385 older people. 140 M and 245 F
Prevalence	…
Included participants	First 385 participants. Mean age 80 (range 65 to 96) years
Excluded participants	…
Self-referred or not	N/R
Definitions	…
Reference standard	…
Source of funding	National Institute of Diabetes and Digestive and Kidney Diseases. Weight Watchers Foundation
Results	WHR was more strongly correlated with the truncal fat:leg fat ratio in women than in men. WHR correlated significantly with the subscapular:triceps skinfold thickness ratio in women only. In both sexes, WC was more strongly correlated with BMI and the % body fat by bioelectric impedance analysis and dual-energy X-ray absorptiometry (DEXA) than with the WHR. In those aged >80 years, age stratification showed that the WHR was not correlated with any other measurement of obesity or fat distribution in men and correlated only with subscapular skinfold thickness in women. WC correlated significantly with almost all other measures of central obesity in older and younger men and women.

Authors' conclusions	Estimates of upper body (central) fat distribution appear to be age specific. After age 80 years, the WHR is a poor method of assessing central or visceral adiposity, and WC is a better measure of body fat distribution. But suggest that several measures should be done.
Quality and notes	– Possible some blinding as several tests were done that may have required different operators (e.g. DEXA and bioimpedance). Study not designed to evaluate the validity of different measures but to compare the concordance.

Han 1997	
Country	UK and Netherlands
Setting	Not clear – samples from World Health Organization study 1989.
Aim or objective	To assess the influences of height and age on the differences in waist circumference between individuals of different stature
Adults or children	Adults (assumed)
No. of participants	Four samples; 4881 and 384 from the Netherlands, and 1918 and 494 from Scotland. Overall 3319 M and 4358 F
Prevalence	Overall, mean (SD) BMI (kg/m^2) 25.8 (3.6) for men and 25.7 (4.9) for women.
Included participants	Samples from four previous anthropometric studies.
Excluded participants	…
Self-referred or not	Not clear.
Definitions	…
Reference standard	N/R?
Source of funding	N/R
Results	Analysis of the samples found that height had a very limited influence on the differences in WC between individuals. Without adjusting for age, height accounted for 0.3 to 3.5% of variance in WC in men and 0.1 to 2.5% in women. When age was adjusted for, this became 0.4 to 7.5% for men and 0.0 to 2.6% in women.
Authors' conclusions	Height and weight had limited influences on the differences in WC between white people of difference stature. WC alone may be used to indicate adiposity or to reflect metabolic risk factors. In contrast, the effect of height on body weight is important.
Quality and notes	+

Lean 1995	
Country	UK
Setting	Community
Aim or objective	To test the hypothesis that a single measurement, waist circumference, might be used to identify people at health risk both from being overweight and from having a central fat distribution
Adults or children	Adults
No. of participants	904 M and 1014 F in determination sample. 86 M and 202 F in validation sample. Total 2206.
Prevalence	52.13% for Action level 1 and 18.64% for Action level 2
Included participants	Randomly recruited participants. Age range 25 to 74 years.
Excluded participants	People who were chair-bound
Self-referred or not	N/R
Definitions	Defined as Action level 1. Low WC <94 cm for men, <80 cm for women. Low BMI <25 kg/m^2. Defined as Action level 2. Low WC<102 cm for men, <88 cm for women. Low BMI <30 kg/m^2.
Reference standard	BMI
Source of funding	Scottish Home and Health Department. University.
Results	WC ≥94 cm for men and ≥ 80 cm for women identified

	participants with high BMI ≥25 kg/m^2) and those with lower BMI but high WHR (≥0.95 for men, ≥0.80 women) with a sensitivity of >96% and specificity >97.5%. WC ≥102 cm for men or ≥88 cm for women identified participants with BMI ≥30 kg/m^2 and those with lower BMI but high WHR with a sensitivity of >96% and specificity >98%, with only about 2% of the sample being misclassified.
Authors' conclusions	WC could be used in health promotion programmes to identify individuals who should seek and be offered weight management. Men with WC ≥94 cm and women with waist circumference ≥80 cm should gain no further weight; men with waist circumference ≥102 cm and women with waist circumference ≥88 cm should reduce their weight.
Quality and notes	+ No blinding, some validation.

Logue 1995	
Country	USA
Setting	Family practice community
Aim or objective	To describe the prevalence of general and central obesity, and to compare different measurements
Adults or children	Adults
No. of participants	414. 130 M and 284 F
Prevalence	56.2% M and 57.6% F had BMI (kg/m^2) >27.8 for men and >27.3 for women)
Included participants	Adults aged ≥45 years who attended family practice centres.
Excluded participants	…
Self-referred or not	N/R
Definitions	Men with BMI >27.8 kg/m^2 and women with BMI >27.3 kg/m^2 classified as having some degree of obesity. Men with WHR >0.95 and women with WHR >0.80 classified as having some degree of central obesity.
Reference standard	BMI
Source of funding	Summa Heath System Foundation and the family practice centres
Results	57% of patients had an elevated BMI. 50% of men (95% CI 46 to 55) and 78% of women (95% CI 75 to 80) had central obesity based on elevated WHRs. Using an elevated WHR as the standard for central obesity, elevated WHR as the standard for central obesity, elevated BMI had a positive predictive value of only 64% and a negative predictive value of 68% in men. For women, the corresponding positive and negative predictive values were 84% and 31%, respectively.
Authors' conclusions	The data indicate that the practice of using only scales to identify 'overweight' patients should be re-evaluated since doing so will miss patients at risk. In primary care patients, particularly those ≥50 years of age, weight-for-height indices such as BMI result in under-diagnosis of central obesity.
Quality and notes	– No blinding

Molarius 1999	
Country	Various, including UK
Setting	Community
Aim or objective	To examine the sensitivity and specificity of WC cut-off points when applied to 19 populations with widely different prevalences of overweight.
Adults or children	Adults
No. of participants	>32,000 men and women aged 25–64 years from 19 (18 in women) populations participating in the second MONItoring trends and determinants in CArdiovascular disease (MONICA)

	survey from 1987–92
Prevalence	54.87% for Action level 1 and 31.74% for Action level 2
Included participants	Aged 25–64 years from 19 (18 in women) populations.
Excluded participants	…
Self-referred or not	N/R
Definitions	Defined as Action level 1. Low WC <94 cm for men, <80 cm for women. Low BMI <25 kg/m^2. Defined as Action level 2. Low WC<102 cm for men, <88 cm for women. Low BMI <30 kg/m^2.
Reference standard	BMI
Source of funding	Governments, research councils and charities. Also the World Health Organization (WHO).
Results	At waist action level 1 (WC ≥94 cm in men and ≥ 80 cm in women), sensitivity varied between 40% and 80% in men and between 51% and 86% in women between populations when compared with the cut-off points based on BMI (≥25 kg/m^2) and WHR (≥0.95 for men, ≥0.80 for women). Specificity was high (≥90%) in all populations. At waist action level 2 (WC ≥102 cm and ≥88 cm in men and women, respectively, BMI ≥30 kg/m^2), sensitivity varied from 22% to 64% in men and from 26% to 67% in women, whereas specificity was >95% in all populations. Sensitivity was in general lowest in populations in which overweight was relatively uncommon, whereas it was highest in populations with relatively high prevalence of overweight.
Authors' conclusions	Cut-off points based on WC as a replacement for cut-off points based on BMI and WHR should be viewed with caution. Based on the proposed waist action levels, very few people would unnecessarily be advised to have weight management, but a varying proportion of those who would need it might be missed. The optimal screening cut-off points for WC may be population specific.
Quality and notes	+ Used UNK-GLA data only. Action level 1 from files on internet. No blinding.

Molarius 1999	
Country	Various, including UK
Setting	Community
Aim or objective	To assess differences in waist and hip circumferences and WHR measured using a standard protocol among populations with different prevalences of overweight. In addition, to quantify the associations of these anthropometric measures with age and degree of overweight.
Adults or children	Adults
No. of participants	>32,000 men and women aged 25–64 years from 19 (18 in women) populations participating in the second MONItoring trends and determinants in CArdiovascular disease (MONICA) survey from 1987–1992
Prevalence	…
Included participants	Aged 25–64 years from 19 (18 in women) populations
Excluded participants	…
Self-referred or not	…
Definitions	Defined as Action level 1. Low WC <94 cm for men, <80 cm for women. Low BMI <25 kg/m^2. Defined as Action level 2. Low WC<102 cm for men, <88 cm for women. Low BMI <30 kg/m^2.
Reference standard	N/R
Source of funding	Governments, research councils and charities. Also WHO.
Results	Age-standardised mean WC range between populations 83–98 cm in men and 78–91 cm in women. Mean hip circumference range 94–105 cm and 97–108 cm in men and women, respectively, and mean WHR 0.87–0.99 and 0.76–0.84,

	respectively. Together, height, BMI, age group and population explained about 80% of the variance in WC. BMI was the predominant determinant (77% in men, 75% women). Similar results were obtained for hip circumference. However, height, BMI, age group and population, accounted only for 49% (men) and 30% (women) the variation in WHR.
Authors' conclusions	Considerable variation in waist and hip circumferences and WHR were observed among the study populations. WC and WHR, both of which are used as indicators of abdominal obesity, seem to measure different aspects of the human body: WC reflects mainly the degree of overweight whereas WHR does not
Quality and notes	+

Molarius 2000	
Country	The Netherlands
Setting	Community
Aim or objective	To examine the applicability of the suggested waist action levels in an older population
Adults or children	Adults
No. of participants	Total 6423 men and women aged ≥55 years. 2640 M and 3783 F.
Prevalence	61.09% for Action level 1 and 14.56% for Action level 2
Included participants	Aged between 55 and >85 years. Nursing home residents accounted for approx 11% of sample.
Excluded participants	…
Self-referred or not	N/R
Definitions	Defined as Action level 1. Low WC <94 cm for men, <80 cm for women. Low BMI <25 kg/m^2. Defined as Action level 2. Low WC <102 cm for men, <88 cm for women. Low BMI <30 kg/m^2.
Reference standard	BMI
Source of funding	N/R
Results	At waist action level 1 (WC ≥94 cm in men, ≥80 cm in women), sensitivity was 71% in men and 86% in women for detecting those with high BMI (≥25 kg/m^2) and/or WHR (≥0.95 in men, or ≥0.80 in women). At waist action level 2 (WC ≥102 cm in men, ≥88 cm in women in comparison with BMI ≥30 kg/m^2 and/or WHR ≥0.95 in men, ≥0.80 in women), sensitivity was considerably lower: 35% in men and 59% in women. This was mainly due to a large proportion of participants with low waist and BMI but high WHR. Specificity was high (>90%) at both action levels. Cardiovascular disease (CVD) risk factors, except smoking, tended to increase with increasing WC, WHR and BMI.
Authors' conclusions	The suggested cut-off points for WC were only to a limited degree useful in identifying participants with overweight and obesity and/or central fat distribution in an older population. This concerned especially the upper cut-off point (waist action level 2) and was mainly due to the increased central distribution of fat with advancing age
Quality and notes	+

Sonmez 2003	
Country	Turkey
Setting	Clinic?
Aim or objective	To determine BMI, WC and WHR in cases with angiographically established coronary artery disease (CAD) and to compare the obesity degrees established according to the ranges determined by the International Guidelines Committees for BMI, waist circumference and WHR

Adults or children	Adults
No. of participants	617. 516 M and 101 F
Prevalence	46.99% for Action level 1 and 17.99% for Action level 2
Included participants	Consecutive cases undergoing first coronary angiography with at least 50% narrowing of at least one artery. Mean age 57.2±10.8 years
Excluded participants	…
Self-referred or not	…
Definitions	Defined as Action level 1. Low WC <94 cm for men, <80 cm for women. Low BMI <25 kg/m^2. Defined as Action level 2. Low WC <102 cm for men, <88 cm for women. Low BMI <30 kg/m^2.
Reference standard	BMI
Source of funding	None reported
Results	Overweight cases comprised approximately half of the patients in both sexes. In males, the percentage of obese cases with regard to BMI was 15%, while males with action level 2 WC were 20%. Obese male patients whose WHRs were ≥0.95 were 51%. In female cases, corresponding percentages of obesity were estimated to be 32, 72 and 86%, respectively.
Authors' conclusions	In the same patient groups, the prevalence of obesity, defined by BMI, WC and WHR, could vary threefold.
Quality and notes	– Not blinded to anthropometric measures

Taylor 1998	
Country	New Zealand
Setting	Community
Aim or objective	To construct receiver operating characteristic (ROC) curves to assess the value of BMI as a screening measure for total adiposity and to examine WHR and WC as measures of central fat distribution.
Adults or children	Adults
No. of participants	96 F
Prevalence	…
Included participants	Recruited women by advertisement. Aged 16 to 80 years.
Excluded participants	…
Self-referred or not	N/R
Definitions	…
Reference standard	…
Source of funding	N/R
Results	BMI (75th percentile=27.3) performed well as a screening measure of total adiposity, correctly identifying 83% of participants with a high body fat mass while misclassifying only eight participants (four false-negatives [participants with high fat mass who were in the low BMI category] and four false-positives [participants with a low fat mass who were in the high BMI category]). The screening performance of WHR (75th percentile=0.81) was lower, accurately categorising 58% of participants while misclassifying 28 participants. By contrast, WC (75th percentile=86.9 cm) was significantly better than WHR at screening for regional fat distribution, accurately classifying 83% of participants and misclassifying eight participants (p<0.05).
Authors' conclusions	BMI and WC provide simple yet sensitive methods for the estimation of total and central adiposity in groups of adult women.
Quality and notes	+ Did not use BMI as the reference standard

1.2 Measures and morbidity in ethnic populations*

Bose 1995 and Bose 1996	
Country	UK
Setting	GP practice
Aim or objective	To compare the anatomical distribution of subcutaneous fat in adult White and Pakistani migrant males
Adults or children	Adults
No. of participants	Letters sent to 400 Asian males and 1000 randomly selected white males. 25% response rate. Participants=362 (100 Pakistani, 262 white males)
Included participants	Adult males
Excluded participants	Adult females
Self-referred or not	Letter invitation
Measures	BMI and skinfold thickness tests (subscapular, suprailiac, abdomen, midaxillary, forearm)
Results	There were no significant differences in the distribution of BMI between the two groups. However, Pakistani groups had significantly higher truncal adiposity and total subcutaneous adiposity. Upper extremity adiposity was significantly lower. For a given level of generalised obesity, the amount and distribution of fat is significantly different in these two ethnic groups.
Authors' conclusions	These preliminary results clearly indicate that there is a tendency for accumulation of truncal adiposity in the abdominal region in Asian men of Pakistani origin compared with White men irrespective of the level of generalised (BMI) adiposity.
Quality and notes	– Consistent with previous UK-based study by MeKeigue et al 1991. Note that white group significantly older than Pakistani group.

Lovegrove 2003	
Country	UK
Setting	Community
Aim or objective	To determine whether the positive statistical associations between measures of total and regional adiposity and measures of glucose, insulin and TAG (TAG) metabolism reported in white men, are also observed in UK Sikhs.
Adults or children	Adults
No. of participants	55 healthy white and 55 healthy UK Sikh men
Included participants	Included if non-smoker, not on any hypolipidaemic medication, or any other medication known to affect lipoprotein metabolism.
Excluded participants	Excluded if had diabetes, liver or endocrine dysfunction, malabsorption syndrome, anaemia, or had previously had a coronary event. Also excluded if BMI <20 or >37 kg/m^2, if aged <27 or >68 years, had total cholesterol (TC) >8 mmol/l, TAG >4 mmol/l, glucose >8 mmol/l, gamma-glutamyltransferase >80 IU/l, haemoglobin <12.5 g/dl, activity levels exceeded more than two 20 min sessions of aerobic exercise per week. Sikh men had to be resident in UK for at least 2 years prior to inclusion.
Self-referred or not	Recruited through posters, leaflets, advertisements, letters, interviews on radio and television, and word of mouth.
Measures	BMI, WC, sum of skinfold thicknesses, subscapular skinfold thickness, suprailiac skinfold thickness
Results	Sikh men had significantly higher body fat, with the sum of the

* Evidence tables only done for UK studies.

	four skinfold thickness measurements (p=0.0001) and subscapular skinfold thickness value (p=0.009) higher compared with the white men. Sikh volunteers also had characteristics of the metabolic syndrome: lower HDL-cholesterol (p=0.07), higher TAG (p=0.004), higher % LDL_3 (p=0.0001) and insulin resistance (p=0.05). Both ethnic groups demonstrated positive correlations between insulin and WC (white: r=0.661, p=0.0001; Sikh: r=0.477, p=0.0001). White men demonstrated significant positive correlations between central adiposity (r=0.275, p=0.04), other measures of adiposity (BMI and suprailiac skinfold thickness) and plasma TAG, whereas Sikh men showed no correlation for central adiposity (r=0.019, NS) and TAG with a trend to a negative relationship between other measures (Ssk and suprailiac) which reached near significance for subscapular skinfold thickness and TAG (r=–0.246, p=0.007). The expected positive association between insulin and TAG was observed in white men (r=0.318, p=0.04) but not in Sikh men (r=0.011, NS).
Authors' conclusions	In white men, expected positive association between plasma TAG and centralised body fat was observed. However, a lack of association between centralised, or any other measure of adiposity, and plasma TAG was observed in matched Sikh men, although both groups showed a positive association between centralised body fat and insulin resistance,(less strong for Sikhs). These findings in the Sikh men were not consistent with the hypothesis that there is a clear causal relationship between body fat and its distribution, insulin resistance, and lipid abnormalities associated with the metabolic syndrome, in this ethnic group.
Quality and notes	+ Seem to be very restrictive inclusion/exclusion criteria, so not sure how generalisable

McKeigue 1991	
Country	UK
Setting	Recruitment from GP practices and factories
Aim or objective	To compare the relation of central obesity with diabetes and cardiovascular risk between Europeans, South Asians and Afro-Caribbeans
Adults or children	Adults
No. of participants	Males: European 1515, South Asian 1421, Afro-Caribbean 209. Females: European 246, South Asian 291
Included participants	Factory sample – males >40 years old (of 1141 men, 808 took part)/GP sample 16 GP practices – males 40–64 years (for three practices women included) 63% response rate.
Excluded participants	GP sample – all those already included in industrial sample. Patients with cancer, renal failure, severe disability or severe psychiatric disturbance.
Self-referred or not	Invitation by letter
Measures	Skinfold thickness, BMI, WHR
Results	The key findings were that ethnicity differences were not found in the correlation of WHR with HDL, TAG and blood pressure (BP). However, controlling for WHR did not explain South Asian–European differences in diabetes prevalence and serum insulin
Authors' conclusions	These results confirm the existence of an insulin resistance syndrome, prevalent in South Asian populations and associated with a pronounced tendency to central obesity in this group.
Quality and notes	+ A potential implication of this study is that WHR cut-offs for obesity as a predictor of diabetes may need to be lower for South Asian

Patel 1999	
Country	UK
Setting	Recruitment from community (conducted in research centre)
Aim or objective	To assess how four proxy measures of abdominal obesity (WC, WHR, waist:height ratio, C index) were associated with features of metabolic syndrome in three ethnic groups
Adults or children	Adults
No. of participants	629 Europeans (320 men, 309 women), 380 Chinese (183 men, 197 women), 597 South Asians (275 men, 322 women) aged 25–64 years
Included participants	Aged 25 to 64 years (further details in additional publications)
Excluded participants	…
Self-referred or not	Recruited from name analysis, and invited to participate.
Measures	WC, WHR, waist to height ratio, C index
Results	Most proxy measures of abdominal obesity were associated with features of metabolic syndrome. However, across ethnic groups, WC and waist-to-height ratio were the most consistent and WHR and C index were least.
Authors' conclusions	Not all the proxy measures of abdominal obesity were consistently related to features of the metabolic syndrome across the ethnic groups studied. However, WC and waist:height ratio were the most consistent and WHR the least when comparing across the ethnic groups.
Quality and notes	+ Implication of this study is that some measures of abdominal obesity are more consistently associated with metabolic syndrome than others. It is suggested that the problems with WHR are due to genetic differences in pelvic dimensions.

1.3 Dietary interventions

1.3.1 2.51 MJ (600 kcal)/day deficit or low-fat diet† compared with control

Weight loss

Cohen 1991 (in HTA) cluster RCT	
Aim	To test the feasibility of a low-technology office-based approach to weight reduction in obese hypertensive patients
Participants	People aged 20 to 75 years who were overweight (BMI [kg/m^2] ≥27.8 men, 27.3 women) with hypertension *30 total – 22 F, 8 M. Mean age 59.3 years intervention (*n=*15), 59.7 years control (*n=*15). Mean BMI (kg/m^2) 34.2 intervention, 34.0 control.*

† Due to lack of reporting, healthy eating advice and diets where the fat or energy restriction was not estimable are included in this category.

Intervention (including details of diet)	Physicians received special instruction and materials in weight reduction methods; reviewed diet of participant using questionnaire and suggested dietary changes, gave participant diet history sheet, information and advice sheet; advised participants to reduce energy content of diet and set short-term goals; used methods of encouragement such as reinforcement, each month reviewed participants previous days food intake. *Goal of diet to reduce energy content without radically changing patients' lifestyle. Given instruction sheet on low-energy alternatives to high-energy foods.*
Control	*Participants received usual care, physicians free to refer patients for dietary advice or provide themselves but did not receive any special weight reduction instructions or materials.*
Length of follow-up	12 months
Results	*At 6 months, mean (SD) weight change in kg was –1.80 (3.4) in the diet group, and 0.56 (2.5) in the control group. The difference was statistically significant (p=0.04).* At 12 months, mean (SD) weight change in kg was –0.88 (4.0) in the diet group, and 1.3 (3.0) in the control group. The difference was not statistically significant.
Quality and comments	Possible intention to treat (ITT) analysis. Blinded assessment not reported. Random allocation but no description of concealment. *Mean BMI noted as highest mean BMI in HTA. No details of accounting for cluster effect.*

DISH 1985 (in HTA) RCT	
Aim	To determine whether dietary modification can increase the number of patients who remain normotensive after drug withdrawal
Participants	Hypertension Detection and Follow-up Program Stepped Care participants (*n*=496 in study overall) who had greater than 5 years antihypertensive therapy and stratified by weight (120% or more of ideal body weight [IBW]) to no dietary intervention, sodium control, or weight control diets. 176 total – *116 F, 60 M. Mean age 56.1 years intervention (*n=*87), 57.2 years no intervention (*n=*89). Mean weight (SD) 86.0 (17.3) kg intervention, 89.9 (17.8) kg no dietary intervention.*‡
Intervention (including details of diet)	Standardised stepped withdrawal of antihypertensives medication during weeks 2 to 8. Medication restarted if diastolic blood pressure DBP 95–99 mmHg three times in 3 months, 100–104 mmHg twice in a month, or 105 mmHg at any time. Dietary intervention began at 1 to 2 weeks post baseline with the aim of desirable weight according to the Metropolitan Life Insurance standards. Diet involved decreasing energy, with relatively little emphasis on physical activity and keeping electrolytes constant. Little emphasis on physical activity.
Control	*As above, but no dietary intervention.*
Length of follow-up	56 weeks
Results	At 12 months (*56 weeks*), mean (SD) weight change in kg was –4.00 (5.00) in the intervention group, and –0.46 (3.60) in the no dietary intervention group. Mean weight change in the intervention group compared to no dietary intervention was –3.54 (95% CI –4.98 to –2.10). No significant differences were seen in weight loss between men and women.
Quality and comments	Study also included continued medication control, and no medication sodium restriction group. Possible ITT analysis. Blinded assessment not done. Random allocation but no description given. *Only reported weight control results.*

Frey-Hewitt 1990 (in HTA) RCT	
Aim	To determine the effect of energy restriction and exercise training on weight loss and resting metabolic rate

‡ Text in italics taken from either evidence tables or text published in the original review.

Participants	Sedentary men (age 30–59) who were overweight (120–160% of IBW) *155 total – all men. Mean (SD) weight 93.63 (9.16) kg in diet group (*n=*51), 94.14 (8.8) kg in physical activity group (*n=*52), 94.99 (10.63) kg in control group (n=52) (weight for completers only).*
Intervention (including details of diet)	Energy requirements for individuals determined at baseline by 7-day food records. Diet designed to reduce total body fat by one-third. Advised to reduce food quantity without changing proportions of fat, carbohydrate, protein, alcohol. Individual weigh loss goals determined by amount of body fat; 300–500 kcal/day deficit to produce 0.3–0.6 kg fat loss per week. Instruction and behavioural strategies to for weight loss for first 9 months, then weight maintenance for about 2 months. Monthly activity and 24 h energy intake monitored, and if changed activity for more then 3 months, counselled to return to baseline habits. (See physical activity review for detail of physical activity intervention)
Control	*Energy requirements determined at baseline by 7-day food records. Advised to keep weight stable with no added energy restriction or physical activity.*
Length of follow-up	12 months
Results (3, 6 and 12 months, control and intervention results)	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –6.68 (3.94) in the diet group, and 0.38 (3.66) in the control group. Mean weight change in the intervention group compared to control was –7.06 (95% CI –8.77 to –5.35).
Quality and comments	Not ITT analysis. Blinded assessment not done. Random allocation but no description of concealment. Not in BT review, as no detail of techniques used. Also results for diet-only group reported here.

Hankey 2001 (in HTA) RCT (pilot)	
Aim	To determine the effectiveness of comprehensive dietary counselling, including weight management advice, in people post MI.
Participants	Survivors of myocardial infarction (MI) participating in cardiac rehabilitation programmes. (Results reported for people BMI >25 kg/m^2 only.) *54 total – 10 F, 44 M. Mean age 57 (range 41 to 72) years in the intervention group (*n=*28), and 57 (range 40 to 75) years in the control group (*n=*26). Mean BMI (SD) (kg/m^2) 28.6 (2.8) intervention group, and 30.4 (3.9) in control group.*
Intervention (including details of diet)	Cardiac rehabilitation; one group session of 30–60 min with a dietitian and 12 practical physical activity sessions of about 30 min each. Four 1 h sessions of individual dietary counselling during the initial 12 weeks, including weight management advice, individualised 2.51 MJ (600 kcal)/day deficit, and following Scottish dietary targets *(minimum five portions of fruits and vegetables daily, two to three portions of oily fish weekly, reduction in saturated fat to <10% dietary energy).*
Control	*As above for cardiac rehabilitation, but no specific weight management advice.*
Length of follow-up	52 weeks
Results	*Only 12 month outcomes reported.* At 12 months, mean (SD) weight change in kg was –0.60 (5.30) in the diet group, and 2.40 (5.00) in the control group. Mean weight change in the intervention group compared to control was –3.00 (95% CI –5.86 to –0.14) kg.
Quality and comments	Baseline BMI appears different between groups. ITT analysis done. Results from contact with the author, and refer only to those individuals with BMI >25 kg/m^2. Blinded assessment not done. Random allocation but no description of concealment.

HOT 1999 (in HTA) RCT	
Aim	To determine whether a dietary behavioural intervention resulting in weight loss would allow fewer medications or lower doses of medication to achieve goal BP in very obese, older people with hypertension

Participants	Older people with a BMI ≥27 kg/m^2, who met the HOT study criteria Patients were randomised to reach a target diastolic BP (DBP): ≤90, ≤85 or ≤80 mmHg by taking a five-step drug treatment. *102 total – 53 F, 49 M. Mean (SD) age, 57 (9) years in the diet group (*n=*55), 59 (7) years in the control group (*n=*56) (data for completers only). Mean (SD) BMI (kg/m^2) 34 (6) in the diet group and 34 (6) in the control.*
Intervention (including details of diet)	Weight loss counselling (food selection and preparation, establishing weight reduction goals, energy and fat restriction) by weight loss dietitian with 10 days of randomisation. *Not counselled to exercise.* Counselled again at 2–4 weeks, and attended group support sessions twice monthly for first 3 months, then every 3–6 months, weight measured at 6-monthly intervals.
Control	*Research nurses told participants to lose weight, but no formal diet counselling or group support given. Weight measured only at 6-monthly intervals.*
Length of follow-up	30 months.
Results	*At 3 months, mean weight change (SD) was –2.7 (3.4) kg in the weight loss group compared with –1.7 (2.3) kg in the control group. But the difference was not significant (*p=*0.09).* *At six months, mean weight change (SD) was –3.2 (4.3) kg in the weight loss group compared with –1.8 (2.7) kg in the control group. The difference was significant (*p=*0.05).* *After 6 months, the weight loss group showed a gradual, continuous return to baseline, but the control group showed a tendency towards weight loss.* At 12 months, mean weight change (SD) was –1.70 (6.40) kg in the weight loss group compared with –1.30 (6.28) kg in the control group. Mean weight change in the intervention group compared with control was –0.40 (95% CI –2.86 to 2.06). At 18 months, mean weight change (SD) was –1.80 (6.42) kg in the weight loss group compared with –1.40 (6.31) kg in the control group. Mean weight change in the intervention group compared with control was –0.40 (95% CI –2.87 to 2.07). At 24 months, mean weight change (SD) was –1.70 (6.40) kg in the weight loss group compared with –1.90 (6.45) kg in the control group. Mean weight change in the intervention group compared with control was 0.20 (95% CI –2.29 to 2.69). At 30 months, mean weight change (SD) was –1.30 (6.28) kg in the weight loss group compared with –2.00 (6.48) kg in the control group. Mean weight change in the intervention group compared with control was 0.70 (95% CI –1.78 to 3.18).
Quality and comments	Diet (weight loss) group were considerably taller than control (*p*=0.05). Possible ITT analysis. Blinded assessment not done. Author contacted for results by treatment group. Random allocation but no description of concealment.

HPT 1990 (in HTA) RCT	
Aim	To assess the effect of dietary counselling and dietary changes on BP in healthy people
Participants	In reduced energy counselling group, *healthy adults aged 25 to 49 years with 'high-normal' BP* who were overweight (BMI [kg/m^2] >25 men, >23 for women). In other groups (control, other counselling), participants did not have to be overweight. *251 total – 82 F, 169 M. Mean age 38 years intervention (*n=*126), 39.4 control (*n=*126). Mean BMI (kg/m^2) 29.0 intervention, 28.0 control.*
Intervention (including details of diet)	Energy restriction dietary counselling where individual goal was for participants to attain IBW and group goal was to reduce mean body weight by 5%. Participants recommended to include daily servings of low-fat milk and dairy products, choose fish, poultry or lean cuts of meat, decrease fats in cooking and at the table. Decrease high-energy desserts, snacks and drinks. Limit alcohol and increase fruit and vegetable intake. Dietary change counselling related to meal planning and rationing, food purchase, label reading. Included didactic presentation and demonstrations, token incentives, bimonthly newsletters, telephone calls if missed session, daily food records.
Control	*No dietary counselling.*
Length of follow-up	3 years

Results	*At 6 months, mean (SD) weight change (kg) was –5.58 (2.86) in the diet group, and 0.18 (2.95) in the control group. Mean weight change in the intervention group compared with control was –5.76 (95% CI –6.51 to –5.01).* At 36 months, mean (SD) weight change in kg was –1.63 (4.43) in the diet group, and 1.86 (4.36) in the control group. Mean weight change in the intervention group compared with control was –3.49 (95% CI –4.63 to –2.35).
Quality and comments	Baseline unequal for genders. 24.8% in intervention group vs 40.5% control. ITT analysis done. Blinded assessment done. Random allocation but no description of concealment.

ODES 1995 (in HTA) RCT	
Aim	The primary aim of the trial was to compare the isolated and combined effects of the diet and exercise on the variables fibrinogen, fibrinolytic capacity, coagulation factor VII, and platelet volume. Secondary aims were the effects on other coagulation and fibrinolytic components and activities; lipids and lipoproteins; fatty acids; glucose and insulin response to a glucose load; clinical, physiological, and anthropometric variables; and quality of life
Participants	*Men and women aged 41 to 50 years who were overweight (BMI >24 kg/m^2) and sedentary.* *219 total – 21 F, 198 M. Mean (SD) age 44.9 (2.5) years. Mean (SD) BMI (kg/m^2) 29.54 (3.89) diet group (*n=*55), 28.56 (3.22) exercise group (*n=*54), 28.57 (3.47) diet and exercise group (*n=*67), 28.30 (3.15) control group (*n=*43).*
Intervention (including details of diet)	Dietary counselling with spouse at baseline then individually at 3- and 9-month follow-up sessions. Diet adapted to individual's risk profile with main focus on energy restriction in those overweight, increase in fish and vegetables, decrease in saturated fat, cholesterol, sugar, and salt restriction for those with elevated BP. Weight targets agreed and set. 180 food-frequency questionnaire at baseline and 12 months. Advised to stop smoking. (See physical activity review for details of exercise intervention)
Control	*Told not to change lifestyle and that after 12 months would receive dietary advice and supervised physical training. Advised to stop smoking.*
Length of follow-up	12 months
Results	*Only 12 month outcomes reported.* At 12 months, mean (SD) weight change in kg was –4.00 (5.05) in the diet group, and 1.10 (2.62) in the control group. Mean weight change in the intervention group compared with control was –5.10 (95% CI –6.68 to –3.52).
Quality and comments	TC and LDL levels significantly lower in the exercise and the diet and exercise groups ($p<0.05$). ITT not done. Only blood analyses blinded. Discrepancy between results in published papers. Good concealment of allocation.

Pritchard 1997 (in HTA) RCT	
Aim	To compare the effects of two weight loss interventions, diet or exercise, on changes in bone, fat and lean tissue
Participants	*Healthy men aged 35 to 55 years who were overweight (BMI 26 to 35 kg/m^2).* *66 total – all men. Mean age (SD) 43.6 (6.0) years in the diet group (*n=*24), 42.3 (4.5) years in the control group (*n=*20). Mean BMI (SD) (kg/m^2) 29.0 (2.8) in the diet group, 28.6 (2.8) in the control. Data for 12-month completers only (*n=*58 overall).*
Intervention (including details of diet)	Advised to follow low-fat intake of *20 to 22*% energy as fat per day, to avoid foods rich in fat, discouraged from eating more than one sweet per day and more than two alcoholic drinks per day. Personalised diet plan to meet recommended daily intakes for use in Australia, given in *The Weight Loss Guide* by the Australian Heart Foundation. Exercise restricted to pre-study level. Completion of daily adherence calendar. At 13 months, exercise intervention was added. (See physical activity review for detail of exercise intervention)
Control	*Attended monthly weight monitoring sessions where counselled to follow usual food and exercise habits. Told participants that they would be able to enter the weight loss study at the end of the study. Both diet and physical activity interventions were added at 13 months.*

Length of follow-up	18 months
Results	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –6.40 (3.30) in the diet group, and 0.30 (2.40) in the control group. Mean weight change in the intervention group compared with control was –6.70 (95% CI –8.57 to –4.83).
Quality and comments	ITT analysis done. Blinded assessment not done. Real possibility of disclosure of allocation, although some attempt made at concealment. Author provided unpublished report. Data up to 12 months only used. Discrepancy in data between reports.

Pritchard 1999 (in HTA) RCT	
Aim	To study the clinical and cost outcomes of providing nutritional counselling to people with one or more of the following conditions: overweight, hypertension, type 2 diabetes.
Participants	*Men and women aged between 25 and 65 years with either hypertension, type 2 diabetes or were overweight (BMI >25 kg/m^2).* *273 total – 198 F, 75 M. 199 participants were aged <50 years. Mean weight (kg) 91.7 in the dietitian led intervention group (*n=*92), 85.5 in the doctor and dietitian led intervention group (*n=*88), 89.1 in the control group (*n=*90).* Majority were from disadvantaged socioeconomic groups (58% most disadvantaged quartile and 20% more disadvantaged quartile).
Intervention (including details of diet)	Counselling focused on principles of good nutrition and exercise and addressed problem areas in lifestyle and dietary patterns. Counselled on food, shopping, cooking, food selection, meal planning, exercise programmes. Advised to complete food records and diet history. Advised to reduce total energy intake and to reduce % energy from fat to ≤30% (carbohydrate ≥50% and protein 20%). Discouraged from smoking and to have two or more alcohol-free days per week, with two or fewer alcoholic standard drinks for women and four for men. In the doctor and dietitian group, as well as counselling above, participants were seen by the GP at baseline and saw same GP on two other occasions during the 12 months for 5 min each time to encourage and monitor the participant.
Control	*Received results of initial screening and advised to discuss queries with the GP at appointment. Received usual care from GP but no dietitian counselling. Mailed to re-attend at 12 months.*
Length of follow-up	12 months
Results	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –5.10 (7.36) in the dietitian group and 0.60 (6.08) in the control group. Mean weight change in the intervention group compared with control was –5.70 (95% CI –8.05 to –3.35). At 12 months, mean (SD) weight change in kg was –6.20 (7.67) in the dietitian and doctor group, and 0.60 (6.08) in the control group. Mean weight change in the intervention group compared with control was –6.80 (95% CI –9.17 to –4.43).
Quality and comments	*Control groups halved.* ITT analysis done. Blinded assessment not done. Real possibility of disclosure of allocation, although some attempt made at concealment. *Results only for overweight group.*

TAIM 1992 (in HTA) RCT	
Aim	To determine the relative efficacy of drug and dietary measures in mild hypertension.
Participants	*People aged 21 to 65 years, who were overweight (110 to 160% IBW) and with mild hypertension.* *179 total at 6 months – 'significantly more men than women' – no details. Mean age 48.6 years intervention (*n=*100), 46.8 years control (*n=*100). Mean BMI (kg/m^2) 30.45 intervention and 30.14 control.*

Intervention (including details of diet)	Diet counselling and nutrition education aimed at behaviour change, related activities (exercise) aimed at weight loss to achieve BP control, given individual goal of energy intake and weight loss of 10% baseline weight or 4.5 kg (whichever is the larger). Also given placebo. Participants given step-up medication if necessary to control BP, administered in double blind fashion; if DBP ≥99 mmHg or 90 to 94 mmHg at two visits with 3 month interval or 95 to 99 mmHg at two visits with 2 week interval then 25 mg chlorthalidone or 50 mg atenolol prescribed, if still not controlled then open-label therapy used (known antihypertensive medication).
Control	*No change in diet and given placebo. As above for drug treatment of BP.*
Length of follow-up	2.5 years minimum
Results	*At 6 months, mean (SD) weight change in kg was –4.40 (6.60) in the diet group, and –0.70 (3.79) in the control group. Mean weight change in the intervention group compared with control was –3.70 (95% CI –5.28 to –2.12).* At 12 months, mean (SD) weight change in kg was –3.70 (6.79) in the diet group, and –0.50 (3.12) in the control group. Mean weight change in the intervention group compared with control was –3.20 (95% CI –5.13 to –1.27). At 18 months, mean (SD) weight change in kg was –2.70 (7.55) in the diet group, and –1.00 (3.12) in the control group. Mean weight change in the intervention group compared with control was –1.70 (95% CI –3.81 to 0.41). At 24 months, mean (SD) weight change in kg was –1.90 (7.55) in the diet group, and –0.40 (3.91) in the control group. Mean weight change in the intervention group compared with control was –1.50 (95% CI –3.69 to 0.69). *Gender was not associated with weight loss at 6 months.*
Quality and comments	Significantly more men than women in the intervention group. Assessors blinded to drug status only. ITT not done. Good concealment of allocation. *Results for 12 months onwards for 24-month completers only.*

Wood 1988 (in HTA) RCT	
Aim	To determine the influence of two methods for losing fat weight on the levels of plasma lipids and lipoproteins in overweight sedentary men – decreasing energy intake without increasing exercise (diet), and increasing energy expenditure without altering energy intake (exercise, primarily running)
Participants	*Men aged 30 to 59 years, overweight (120 to 160% IBW) and no regular exercise for past 3 months.* *155 M. Mean (SD) age 44.2 (8.2) years diet group (n=51), 44.1 (7.8) years exercise group (*n=*52), 45.2 (7.2) years control (*n=*52). Mean (SD) weight 93.0 (8.8) kg diet group, 94.1 (8.6) exercise group, and 95.4 (10.6) control (results for 131 assessed participants).* Noted in HTA as highest mean reported weight (kg)
Intervention (including details of diet)	Diet group 1: baseline 7-day diet recall and body fat mass used to provide individual counselling including behavioural strategies, to reduce energy intake to produce gradual weight loss and to lose one-third of body fat (assumed a reduction of 7762 kcal for loss of 1 kg adipose tissue). No change in nutrient composition, requested to remain sedentary, included weight stabilisation for last 6 weeks. (See PA review for details of exercise group)
Control	*Advised not to make any changes in diet, including composition, exercise or body weight, offered weight loss programme of diet and exercise at end of study.*
Length of follow-up	12 months *(24 months follow-up for other groups not relevant to this review)*
Results	*At 7 months, mean (SD) weight change in kg was –7.60 (3.90) in the diet group and 0.20 (2.50) in the control group. Mean weight change in the intervention group compared with control was –7.80 (95% CI –9.20 to –6.40).* At 12 months, mean (SD) weight change in kg was –7.20 (3.70) in the diet group, and 0.60 (3.70) in the control group. Mean weight change in the intervention group compared with control was –7.80 (95% CI –9.38 to –6.22).
Quality and comments	ITT analysis not done. Blinded assessment only in year 2. Random allocation but no description of concealment. Only 12-month outcomes reported in published papers.

Wood 1991 (in HTA) RCT	
Aim	To test the hypothesis that exercise (walking or jogging) will increase HDL-cholesterol levels in moderately overweight, sedentary people who adopt a hypoenergetic National Cholesterol Education Programme (NCEP) diet
Participants	*Sedentary people (exercise less than twice per week) who were moderately overweight (BMI 28 to 34 kg/m^2 for men, 24 to 20 for women).* *264 total – 132 F, 132 M. Mean (SD) age 39.1 (6.4) years women, 40.3 (6.3) years men. Mean BMI (SD) (kg/m^2) 27.9 (2.2) women, 30.7 (2.2) men.* (Noted as lowest mean BMI in HTA.) *Eighty-seven allocated to diet, 90 to diet and exercise, and 87 to control.*
Intervention (including details of diet)	*NCEP step 1 diet consisting of 55% energy as carbohydrate, 30% as fat (saturated fat ≤10%), dietary cholesterol <300 mg/day, energy reduction, no change in exercise (See physical activity review for details of exercise)*
Control	Instructed to maintain usual diet and exercise patterns.
Length of follow-up	*12 months*
Results	*Only 12 months outcomes reported.* Women: At 12 months, mean (SD) weight change in kg was –4.10 (5.50) in the diet group, and 1.30 (5.20) in the control group. Mean weight change in the intervention group compared with control was –5.40 (95% CI –7.93 to –2.87). Men: At 12 months, mean (SD) weight change in kg was –5.10 (5.80) in the diet group, and 1.70 (4.80) in the control group. Mean weight change in the intervention group compared with control was –6.80 (95% CI –9.13 to –4.47).
Quality and comments	Significant differences between men in both intervention groups vs control for DBP (p<0.001), TC for women in diet group vs control (p≤0.01), and diet and exercise group vs control (p≤0.05), and LDL levels in women in both intervention groups vs control (p≤0.05). Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment.

Other outcomes

Cohen 1991 (in HTA) cluster RCT	
Results	*At 6 and 12 months, there was no difference between groups in mean arterial pressure change from baseline (*p*>0.10).* *At 6 months, there was a change in the number of antihypertensive medications from baseline of –0.6 (SD 1.0) in the diet group compared with 0 (SD 0.5) in the control group. This was significantly different (*p*=0.04) but this was not maintained at 12 months (–0.3 vs –0.2,* p*>0.10).* *After 12 months, subjects who lost weight had more physician visits (*p*=0.006) and took fewer antihypertensive medications (*p*=0.01) but had no significant change in BP (*p*>0.10) than those who gained weight.*
Quality and comments	…

DISH 1985 (in HTA) RCT	
Results	At 12 months, 59.5% of people allocated to dietary intervention remained off antihypertensive medication compared with 35.5% of those with no dietary intervention (p=0.0015). *Dietary estimates, obtained by analysis of 3-day food records, showed that the overweight participants were more likely to underestimate than the non-overweight participants.*
Quality and comments	…

Frey-Hewitt 1990 (in HTA) RCT	
Results	*At 12 months, mean change (SD) in energy intake (kcal/day) in the diet group was –335.39 (412.55) from a baseline of 2489.56 (474.36) in the diet group compared with –121.70 (514.83) from a baseline of 2517.24 (557.40) in the control group. The difference was not significant.* *Also reported were changes in fat free mass, fat mass, % body fat,* VO_{2max} *and resting metabolic rate at 12 months, which were all significant (*p*≤0.01) in the diet group compared with control.*
Quality and comments	Energy intake estimated from participants' 7-day food diaries and recall checks periodically from trained interviewers by telephone.

Hankey 2001 (in HTA) RCT (pilot)	
Results	*At 52 weeks anthropometric measurements were unchanged in the 25 overweight patients provided with weight management advice, but increased significantly in overweight control patients, but the difference between the groups was not significant (WC +0.7 vs +2.6 cm,* p*=0.10, and % body fat –1.1 vs 0.6,* p*=0.16).*
Quality and comments	…

HOT 1999 (in HTA) RCT	
Results	*No difference was found between the proportions of people who reached their target DBP at any time point in either the weight loss group or the control. Stratified analysis showed no difference between DBP in weight loss compared with control.* People in the weight loss group required fewer medications between 6 months and 30 months (difference consistently statistically significant). The weight loss group tended to regain weight after the first 6 months of the study.
Quality and comments	…

HPT 1990 (in HTA) RCT	
Results	*At 6 months, mean (SD) DBP change in mmHg was –5.30 (7.41) in the diet group, and –2.50 (7.70) in the control group. Mean DBP change in the intervention group compared with control was –2.80 (95% CI –4.74 to –0.86).* *At 6 months, mean (SD) SBP change in mmHg was –6.90 (7.41) in the diet group, and –1.80 (7.70) in the control group. Mean SBP change in the intervention group compared with control was –5.10 (95% CI –7.04 to –3.16).* At 36 months, mean (SD) DBP change in mmHg was –4.20 (8.65) in the diet group, and –2.40 (8.58) in the control group. Mean DBP change in the intervention group compared with control was –1.80 (95% CI –4.02 to 0.42). At 36 months, mean (SD) SBP change in mmHg was –5.00 (9.73) in the diet group, and –2.69 (9.65) in the control group. Mean SBP change in the intervention group compared with control was –2.31 (95% CI –4.80 to 0.18). 9% in the intervention and control groups needed drug treatment for hypertension during the 3-year study. *Energy restriction alone did not affect sodium and potassium excretion rates.*
Quality and comments	…

ODES 1995 (in HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.23 (0.65) in the diet group, and –0.16 (0.59) in the control group. Mean TC change in the intervention group compared with control was –0.07 (95% CI –0.32 to 0.18). At 12 months, mean (SD) LDL change in mmol/l was –0.18 (0.72) in the diet group, and –0.22 (0.59) in the control group. Mean LDL change in the intervention group compared with control was 0.04 (95% CI –0.22 to 0.30). At 12 months, mean (SD) HDL change in mmol/l was 0.05 (0.12) in the diet group, and 0.02 (0.10) in the control group. Mean HDL change in the intervention group compared with control was 0.03 (95% CI –0.01 to 0.07). At 12 months, mean (SD) TAG change in mmol/l was –0.23 (1.01) in the diet group, and 0.17 (0.92) in the control group. Mean TAG change in the intervention group compared with control was –0.04 (95% CI –0.79 to 0.01). At 12 months, mean (SD) DBP change in mmHg was –3.40 (7.21) in the diet group, and –0.70 (8.52) in the control group. Mean DBP change in the intervention group compared with control was –2.70 (95% CI –5.91 to 0.51). At 12 months, mean (SD) systolic BP (SBP) change in mmHg was –6.40 (10.10) in the diet group, and –0.50 (11.15) in the control group. Mean SBP change in the intervention group compared with control was –5.90 (95% CI –10.22 to –1.58). At 12 months, mean (SD) fasting plasma glucose (FPG) change in mmol/l was –0.21 (0.50) in the diet group, and 0.07 (0.46) in the control group. Mean FPG change in the intervention group compared with control was –0.28 (95% CI –0.47 to –0.09). *The diet group had a mean (SD) change in total energy intake of –1679 (3245) kJ/day, which was significantly different compared with control (*p*<0.05). No values were reported for the control group.* *The diet group had a mean (SD) change in energy from fat of –4.9 (7.93)%, which was significantly different compared with control (*p*<0.05). No values were reported for the control group.* *At 12 months, significant changes from baseline were seen in the diet group for energy intake (–550 kcal), protein (–13.4 g), fat (–32.5 g), % energy as fat (–5.1%), carbohydrate (–42.3 g), sugar (–16.8 g), alcohol (–2.5 g), cholesterol (–121 mg), saturated fatty acids (–13.6 g), monounsaturated fatty acids (–12.3 g) and polyunsaturated fatty acids (–4.9 g).* *Within the upper tertile of baseline BP, the decline in blood pressure in the diet group were almost comparable with those obtained with drug treatment.* *The 1-year diet intervention gave a significant decrease in the calculated insulin resistance from 4.6 to 4.2 and a positive correlation between the changes in insulin resistance and changes in BMI (*r*=0.40).*

Quality and comments	Dietary intake assessed through a validated food-frequency questionnaire.

Pritchard 1997 (in HTA) RCT	
Results	*At 12 months, significant differences from baseline were seen in the diet group compared with control for energy intake (–30.4 vs +4.0%), % energy as fat (–32.0 vs +1.7%) (*p<*0.001) and % energy protein (+23.3 vs –1.1%) (*p<*0.05).* *No significant differences were seen between diet and control for dietary calcium or index of activity (used to calculate daily energy expenditure).* *Also at 12 months, significant differences were seen from baseline between diet and control in bone mineral density (–1.5 vs +0.4%) (*p<*0.05), bone mass (–1.4 vs –0.1%) (*p<*0.01), fat mass (–19.4 vs +0.4%) and lean mass (–3.9 vs +0.1%) (*p<*0.001).* *DEXA scans revealed that 40% of dieters' weight loss was lean tissue.*
Quality and comments	Dietary intake estimated from participants' 3-day food diaries

Pritchard 1999 (in HTA) RCT	
Results	*No other results reported for overweight participants only.* The cost of an additional kg weight loss was A$9.76 in the doctor and dietitian group compared with A$7.30 in the dietitian group.
Quality and comments	…

TAIM 1992 (in HTA) RCT	
Results	*At 6 months, the weight loss group showed a change (SD) in pulse beats per min of –4.9 (9.43) vs control of –1.8 (11.4), and a change in dietary intake of –442.5 kcal vs –122.6. No* p *values were reported.*
Quality and comments	Energy intake calculated from participants' diet diaries.

Wood 1988 (in HTA) RCT	
Results	*At 7 months, changes in TAG, TC, HDL and HDL_2 levels were significantly different to controls (–0.40 vs –0.01* p≤*0.01, –0.40 vs –0.21* p≤*0.05, 0.06 vs 0.00* p≤*0.01, 0.06 vs 0.00* p≤*0.001 respectively). Changes in LDL and HDL_3 levels were not significantly different between groups.* At 12 months, mean (SD) TC change in mmol/l was –0.36 (0.56) in the diet group, and –0.23(0.65) in the control group. Mean TC change in the intervention group compared with control was –0.13 (95% CI –0.39 to 0.13). At 12 months, mean (SD) LDL change in mmol/l was –0.31 (0.64) in the diet group, and –0.21 (0.67) in the control group. Mean LDL change in the intervention group compared with control was –0.10 (95% CI –0.38 to 0.18). At 12 months, mean (SD) HDL change in mmol/l was 0.12 (0.16) in the diet group, and –0.02 (0.11) in the control group. Mean HDL change in the intervention group compared with control was 0.14 (95% CI 0.08 to 0.20). At 12 months, mean (SD) TAG change in mmol/l was –0.27 (0.72) in the diet group, and 0.08 (0.60) in the control group. Mean TAG change in the intervention group compared with control was –0.35 (95% CI –0.63 to –0.07). At 12 months, mean (SD) DBP change in mmHg was –5.60 (7.30) in the diet group, and –2.60 (8.10) in the control group. Mean DBP change in the intervention group compared with control was –3.00 (95% CI –6.55 to 0.55). At 12 months, mean (SD) SBP change in mmHg was –5.70 (7.90) in the diet group, and –4.10 (8.00) in the control group. Mean SBP change in the intervention group compared with control was –1.60 (95% CI –5.25 to 2.05). *TC/HDL-cholesterol ratios were significantly lower in the diet group compared with control at both 7 and 12 months (*p≤*0.01).* *At 12 months, the diet group showed significant changes from baseline compared with control for body fat (–4.6% vs –0.9%) (*p<*0.01), energy intake per day (–306*

	vs –112) and g of fat per day (2.0 vs 1.4) (p<0.05). No other changes in outcomes were significant (saturated fat, poly- and monounsaturated fat, alcohol, calcium, potassium, sodium levels). *At 12 months, VO_{2max} and treadmill test duration decreased significantly less in the diet group compared with control (p≤0.001) (0.0 vs –2.4 VO_{2max}, and –0.8 vs –1.6 treadmill test duration in min).*
Quality and comments	Dietary intake estimated from participants' 7-day food diaries.

Wood 1991 (in HTA) RCT	
Results	Women: At 12 months, mean (SD) TC change in mmol/l was –0.39 (0.61) in the diet group, and –0.03 (0.47) in the control group. Mean TC change in the intervention group compared with control was –0.36 (95% CI –0.62 to –0.10). Women: At 12 months, mean (SD) LDL change in mmol/l was –0.28 (0.63) in the diet group, and –0.03 (0.41) in the control group. Mean LDL change in the intervention group compared with control was –0.25 (95% CI –0.51 to 0.01). Women: At 12 months, mean (SD) HDL change in mmol/l was –0.15 (0.26) in the diet group, and –0.05 (0.24) in the control group. Mean HDL change in the intervention group compared with control was –0.10 (95% CI –0.22 to 0.02). Women: At 12 months, mean (SD) TAG change in mmol/l was 0.09 (0.36) in the diet group, and 0.13 (0.37) in the control group. Mean TAG change in the intervention group compared with control was –0.04 (95% CI –0.79 to 0.01). Women: At 12 months, mean (SD) DBP change in mmHg was –2.20 (5.10) in the diet group, and 0.90 (5.30) in the control group. Mean DBP change in the intervention group compared with control was –3.10 (95% CI –5.55 to –0.65). Women: At 12 months, mean (SD) SBP change in mmHg was –4.10 (6.00) in the diet group, and –0.20 (6.60) in the control group. Mean SBP change in the intervention group compared with control was –3.90 (95% CI –6.86 to –0.94). Men: At 12 months, mean (SD) TC change in mmol/l was –0.42 (0.51) in the diet group, and –0.14 (0.64) in the control group. Mean TC change in the intervention group compared with control was –0.28 (95% CI –0.53 to –0.03). Men: At 12 months, mean (SD) LDL change in mmol/l was –0.39 (0.48) in the diet group, and –0.20 (0.59) in the control group. Mean LDL change in the intervention group compared with control was –0.19 (95% CI –0.43 to 0.05). Men: At 12 months, mean (SD) HDL change in mmol/l was 0.02 (0.17) in the diet group, and –0.05 (0.15) in the control group. Mean HDL change in the intervention group compared with control was 0.07 (95% CI 0.00 to 0.14). Men: At 12 months, mean (SD) TAG change in mmol/l was –0.12 (0.59) in the diet group, and 0.18 (0.67) in the control group. Mean TAG change in the intervention group compared with control was –0.30 (95% CI –0.58 to –0.02). Men: At 12 months, mean (SD) DBP change in mmHg was –2.40 (6.60) in the diet group, and 2.10 (5.00) in the control group. Mean DBP change in the intervention group compared with control was –4.50 (95% CI –7.70 to –1.93). Men: At 12 months, mean (SD) SBP change in mmHg was –4.10 (8.10) in the diet group, and 0.10 (7.70) in the control group. Mean SBP change in the intervention group compared with control was –4.20 (95% CI –7.66 to –0.74). *Women: at 12 months, significant changes in baseline were seen in the diet group compared with the control groups for total energy intake (–2180 vs 60 kJ/day* p*≤0.001), total fat intake (–7.8% vs –0.9%,* p*≤0.001), saturated fat (–3.7 vs –0.4%* p*≤0.001) and cholesterol intake (–123 vs –5 mg/day,* p*≤0.001). No significant difference was seen for aerobic capacity. Also, the estimated 12 year CHD risk decreased by 1.0 events/1000 persons in the diet group compared with an increase of 1.3 in the control group, but the difference was not significant between groups.* *Men: at 12 months, significant changes in baseline were seen in the diet group compared with the control groups for total energy intake (–2915 vs 155 kJ/day,* p*≤0.001), total fat intake (–6.0 vs 0.8%,* p*≤0.001), saturated fat (–3.2 vs –0.2%,* p*≤0.001) and cholesterol intake (–159 vs 7 mg/day,* p*≤0.001). No significant difference was seen for aerobic capacity. Also, the estimated 12 year CHD risk*

Quality and comments	*decreased by 12.9 events/1000 persons in the diet group compared with an increase of 0.6 in the control group (*p≤*0.01).* *Men and women in the weight-loss (diet only) programme reported greater restraint, less disinhibition, and less hunger at 1 year than those in no programme. Significant differences between men in both intervention groups vs control for DBP (*p<*0.001), TC for women in diet group vs control (p≤0.01), and diet and exercise group vs control (*p≤*0.05), and LDL levels in women in both intervention groups vs control (*p≤*0.05).* Dietary intake estimated from participants' 7-day food diaries, with further probing for more detail by trained interviewers when collecting the data by telephone.

Reported harms

Cohen 1991 (in HTA) cluster RCT	
Harms	None reported
Quality and comments	…

DISH 1985 (in HTA) RCT	
Harms	None reported
Quality and comments	

Frey-Hewitt 1990 (in HTA) RCT	
Harms	None reported
Quality and comments	…

Hankey 2001 (in HTA) RCT (pilot)	
Harms	Two deaths occurred in the intervention group and one in the control group.
Quality and comments	Participants by definition at high risk of death. Serious illness was also reported, but not by overweight group only.

HOT 1999 (in HTA) RCT	
Harms	Of the participants who dropped out, thee died and one had a serious illness. No details of group allocation were given.
Quality and comments	…

HPT 1990 (in HTA) RCT	
Harms	*One death occurred in the control group.*
Quality and comments	…

ODES 1995 (in HTA) RCT	
Harms	*One death and two cancers (allocation not known).*
Quality and comments	…

Pritchard 1997 (in HTA) RCT	
Harms	Two participants withdrew before completion due to ill health unrelated to the study.
Quality and comments	…

Pritchard 1999 (in HTA) RCT	
Harms	None reported
Quality and comments	…

TAIM 1992 (in HTA) RCT	
Harms	*Two deaths reported in the intervention group (Phase I study)*
Quality and comments	…

Wood 1988 (in HTA) RCT	
Harms	*One diagnosis of cancer reported in year 2.*
Quality and comments	…

Wood 1991 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Cohen 1991 (in HTA) cluster RCT	
Country and setting	USA. Family health centre – primary care.
Participants (included/excluded)	*Included if aged 20–75 years, BMI (kg/m^2) 27.8 for men and ≥27.3 for women; average SBP 140 mmHg or more on two or more readings, or average DBP more than 90 mmHg on two or more readings.* *No details of exclusion given.*
Recruitment	Patients who attended the health centre who met the eligibility criteria – no further details.
Intervention (mode and intensity)	12 months intervention, contacted 13 times (baseline then monthly)
Control (mode and intensity)	*Assessed three times (baseline, 6 and 12 months)*
Delivery of intervention/control (who)	Physicians were taught by a behavioural psychologist with a special interest in weight reduction The 'trained' physician then reviewed individual patient's diet using a questionnaire. Management of hypertension was the responsibility of the treating physician.
Dropout rates	*0% intervention and 0% control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	No dropouts

DISH 1985 (in HTA) RCT	
Country and setting	*USA. Multicentred.*
Participants (included/excluded)	*Included if no SBP >180 mmHg in past year, average DBP <95mmHg, average of last two DBP ≤90 mmHg and neither >95 mmHg.* *Excluded if congestive cardiac failure, ECG evidence of MI, stroke, transient ischaemic attacks, creatinine ≥2.5 mg/dl on at least two occasions, personal problems, compliance with diet difficult, severe alcoholism, pregnancy, □-blockers for angina, glucocorticosteroids.*
Recruitment	Recruited from Stopped Care clinic populations in the Hypertension Detection and Follow-up programme (initially found by population screening).
Intervention (mode and intensity)	Intervention lasted 56 weeks. Participants contacted about 38 times, (baseline then every 2 weeks for initial 16 weeks, monthly to week 56, plus eight initial weekly nutritional visits, then monthly to week 56).
Control (mode and intensity)	*No dietary intervention for 56 weeks. Contacted 20 times, (baseline then every 2 weeks for initial 16 weeks, then monthly to week 56).*

Delivery of intervention/control (who)	N/R
Dropout rates	*23% in intervention group, 13% in no dietary intervention group at 56 weeks.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Frey-Hewitt 1990 (in HTA) RCT	
Country and setting	*USA. University.* No further details.
Participants (included/excluded)	*Included men aged 30 to 59 years, 120–160% IBW, non-smokers, weight-stable (±2.27 kg during previous year).* *Excluded if BP >160/100, medications known to affect lipids, plasma TC >7.76 mmol/l or TAG >5.65 mmol/l, exercising more than three times per week.*
Recruitment	Volunteers – no further details.
Intervention (mode and intensity)	Dietary and physical activity groups were contacted 25 times (every 2 weeks) over the 12-month intervention period.
Control (mode and intensity)	*Over the 12 months, contact was unclear (possibly twice – baseline and 12 months).*
Delivery of intervention/control (who)	Dietitian met participants in the diet group every 2 weeks.
Dropout rates	4% in diet group, (2% in physical activity group), 6% in control at 12 months.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Hankey 2001 (in HTA) RCT (pilot)	
Country and setting	UK. Cardiac rehabilitation programme. *Glasgow Royal Infirmary.*
Participants (included/excluded)	People attending cardiac rehab at two study hospitals, aged 35 to 75 years, survived acute MI about 3 months before study. No exclusion criteria stated.
Recruitment	Participants (assumed to be) recruited from cardiac rehabilitation programmes. No further details reported in published paper.
Intervention (mode and intensity)	Intervention for 12 weeks, with follow-up at 52 weeks. *Not clear about number of contacts, but routine cardiac rehabilitation plus four 1 h sessions of nutritional counselling.*
Control (mode and intensity)	*Assessed at baseline, 12 weeks and 52 weeks* with one 30–60 min group session
Delivery of intervention/control (who)	Nutrition counselling – assume dietitian? Routine cardiac rehabilitation – no details
Dropout rates	11% in diet group and 4% in control group at 52 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

HOT 1999 (in HTA) RCT	
Country and setting	Multicentre trial conducted in 26 countries (Europe, North and South America and Asia). No further details.
Participants (included/excluded)	*People with a BMI or ≥27 kg/m^2 from the HOT study.* (Inclusion for the HOT study was male or female patients aged 50–80 years with hypertension and office average sitting DBP between 100 and 115 mmHg at three consecutive measurements taken on two occasions, at least 1 week apart.) *Excluded for this sub-study if BMI <27 kg/m^2.*
Recruitment	N/R

Intervention (mode and intensity)	Intervention lasted 30 months, with maximum 24 contacts (baseline, at 2–4 weeks, twice per month to 3 months, every 3–6 months to 30 months).
Control (mode and intensity)	*30 months of control, with six contacts (baseline, 6, 12, 18, 24, 30 months).*
Delivery of intervention/control (who)	*Counselling in the intervention group was by the dietitian. Research nurses gave information to the control group.*
Dropout rates	7% in the weight loss group and 9% in the control group at 30 months.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

HPT 1990 (in HTA) RCT	
Country and setting	USA. Four *university?* clinics and four resource centres. No further details.
Participants (included/excluded)	*Included men and women aged 25 to 49 years, BMI <35 kg/m^2 or <150% IBW (Metropolitan Life Insurance tables), DBP ≥76mmHg or <99 mmHg at first baseline visit and DBP ≤89mmHg at second visit (7 to 30 days later).* *Excluded if antihypertensive medications or medication that may affect sodium metabolism, major chronic disease, BMI ≥35 kg/m^2, dietary requirements incompatible with dietary regimens, 21 or more alcoholic drinks per week, perceived unable to comply with study.*
Recruitment	No details in the papers reporting results.
Intervention (mode and intensity)	Dietary change counselling included didactic presentation and demonstrations, token incentives, bimonthly newsletters, telephone calls if missed session, daily food records. 3 years of intervention. About 38 contacts (three times at baseline, then at clinic sessions other than those of treatment sessions, six times at 6 monthly intervals, treatment group sessions weekly for 10 weeks, then every other month to 3 years. Also individual counselling sessions.)
Control (mode and intensity)	*3 years of control. Contacted ten times (assessed three times at baseline, then at 3, 6, 12, 18, 24, 30, 36 months).*
Delivery of intervention/control (who)	Counselling was provided by 'personnel trained and experienced in effecting behaviour changes related to shopping, cooking, and eating practices'.
Dropout rates	*6% in diet group and 10% in control at 36 months.*
Treatment of dropouts (return to baseline, or last measurement?)	People with missing follow-up data were excluded from the analysis of change for that time point. For BP, values were imputed for all follow-up visits after the initiation of antihypertensive therapy to avoid distortion of results by including BP lowered by such therapy. For DBP, 95 mmHg was used if observed DBP 95 mmHg or less, if not observed value used. For SBP, value imputed was value at last visit before initiation of therapy or current observed value, whichever was higher.

ODES 1995 (in HTA) RCT	
Country and setting	Norway. Community-based?
Participants (included/excluded)	*Included if aged 41 to 50 years, sedentary (exercise no more than once per week), BMI >24 kg/m^2, DBP 86 to 99 mmHg, TC 5.2 to 7.74 mmol/l, HDL <1.2 mmol/l, fasting serum TAG >1.4mmol/l.* *Excluded if overt diabetes or CVD, other disease or drugs that could interfere with test results, treatment with antihypertensive drugs, acetylsalicylic acid, lipid-lowering diet, personal traits unsuitable for inclusion.*
Recruitment	Participants recruited from continuous screening programme of 40-year old men and women in Oslo. No further details reported.
Intervention (mode and intensity)	Dietary intervention lasted 12 months. Four contacts (baseline, 3, 9, 12 months).

Control (mode and intensity)	*12-month control. Contacted at baseline and 12 months.*
Delivery of intervention/control (who)	N/R
Dropout rates	5% in diet group and 0% in control at 12 months (includes five excluded)
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Pritchard 1997 (in HTA) RCT	
Country and setting	Australia. Work-based.
Participants (included/excluded)	*Included men aged 35 to 55 years of age, satisfactory cardiovascular fitness test, BMI 26–35 kg/m^2, 110 to 130% of IBW, otherwise healthy. No details of exclusion criteria given.*
Recruitment	Volunteers recruited from a national business corporation, previously screened as being overweight in a corporate health programme.
Intervention (mode and intensity)	18 months of intervention. Contacted 19 times (baseline then monthly. Also encouraged to attend bimonthly motivational group breakfasts or lunch meetings with guest speakers or videos relevant to diet, exercise and health issues).
Control (mode and intensity)	12 months of control. 6 months of diet and exercise. Contacted at baseline and weight monitored monthly
Delivery of intervention/control (who)	N/R
Dropout rates	*25% in the diet group and 5% in the control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Pritchard 1999 (in HTA) RCT	
Country and setting	Australia. University group general practice.
Participants (included/excluded)	*Included if aged between 25 and 65 years. Also if BMI >25 kg/m^2, or screened BP >140/90 mmHg and recorded BP >140/90 mmHg at least twice in medical records, history of type 2 diabetes.* *Excluded if mentally ill, intellectually disabled, terminally ill, acutely ill, pregnant, or participating in other health education programmes.*
Recruitment	Participants were screened opportunistically when attending the GP. People with recorded diagnosis of overweight, hypertension or type 2 diabetes in their patient notes were invited to participate. People who appeared to be overweight on presentation at reception were also invited to participate.
Intervention (mode and intensity)	Intervention lasted 12 months. Contacted seven times (baseline then six times by dietitian over 12 months). *Also supplemented with baseline contact with GP and 25 min sessions with the GP in the doctor and dietitian group.*
Control (mode and intensity)	*Contacted twice (baseline and 12 months).*
Delivery of intervention/control (who)	*Initial screening and counselling done by dietitian. Dietitian invited those allocated to the dietitian group to participate. GP invited those allocated to the doctor and dietitian group, after screening by the dietitian. Mailed invite to attend for final measurement in control group.*
Dropout rates	*45% dietitian group, 29% doctor and dietitian group, and 29% control at 12 months (as reported in original paper, not HTA.) Dropouts were significantly higher in the dietitian group (*p=*0.022) than either the doctor and dietitian group or the control.*
Treatment of dropouts (return to baseline, or last measurement?)	If missing data, the last measurement recorded was taken to populate subsequent data values.

TAIM 1992 (in HTA) RCT	
Country and setting	USA. Multicentre (clinical centres), but no details given in the results paper.
Participants (included/excluded)	*Included if 21 to 65 years of age, 100 to 160% IBW, BP untreated or discontinued medication 2 weeks before start of study, one member per household treated DBP ≤99 mmHg or untreated DBP 90 to 104 mmHg at preliminary screening, 90 to 100 mmHg at first clinic visit, <115 mmHg at second visit (pre-randomisation).* *Excluded if MI during past year or history of MI, history or other evidence of stroke, bronchial asthma, diabetes mellitus requiring insulin, history or other evidence of allergy to thiazides or □-blockers, creatinine ≥180 µmol/l at baseline, other major disease (e.g. kidney disease, liver disease, cancer), pregnancy or likelihood of pregnancy during study, lifestyle or other conditions likely to affect compliance.*
Recruitment	N/R
Intervention (mode and intensity)	30 months intervention. Contacted at least 25 times (baseline, 10 weekly group sessions, monthly assessment in initial 6 months then every 6 to 12 weeks up to maximum of 30 months).
Control (mode and intensity)	*Contacted 5 times (baseline, 6, 12, 18, 24 months).*
Delivery of intervention/control (who)	N/R
Dropout rates	Not clear.
Treatment of dropouts (return to baseline, or last measurement?)	*Excluded from analysis if attendance not 100%.*

Wood 1988 (in HTA) RCT	
Country and setting	USA. University clinic.
Participants (included/excluded)	*Included men aged 30 to 59 years, 120 to 160% IBW, no regular exercise for past 3 months, non-smokers, clinically healthy, resting clinic BP <160/100 mmHg, plasma cholesterol <8.28 mmol/l, plasma TAG <5.65 mmol/l, average<4 alcoholic drinks per day, expected to reside in Stanford area for at least 12 months, normal ECG during grade treadmill test.* *Excluded if orthopaedic limitations, medications known to effect BP or plasma lipids.*
Recruitment	Potential participants invited to be screened via mass media. Interviewed by telephone, and scheduled for orientation session if criteria met and still interested.
Intervention (mode and intensity)	First 12 months, no details of frequency of contact. In year 2, monthly mailings, telephone contact of 5 to 10 min each during months 13, 14, 15, 18, 21, 24 (for contact groups). In year 2, contacted twice at 18 and 24 months (no contact groups).
Control (mode and intensity)	Contacted three times in year 1 – baseline and 7, 12 months.
Delivery of intervention/control (who)	Registered dietitian provided individual counselling.
Dropout rates	4% diet, 6% control in first 12 months. 17% diet 2 (contact) group, 20% in diet 3 (no contact) group at 24 months.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Wood 1991 (in HTA) RCT	
Country and setting	USA. University clinic?
Participants (included/excluded)	*Included if aged between 25 and 49 years, 120 to 150% IBW, BMI 28 to 34 kg/m^2 for men, BMI 24 to 30 kg/m^2 for women, non-smokers, sedentary (exercise less than twice per week, <30 min per time), resting BP <160/95 mmHg, plasma cholesterol <6.72 mmol/l, plasma TAG <5.65 mmol/l, average less than four alcoholic drinks per day, generally good health.* *Excluded if medication known to affect BP or lipid metabolism, pregnancy, lactating or taking oral contraception in past 6 months or planning pregnancy in subsequent 2 years.*
Recruitment	Potential participants were invited to be screened via mass media, followed with telephone interviews.
Intervention (mode and intensity)	12-month intervention. Contacted 25 times (baseline then weekly for first 3 months, then every other week for 3 months, then monthly)
Control (mode and intensity)	*Contacted twice (baseline and 12 months)*
Delivery of intervention/control (who)	Dietary recommendations were presented by a registered dietitian. Group sessions assumed to be dietitian?
Dropout rates	*10% in diet group and 10% in control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Analyses restricted to individuals with complete data only.

1.3.2 Low-energy diet (1000 to 1600 kcal/day) compared with control

Weight loss

de Waard 1993 (in HTA) RCT	
Aim	To assess the effect of weight reduction in obese postmenopausal breast cancer patients as an adjuvant to primary surgical and radiotherapeutic treatment (feasibility study)
Participants	*Postmenopausal women with breast cancer who were also obese (BMI ≥27 kg/m^2).* *107 total – all women (107 randomised, 102 participated). No details of age reported. Minimum mean BMI 29.3 kg/m^2 intervention (The Netherlands,* n=*30), 29.5 control (The Netherlands,* n=*24), 30.6 intervention (Poland,* n=*29), 32.2 control (Poland,* n=*19).*
Intervention (including details of diet)	Participants received dietary advice from a dietitian of 1500 kcal per day (reduced to 1000 kcal/day if insufficient weight loss was noted) and psychological support.
Control	*No details given.*
Length of follow-up	3 years – The Netherlands. 1 year – Poland.

Results	Other time points shown graphically but not able to determine exact numbers. Women in the Netherlands: at 12 months, mean (SD) weight change in kg was –5.50 (7.50) in the diet group, and 1.50 (6.30) in the control group. Mean weight change in the intervention group compared with control was –7.00 (95% CI –10.75 to –3.25). Women in Poland: at 12 months, mean (SD) weight change in kg was –5.90 (7.60) in the diet group, and –0.60 (6.10) in the control group. Mean weight change in the intervention group compared with control was –5.30 (95% CI –9.51 to –1.09). Women in the Netherlands: at 24 months, mean (SD) weight change in kg was –5.00 (7.30) in the diet group, and 2.00 (6.50) in the control group. Mean weight change in the intervention group compared with control was –7.00 (95% CI –10.99 to –3.01). Women in the Netherlands: at 36 months, mean (SD) weight change in kg was –5.00 (7.30) in the diet group, and 1.10 (6.20) in the control group. Mean weight change in the intervention group compared with control was –6.10 (95% CI –10.71 to –1.49).
Quality and comments	Control group in Poland had significantly fewer women with moderate overweight (p<0.02). Blinded assessment not done. ITT not done. Random allocation but no description of concealment. Some calculations needed on the data presented. Data presented as two trials – The Netherlands and Poland. Small study.

Other outcomes

de Waard 1993 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Reported harms

de Waard 1993 (in HTA) RCT	
Harms	*Three cases of breast cancers occurred in the intervention group and one in the control group. Three women died from breast cancer in the intervention group and five in the control group. Two deaths from other causes also occurred in both the intervention and the control group.*
Quality and comments	…

Generalisability

de Waard 1993 (in HTA) RCT	
Country and setting	*The Netherlands – three hospitals. Poland – two oncology hospitals.*
Participants (included/excluded)	*Included women who had had primary treatment for breast cancer, no signs of distant metastases, aged 50–69 years, postmenopausal (no menses for at least 1 year), overweight by ≥10 kg (according to Broca's 1st rule, equivalent to BMI of ≥27 kg/m^2).* *Excluded initially if tamoxifen use but this exclusion criterion was subsequently omitted.*
Recruitment	Screened for eligibility by treating physician.
Intervention (mode and intensity)	The Netherlands – 3 years. Poland – 1 year. No further details reported.
Control (mode and intensity)	*The Netherlands – 3 years. Poland – 1 year. No further details reported.*

Delivery of intervention/control (who)	*Dietary advice delivered by dietitian.*
Dropout rates	*The Netherlands: 40% intervention, 38% control at 36 months. Poland: 7% intervention, 21% control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

1.3.3 Very-low-energy diet (<1000 kcal/day) compared with control

Weight loss

Stenius-Aarniala 2000 (in HTA) RCT	
Aim	To determine whether weight loss affects lung function, morbidity, symptoms, or health status in obese people with asthma
Participants	People with asthma who were obese (BMI 30–42 kg/m^2). *38 total – 29 F, 9 M. Mean age (range) 49.7 (34–60) years intervention (*n=*19) 48.3 (23–60) years control (*n=*19). Mean BMI (range) 35.8 (31.3–39.4) kg/m^2 intervention, 36.7 (32.8–41.8) kg/m^2 control.*
Intervention (including details of diet)	2–3 weeks pre-treatment phase consisting of lung function tests and laboratory tests to fulfil exclusion and inclusion criteria then 2 weeks of baseline measurements. Then 14 weeks weight reduction programme consisting of 12 × 30 min group sessions and including 8 weeks VLED (Nutrilett) consisting of 420 kcal/day containing daily allowances of all essential nutrients; discussed same themes as controls but at a later date so that each group had the same amount of education about asthma and allergy at end of treatment. *Nutrilett was described as a 'dietary preparation', so assumed to be a meal replacement option?*
Control	*2–3 weeks pre-treatment phase consisting of lung function tests and laboratory tests to fulfil exclusion and inclusion criteria then 2 weeks of baseline measurements. Then 12 × 30 min group sessions during initial 14 weeks where themes chosen by participants were discussed freely.*
Length of follow-up	*52 weeks*
Results	*At 14 weeks, mean (SD) weight change in kg was –14.20 (9.93) in the diet group, and –0.30 (6.00) in the control group. Mean weight change in the intervention group compared with control was –13.40 (95% CI –19.11 to –8.69). At this point, nine participants had lost ≥15% of initial weight, eight had lost between 10 and 14.9%, and two between 5 and 9.9% of initial body weight.* *A*t 12 months, mean (SD) weight change in kg was –11.10 (9.06) in the diet group, and 2.30 (6.57) in the control group. Mean weight change in the intervention group compared with control was –13.40 (95% CI –18.43 to –8.37).
Quality and comments	Some calculation needed for HTA analysis. Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. *Used HTA Appendix 13 for SD calculation.*

Other outcomes

Stenius-Aarniala 2000 (in HTA) RCT	
Results	*At 8 weeks, the difference in forced expiratory volume (FEV) in 1 s between diet and control groups was 7.2% (95% CI 1.9 to 12.5), forced vital capacity (FVC) 8.6% (95% CI 4.8 to 12.4) and peak expiratory flow (PEF) 4.8% (95% CI –0.3 to 9.8).*

	At 14 weeks, the difference in FEV in 1 s between diet and control groups was 6.7% (95% CI 2.1 to 11.4), FVC 7.4% (95% CI 2.8 to 12.1) and peak expiratory flow (PEF) 4.8% (95% CI –1.9 to 11.4). *At 6 months, the difference in FEV in 1 s between diet and control groups was 8.4% (95% CI 3.7 to 13.2), FVC 7.6% (95% CI 4.1 to 11.2) and PEF 4.7% (95% CI –2.5 to 11.9).* At 12 months, the difference in FEV in 1 s between diet and control groups was 7.6% (95% CI 1.5 to 13.8), FVC 7.6% (95% CI 3.5 to 11.8) and PEF 6.2% (95% CI –1.4 to 13.7). During the 12 months, overall reduction in rescue medication was 0.5 doses in the diet group compared with 0 doses in the control group (*p*=0.002). Ten of the intervention group needed a course of oral steroids compared with 13 in the control group (*p*=0.07). Overall median change in dyspnoea was –13 mm in the diet group and –2 mm in the control (*p*=0.03). No significant differences were seen in cough, *After 1 year the differences in the changes between the two groups were –12 for symptom scores (range –1 to –22,* p=*0.04) and –10 for total scores (–18 to –1,* p=*0.02). The median number of exacerbations in the treatment group was 1 (0–4) and in the controls 4 (0–7),* p=*0.001.*
Quality and comments	*Small study so wide CIs.* Not sure how cough, dyspnoea, medication use was measured – self-reported? From St George's questionnaire?

Reported harms

Stenius-Aarniala 2000 (in HTA) RCT	
Harms	*During the 12 months, 16 of 19 of the intervention group and 18 of the 19 control group had at least one exacerbation of asthma. Median exacerbations were 1 (range 0 to 4) in the intervention group and 1 (range 0 to 7) in the control group, which were significantly different (reported* p=*0.001).* *Two of the participants found the consistency or the taste of the dietary preparation intolerable but followed an LED (no details given).*
Quality and comments	Not sure how exacerbation was measured – self-reported? From St George's questionnaire?

Generalisability

Stenius-Aarniala 2000 (in HTA) RCT	
Country and setting	*Finland. Private outpatients clinic.*
Participants (included/excluded)	*Included if aged 18–60 years, BMI 30–42 kg/m^2, diagnosis of asthma with spontaneous diurnal variation or a bronchodilator response of 15% or more; non-smoker or having stopped smoking for 2 years or more and before age 50 years.* *Excluded if pregnant, history of bulimia or anorexia, unstable angina or arrhythmia, untreated thyroid disease, symptomatic liver or gall bladder disorder, any other severe disease, insulin treatment, systemic steroid treatment, history of food allergy or intolerance to any component of the study VLED preparation (Nutrilett) such as soya, fish, chocolate or lactose; history of adverse reactions to peas, beans or peanuts; poor motivation.*
Recruitment	Participants were recruited by advertisements in two daily newspapers, then interviewed by telephone.
Intervention (mode and intensity)	12 months, contacted 16 times (12 half hour group sessions during initial 14 weeks then at week 14, month 6 and month 12).
Control (mode and intensity)	*As for intervention group.*

Delivery of intervention/control (who)	N/R explicitly, but cost of trained nurse supervision noted in the Discussion section, so assume trained nurse?
Dropout rates	0% for intervention and 0% control at 52 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	*N/R*

1.3.4 Low-energy diet compared with 600 kcal/day deficit or low-fat diet

Weight loss

Shah 1996 (in HTA) RCT	
Aim	To compare a energy-restricted diet with a fat-restricted diet (categorised as LED vs low-fat)
Participants	Healthy women who were overweight (20 to 40% above IBW). *122 total – all women. Age range 25 to 45 years, mean age 36 years. Mean (SD) weight 79.92 (4.45) kg, LED (n=61), 79.70 (4.40) kg low fat (*n=*61).*
Intervention (including details of diet)	Participants counselled on diet, exercise, menu planning, eating out, stimulus control, problem-solving, social assertion, goal setting, relapse prevention; cooking demonstrations given, all participants advised to walk for 30 min, 5 days per week, all participants advised to keep a daily record of food intake and physical activity. LED was 1000–1200 kcal/day, fat intake no more than 30% of total energy intake, no more than 170 g (6 oz) meat each day (only poultry, fish and lean red meat), limit fats, oils, eggs and high-fat desserts, snacks and dairy produce and replace with low fat alternatives, increase complex carbohydrates and limit simple sugars.
Control	*Participants counselled on diet, exercise, menu planning, eating out, stimulus control, problem-solving, social assertion, goal setting, relapse prevention; cooking demonstrations given, all participants advised to walk for 30 min, 5 days per week, all participants advised to keep a daily record of food intake and physical activity.* *Also to reduce fat intake to 20 g per day, unlimited complex carbohydrate, limit meat, fish and poultry to 60 g (2 oz) per day or less, (categorised as low fat) specific food recommendations, otherwise the same as LED.*
Length of follow-up	12 months
Results	*At 6 months, changes in BMI, % body fat, WHR were not significantly different between groups.* *At 6 months, mean (SD) weight change in kg was –3.70 (6.96) in the LED group and –4.60 (7.22) in the low-fat group. Mean weight change in the LED group compared with low-fat was 0.90 (95% CI –2.33 to 4.13).* *A*t 12 months, mean (SD) weight change in kg was –0.82 (6.15) in the LED group, and –2.45 (6.61) in the low-fat group. Mean weight change in the LED group compared with low-fat was 1.63 (95% CI –1.26 to 4.52). *A*t 18 months, mean (SD) weight change in kg was 1.80 (5.00) in the LED group and 0.40 (5.00) in the low-fat group, and. Mean weight change in the LED group compared with low-fat was 1.40 (95% CI –0.88 to 3.68).
Quality and comments	Some calculation needed for HTA analysis. Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. *Used 6-month data from Shah paper and HTA formula.*

Dansinger 2005 RCT	
Aim	To assess adherence rates and the realistic clinical effectiveness of four popular diets (Atkins, Zone, Weight Watchers and Ornish) for weight loss and cardiac risk factor reduction. Dietary components only of the programmes were used (see details of intervention later).
Participants	People who were overweight (BMI between 27 and 24 kg/m^2) who also had at least one metabolic cardiac risk factor. 160 total – 81 F, 79 M. Mean (SD) age 49 (10) years LED (*n*=40), 51 (9) years low fat (*n*=40). Mean (SD) BMI 35 (3.8) kg/m^2 LED, 34 (4.5) low fat.
Intervention (including details of diet)	*LED: number of daily points determined by current weight. Each point was roughly 50 kcal, and most participants aimed for 24 to 32 points daily (1200 to 1500 kcal). Lists provided by Weight Watchers determined point values of common foods.* *Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence.* *Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also encouraged to follow the assigned diet to the best of their ability until the 2 month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.*
Control	Low fat: aimed for a 40–30–30 balance of percentage energy from carbohydrate, fat and protein respectively. No further details reported. Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also encouraged to follow the assigned diet to the best of their ability until the 2 month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.
Length of follow-up	*12 months*
Results	*At 2 months, mean (SD) weight change in kg was –3.50 (3.80) in the LED group and –3.80 (3.60) in the low-fat group. Mean weight change in the LED group compared with low-fat was 0.30 (95% CI –1.32 to 1.92).* *At 6 months, mean (SD) weight change in kg was –3.50 (5.60) in the LED group and –3.40 (5.70) in the low-fat group. Mean weight change in the LED group compared with low-fat was –0.10 (95% CI –2.58 to 2.38).* *At 12 months, mean (SD) weight change in kg was –3.00 (4.90) in the LED group and –3.20 (6.00) in the low-fat group. Mean weight change in the LED group compared with low-fat was 0.20 (95% CI –2.20 to 2.60).* *Weight and BMI were significantly lower than baseline for both groups (p≤0.05) but there was no statistically significant difference between the groups.* *Greater effects were observed in study completers.*
Quality and comments	*Weight Watchers categorised as LED (1200–1600 kcal/day). Zone diet categorised as low fat (not able to determine energy intake).* *Blinded assessment done. ITT analysis done. Randomisation done by computer-generated sequence, and good allocation concealment.* *See other sections for comparisons of protein-sparing modified fast (PSMF), LED, low-fat, and very-low-fat (Atkins, Weight Watchers, Zone and Ornish respectively).*

Other outcomes

Shah 1996 (in HTA) RCT	
Results	*Significant differences were seen between the groups over time for changes in energy from fat (–3.4 vs –8.9%,* p=*0.0002) and energy from carbohydrate (2.6 vs 7.3%,* p=*0.015). No differences were seen for changes in energy from protein or alcohol, overall protein, palatability, satiety, quality of life or physical activity.* *Significant differences were seen between the groups over time for changes in intake of vitamin C (–28% recommended daily allowance [RDA] vs 19% RDA,* p=*0.043), calcium (–27% RDA vs –4% RDA,* p=*0.009) and phosphorus (–36 vs –10% RDA,* p=*0.02). No differences were seen for the changes of intake of vitamins A, D, E and C, thiamine, riboflavin, niacin, folacin, B_6, B_{12}, iron, magnesium, zinc or dietary fibre.* *Data on compliance suggested that the low-fat diet may have been more attractive to participants (attendance, completion of diaries, days achieving dietary goals were all higher in this group). Compliance was associated with weight loss at 6 months, but not 12 months.*
Quality and comments	Dietary intake assessed by daily food diary and three random telephone recalls (unannounced).

Dansinger 2005 RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was –0.21 (0.62) in the LED group, and –0.26 (0.90) in the low-fat group. Mean TC change in the LED group compared with low-fat was 0.05 (95% CI –0.29 to 0.39).* *At 12 months, mean (SD) LDL change in mmol/l was –0.24 (0.69) in the LED group, and –0.30 (0.87) in the low-fat group. Mean LDL change in the LED group compared with low-fat was 0.06 (95% CI –0.28 to 0.40).* *At 12 months, mean (SD) HDL change in mmol/l was 0.09 (0.25) in the LED group, and 0.08 (0.26) in the low-fat group. Mean HDL change in the LED group compared with low-fat was 0.01 (95% CI –0.10 to 0.12).* *At 12 months, mean (SD) TAG change in mmol/l was –0.14 (0.69) in the LED group, and 0.03 (1.65) in the low-fat group. Mean TAG change in the LED group compared with low-fat was –0.17 (95% CI –0.72 to 0.38).* *At 12 months, mean (SD) DBP change in mmHg was –1.70 (6.40) in the LED group, and –1.20 (9.50) in the low-fat group. Mean DBP change in the LED group compared with low-fat was –0.50 (95% CI –4.05 to 3.05).* *At 12 months, mean (SD) SBP change in mmHg was –2.70 (13.00) in the LED group, and 1.40 (15.00) in the low-fat group. Mean SBP change in the LED group compared with low-fat was -4.10 (95% CI –10.25 to 2.05).* *At 12 months, mean (SD) FPG change in mmol/l was –0.26 (1.06) in the LED group, and –0.23 (1.00) in the low-fat group. Mean FPG change in the LED group compared with low-fat was –0.03 (95% CI –0.48 to 0.42).* *At 12 months, the mean energy reductions from baseline were 244 for LED and 251 for low fat (*p≤*0.05). These were not significantly different between groups.* *No significant differences were seen in macronutrient content between any of the groups* *In each group, about 25% of participants lost 5% or more of initial body weight, and about 10% lost 10% or more at 12 months.* *Group mean adherence scores according to diet records and self-assessment decreased over time, and to a similar extent in all groups. About 25% of each group sustained a mean adherence level of at least 6/10, which 'appeared to delineate a clinically meaningful adherence level'.* *Amount of weight loss was associated with self-reported dietary adherence level (*r=*0.60;* p<*0.001) but not with diet type (*r=*0.07;* p=*0.40).*
Quality and	Converted mg/dl to mmol/l (see paper for conversion rates and values used).

comments	Dietary intake was assessed from 3-day diet records at 1, 2, 6 and 12 months.

Reported harms

Shah 1996 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Dansinger 2005 RCT	
Harms	Common reasons for discontinuation were that the assigned diet was too hard to follow, or not yielding enough weight loss. No diet-related or adverse events or serious adverse effects were found.
Quality and comments	Reasons for discontinuation not reported by group but overall only.

Generalisability

Shah 1996 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if healthy, non-smoking, women, aged 25–45 years, 20–40% above IBW.* *Excluded if smokers, consumed more than 20 alcoholic drinks per week, pregnant or lactating, suffered from chronic disease or psychiatric problems.*
Recruitment	Recruited through newspaper advertisements.
Intervention (mode and intensity)	26 weeks plus follow-up visit at 12 months, contacted 18 times (baseline, then 16 times in first 26 weeks then at 12 months).
Control (mode and intensity)	*As for intervention.*
Delivery of intervention/control (who)	A dietitian and health educator delivered counselling to participants.
Dropout rates	39% overall at 12 months.
Treatment of dropouts (return to baseline, or last measurement?)	Results for participants with no missing data only.

Dansinger 2005 RCT	
Country and setting	USA. Enrolled at an academic medical centre.
Participants (included/excluded)	Included if adults of any age who were overweight (BMI between 27 and 42 kg/m^2) and having at least one of the following metabolic cardiac risk factors: FPG ≥6.1 mmol/l, TC ≥5.2 mmol/l, LDL ≥3.4 mmol/l, HDL ≤1.0 mmol/l, TAG ≥1.7 mmol/l, SBP ≥145 mmHg, DBP ≥90 mmHg, or current use of oral medication to treat hypertension, diabetes, dyslipidaemia. Excluded if unstable chronic illness, insulin therapy, urinary microalbumin of more than two times normal, serum creatinine ≥123.8 µmol/l, clinically significant abnormalities of liver or thyroid test results, weight loss medication or pregnancy.
Recruitment	Newspaper advertisements and TV publicity (local news coverage).
Intervention (mode and intensity)	*Four classes lasting 1 h during the first 2 months. Assessed at baseline, 2, 6 and 12 months (additional dietary assessment at 1 month).*
Control (mode and intensity)	As above

Delivery of intervention/control (who)	Team consisted of dietitian and physician who facilitated the meetings.
Dropout rates	*35% LED and 35% low-fat at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Weight and cardiac risk factors, baseline values carried forward. Dietary intake, baseline or subsequent values used.

1.3.5 Very-low energy diet compared with 600 kcal/day deficit or low-fat diet

Weight loss

Simonen 2000 (in HTA) RCT	
Aim	To investigate whether cholesterol and lipoprotein metabolism are related to serum variables of glucose metabolism at baseline, and to study the effects of weight reduction on glucose, cholesterol and lipoprotein metabolism during a prolonged follow-up in obese people with type 2 diabetes
Participants	People who were obese (BMI >30 kg/m^2) and who had type 2 diabetes. 1*6 total – 3 F, 13 M. Mean (SD) age 51.1 (8.8) years VLED (*n=*6), 54.3 (3.4) years low-fat (*n=*10). Mean BMI 31.94* kg/m^2 *VLED, 32.32* kg/m^2 *low-fat.*
Intervention (including details of diet)	6 week pre-treatment phase consisting of ad libitum diet at home whilst metabolic tests carried out. Hypoglycaemia treatment discontinued; VLED diet consisted of three daily servings of 140 kcal per serving (Cambridge diet – meal replacement), one serving=14.2 g protein, 15 g carbohydrate, 2.7 g fat, essential minerals, trace nutrients and vitamins for 3 months. From month 4 until month 24 diets individually tailored by dietitian to provide daily energy balance of zero.
Control	*6 week pre-treatment phase consisting of ad libitum diet at home whilst metabolic tests carried out.* *Participants' dose of glibenclamide adjusted so that plasma glucose <7.0 mmol/l and biguanides discontinued; LED where participants advised to consume low-fat, low-cholesterol diet for 3 months.* *From month 4 until month 24 diets individually tailored by dietitian to provide daily energy balance of zero*.
Length of follow-up	24 months
Results	*A*t 24 months, mean (SD) weight change in kg was –6.70 (7.81) in the *VLED* group, and –2.00 (6.48) in the low-fat group. Mean weight change in the *VLED* group compared with low fat was –4.70 (95% CI –11.79 to 2.39).
Quality and comments	Fasting plasma glucose and HbA_{1c} differed significantly between groups (p<0.05). Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. All 16 participants analysed in aggregate, author replied, only weight data outcome used as treatment by hypoglycaemic medications differed between groups.

Other outcomes

Simonen 2000 (in HTA) RCT	
Results	Only weight data outcome used as treatment by hypoglycaemic medications differed between groups. *Other published outcomes not reported by treatment group (VLED or low-fat).*
Quality and	…

comments

Reported harms

Simonen 2000 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Simonen 2000 (in HTA) RCT	
Country and setting	Finland. No further details.
Participants (included/excluded)	*Included if diagnosis of type 2 diabetes in last 2 years (fasting plasma glucose ≥7.0 mmol/l).* (All women were postmenopausal and none had received hormone replacement therapy – but this appeared to be more a coincidence rather than a defined inclusion criteria) *Excluded if on insulin therapy, diabetic microangiopathy, hepatic or thyroid disease; unstable angina pectoris or MI; or invasive coronary artery disease (CAD) treatment in previous year.*
Recruitment	N/R.
Intervention (mode and intensity)	3 months plus follow-up at 2 years.
Control (mode and intensity)	*3 months plus follow-up at 2 years.*
Delivery of intervention/control (who)	Dietitian calculated individual energy intakes in the weight maintenance phase (months 4 to 24).
Dropout rates	0% overall.
Treatment of dropouts (return to baseline, or last measurement?)	No missing values reported.

1.3.6 Very-low energy diet compared with low-energy diet

Weight loss

Viegener 1990 (in HTA) RCT	
Aim	To determine whether the efficacy of behaviour therapy for obesity might be improved by the use of an intermittent, low-fat, LED.
Participants	Women who were obese (25 to 99% overweight based on the Metropolitan Life Insurance Company tables). *85 total – all women. Mean (SD) age 47.10 (7.49) years VLED (*n*=42), 47.13 (8.86) years LED (*n*=43). Mean (SD) weight 94.58 (12.64) kg VLED, 98.57 (15.91) kg LED.*

Intervention (including details of diet)	All participants received behaviour therapy which included self-monitoring, stimulus control, self-reinforcement, cognitive modification and problem-solving; all participants were advised to follow a regimen of programmed aerobic exercise with a target goal of 30 min a day for 6 days per week; all participants required to purchase a nutrition guide book and to complete daily food diary and daily exercise diary. Diet *(classified as VLED)* was 800 kcal/day diet for 4 days per week and 1200 kcal/day for 3 days per week consisting of 15% or less intake from fat on VLED days and 25% or less fat on LED days; each treatment session included significant focus on nutrition education with sample meals and practical guidance regarding low fat and low energy foods.
Control	*All participants received behaviour therapy which included self-monitoring, stimulus control, self-reinforcement, cognitive modification and problem-solving; all participants were advised to follow a regimen of programmed aerobic exercise with a target goal of 30 min per day for 6 days per week; all participants required to purchase a nutrition guide book and to complete daily food diary and daily exercise diary.* *Diet* (classified as LED) *was 1200 kcal/day balanced deficit diet with 55% energy as carbohydrate, 30% as fat and 15% as protein.*
Length of follow-up	52 weeks
Results	At 1 month, mean (SD) weight change in kg was –3.72 (1.65) in the VLED group, and –2.37 (2.00) in the LED group. Mean weight change in the VLED group compared with LED was –1.35 (95% CI –2.25 to –0.45). At 2 months, mean (SD) weight change in kg was –5.91 (2.88) in the VLED group, and –3.91 (3.19) in the LED group. Mean weight change in the VLED group compared with LED was –2.00 (95% CI –3.50 to –0.50). At 3 months, mean (SD) weight change in kg was –7.88 (3.17) in the VLED group, and –5.51 (4.12) in the LED group. Mean weight change in the VLED group compared with LED was –2.37 (95% CI –4.18 to –0.56). At 4 months, mean (SD) weight change in kg was –8.89 (3.78) in the VLED group, and –6.98 (4.67) in the LED group. Mean weight change in the VLED group compared with LED was –1.91 (95% CI –4.00 to 0.18). At 5 months, mean (SD) weight change in kg was –9.63 (4.44) in the VLED group, and –8.02 (5.23) in the LED group. Mean weight change in the VLED group compared with LED was –1.61 (95% CI –4.00 to 0.78). At 6 months, mean (SD) weight change in kg was –10.19 (5.06) in the VLED group, and –8.87 (5.56) in the LED group. Mean weight change in the VLED group compared with LED was –1.32 (95% CI –3.94 to 1.30). *At 12 months, mean (SD) weight change in kg was –8.97 (6.72) in the VLED group, and –8.95 (7.26) in the LED group. Mean weight change in the VLED group compared with LED was –0.02 (95% CI –3.56 to 3.52).*
Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment.

Wing 1984 (in HTA) RCT	
Aim	To compare two weight control strategies: intermittent LED and intermittent booster sessions.
Participants	People who were overweight (≥20% greater than IBW] *48 total – 42 F, 6 M. Mean (SEM) age 44.79 (1.56) years overall. Mean BMI 36.45 kg/m^2 overall. Allocated 25 to VLED and 23 to LED.*

Kg/m2)Intervention (including details of diet)	All participants underwent 10 days pre-treatment assessment prior to randomisation, first 4 days involved food and exercise records, days 5–7 involved individual energy deficit (initial weight in pounds × 12 – 1000 kcal) using Slender breakfast bars and liquid, days 8–10 participants returned to conventional foods but still maintaining same prescribed energy deficit. Post randomisation for initial 10 weeks participants received 60–90 min weekly sessions involving individual weight-in, review, food diaries, presentation of a behavioural lesson (energy balance, strategies for increasing exercise, stimulus control, cognitive restructuring, self-reinforcement and relapse prevention) To maintain weight, individually prescribed energy goal (initial weight in pounds × 12 – 1000 kcal) for 5 days per week and <750 kcal/day for 2 days each week (chosen by participant) for initial 10 weeks, could use low energy menu or return to using Slender bars and liquid *(classified as VLED).* Further randomised by weight loss to maintenance by either massed booster session at weeks 14, 23, 24, 25, 26 and 34 which included problem-solving techniques, coping strategies, nutrition and exercise topics or spaced booster sessions with the same content as the massed booster sessions.
Control	*All participants underwent 10 days pre-treatment assessment prior to randomisation, first 4 days involved food and exercise records, days 5–7 involved individual energy deficit (initial weight in pounds × 12 – 1000 kcal) using Slender breakfast bars and liquid, days 8–10 participants returned to conventional foods but still maintaining same prescribed energy deficit.* *Post randomisation for initial 10 weeks participants received 60–90 min weekly sessions involving individual weight-in, review, food diaries, presentation of a behavioural lesson (energy balance, strategies for increasing exercise, stimulus control, cognitive restructuring, self-reinforcement and relapse prevention)* *To maintain weight, individually prescribed energy goal (initial weight in pounds × 12 – 1000 kcal) for 7 days per week* (classified as LED). *Further randomised by weight loss to maintenance by either massed booster session at weeks 14, 23, 24, 25, 26 and 34 which included problem-solving techniques, coping strategies, nutrition and exercise topics or spaced booster sessions with the same content as the massed booster sessions.*
Length of follow-up	52 weeks
Results	Concentrated sessions: at 6 months, mean (SD) weight change in kg was –4.05 (7.06) in the VLED group, and –1.47 (6.33) in the LED group. Mean weight change in the VLED group compared with LED was –2.58 (95% CI –8.08 to 2.92). Spaced sessions: at 6 months, mean (SD) weight change in kg was –1.31 (6.29) in the VLED group, and –3.12 (6.80) in the LED group. Mean weight change in the VLED group compared with LED was 1.81 (95% CI –3.88 to 7.50). *Concentrated sessions: at 12 months, mean (SD) weight change in kg was –1.95 (6.47) in the VLED group, and 0.38 (6.02) in the LED group. Mean weight change in the VLED group compared with LED was –2.33 (95% CI –7.45 to 2.79).* *Spaced sessions: at 12 months, mean (SD) weight change in kg was –0.58 (6.08) in the VLED group, and –2.69 (6.68) in the LED group. Mean weight change in the VLED group compared with LED was 2.11 (95% CI –3.45 to 7.67).*

Quality and comments	Baseline comparability not stated. Blinded assessment done. ITT analysis done. Random allocation but no description of concealment. Mean change in weight calculated by subtracting pre-randomisation weight loss from weight change at 12 months, SDs calculated. *HTA reported results comparing VLED and LED for two groups: concentrated booster sessions (Wing 1984a) and spaced booster sessions (Wing 1984b).*

Pavlou 1989 1 (in HTA) RCT	
Aim	To determine the role of exercise in relation to the type of diet, rate of weight loss and defined exercise experience on long-term maintenance
Participants	Healthy men. *160 total (for complete study) – all men. Mean (SD) age 46.1 (9.33) years VLED, 41.5 (7.59) years LED (Pavlou 1ga). Mean (SD) age 44.5 (9.60) years VLED, 42.9 (6.63) years LED (Pavlou 1hb). Mean BMI (kg/m^2) 31.89 VLED, 32.54 LED (Pavlou 1ga). Mean BMI 33.78 VLED, 32.4 LED (Pavlou 1hb).* *Data for completers only (18 VLED, 10 LED, 16 VLED, 11 LED respectively completed at 18 months post-treatment). No details of allocation to each group.*
Intervention (including details of diet)	All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts. VLED: DPC 800; assumed VLED 800 kcal/day diet provided in powdered form to be consumed similarly to DPC-70, provided a complete mixture of nutrients and similar nutritionally to balanced energy-deficit diet (BEDD) except for less energy. For groups allocated to exercise (Pavlou 1ga) 90 min supervised exercise programme three times per week from baseline to week 8 which consisted of 35–60 min of aerobic activity, e.g. walk-jog-run (70–85% maximum heart rate), callisthenics and relaxation techniques. For groups allocated to no exercise (Pavlou 1hb) participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks.
Control	*All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts.* *LED: BEDD, where 1000 kcal/day selected from usual four food groups in quantities thought to meet basic requirements.* *For groups allocated to exercise (Pavlou 1ga) 90 min supervised exercise programme three times/week from baseline to week 8 which consisted of 35–60 min of aerobic activity e.g. walk–jog–run (70–85% maximum heart rate), callisthenics and relaxation techniques.* *For groups allocated to no exercise (Pavlou 1hb) participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks.*
Length of follow-up	*86 weeks.*
Results	Only 18-month outcomes reported. Published values showed results over the initial 12 weeks, but difficult to determine the numbers exactly. Supervised exercise: at 18 months, mean (SD) weight change in kg was –12.40 (9.42) in the VLED group, and –9.19 (8.52) in the LED group. Mean weight change in the VLED group compared with LED was –3.21 (95% CI –10.05 to 3.63). No additional exercise: at 18 months, mean (SD) weight change in kg was –3.45 (6.89) in the VLED group, and –3.57 (6.93) in the LED group. Mean weight change in the VLED group compared with LED was 0.12 (95% CI –5.19 to 5.43).

Quality and comments	*HTA reported results for two groups. Pavlou 1ga – VLED (800 kcal) and exercise vs LED and exercise, and Pavlou 1hb – VLED (800 kcal) vs LED.* Blinded assessment not done. Possible ITT analysis. Random allocation but no description of concealment. Weight data derived from graph and SDs calculated.

Other outcomes

Viegener 1990 (in HTA) RCT	
Results	*At months 1, 2, 4 and 6 the VLED group were consuming significantly less energy per day than the LED group (*p<*0.05). Energy intake at months 3 and 5 were not significantly different.* *At 12 months, mean (SD) energy intake (kcal/day) in the diet group was 1283 (391) in the VLED group compared with 1293 (473) in the LED group. The difference was not significant.* *For the first 5 months, the VLED group was consuming significantly less energy from fat per day than the LED group (*p<*0.05). Energy intake from fat at month 6 was not significantly different.* *At 12 months, there was not enough data in the diaries to calculate the energy intake from fat* *No difference was seen between groups in attendance rates, self-reported diet adherence, and self-reported physical activity.*
Quality and comments	Dietary intake calculated from participants' 7-day eating diaries.

Wing 1984 (in HTA) RCT	
Results	*During the 10-week treatment programme, participants in the VLED group reported significantly more days where the energy intake was <750 kcal compared with the LED group (13.4 days vs 5.9 days,* p<*0.001). But the total energy intake was no different between the groups (1106 vs 1199 kcal).* *Significant improvements in eating habits (assessed by the Eating Behaviour Inventory) were seen at 10 weeks and 6 months (*p<*0.01). Significant reductions in the amount of high-energy food stored in the home were also seen (*p<*0.01).*
Quality and comments	Self-reported dietary intake from diaries.

Pavlou 1989 1 (in HTA) RCT	
Results	*No other outcomes by different diet groups were reported.*
Quality and comments	…

Reported harms

Viegener 1990 (in HTA) RCT	
Harms	*None reported.*
Quality and comments	…

Wing 1984 (in HTA) RCT T	
Harms	None reported.
Quality and comments	…

Pavlou 1989 1 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Viegener 1990 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included women aged 21–59 years, 25–99% overweight, with physicians approval, $125 deposit (with return based on attendance and completion of food diaries).* *Excluded if had obesity related disorders.*
Recruitment	Newspaper advertisements
Intervention (mode and intensity)	12 months, contacted maximum of 39 times (baseline, weekly 2 h group and individual sessions for first 26 weeks then opportunity to attend group maintenance sessions twice monthly for 26 weeks).
Control (mode and intensity)	As above.
Delivery of intervention/control (who)	Clinical psychology graduate students facilitated the behavioural treatment groups.
Dropout rates	29% in VLED and 30% in LED at 12 months.
Treatment of dropouts (return to baseline, or last measurement?)	Missing data was imputed by assuming that dropouts relapsed to pre-treatment weight.

Wing 1984 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if aged 20–65 years, 20% or more overweight, $85 deposit, $35 non-refundable, $50 refunded at attendance.* *Excluded if currently involved in other weight control programme.*
Recruitment	Recruited via newspaper articles and physician referrals. Interested people were then invited to an orientation meeting.
Intervention (mode and intensity)	Massed booster sessions: 12 months, contacted 18 times (baseline, weekly for first 10 weeks then at weeks 14, 23, 24, 25, 26, 34 and 52) Concentrated booster sessions: 12 months, contacted 18 times (baseline, weekly for first 10 weeks then at weeks 14, 18, 22, 26, 34 and 52
Control (mode and intensity)	As above
Delivery of intervention/control (who)	No details.
Dropout rates	*8% overall*
Treatment of dropouts (return to baseline, or last measurement?)	Dropouts were assumed to have lost no weight.

Pavlou 1989 1 (in HTA) RCT	
Country and setting	USA. Workplace.
Participants (included/excluded)	*Included men, aged 26–52 years, euthyroid, free from any physical, psychological or metabolic impairment.* *Exclusion criteria not stated.*
Recruitment	Men were recruited from the Boston Police Department and the Metropolitan District Commission. No further details reported.
Intervention (mode and intensity)	8 weeks plus 18 months post-treatment follow-up (weekly from baseline to week 8 then at 8 months and 18 months post-treatment)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	No details.

Dropout rates	31% overall at 18 months post-treatment.
Treatment of dropouts (return to baseline, or last measurement?)	N/R

1.3.7 Low-fat diet compared with another weight-reducing diet

Weight loss

Baron 1986 (in CR Pirozzo) RCT	
Aim	To compare the effects of low-carbohydrate and low-fat/low-fibre diets on weight and metabolic outcomes
Participants	*People who were overweight (above upper limit of acceptable weight for medium framed person from the Metropolitan Life Insurance tables)* *135 total – 115 F, 20 M.* Mean (SE) age 39.7 (1.5) years low-fat, 39.5 (1.3) years other diet. Mean (SE) BMI (kg/m^2) 28.5 (0.5) low-fat, 29.1 (0.6) other diet. *Low-fat group (*n*=69) and other control group (*n*=66).*
Intervention (including details of diet)	Diet: 1000–1200 kcal/day; low fat//high fibre; fat not >30 g/day. General orientation to dieting and limited discussion of behavioural techniques and value of exercise. Given diet instruction sheets and verbal advice. Weekly meetings with group (at diet club) for 3 months.
Control	*Control: 1000–1200 kcal/day; low-carbohydrate/low-fibre; carbohydrate no t>50 g/day.* *General orientation to dieting and limited discussion of behavioural techniques and value of exercise. Given diet instruction sheets and verbal advice. Weekly meetings with group (at diet club) for 3 months.*
Length of follow-up	12 months.
Results	*At 1 month, mean (SD) weight change in kg was –2.80 (6.71) in the low-fat diet group, and –3.9 (7.02) in the other diet group. Mean weight change in the low-fat diet group compared with the other diet group was 1.1 (95% CI –1.26 to 3.46).* *At 3 months, mean (SD) weight change in kg was –3.70 (6.96) in the low-fat diet group, and –5.00 (7.33) in the other diet group. Mean weight change in the low-fat diet group compared with the other diet group was 1.30 (95% CI –0.26 to 2.86).* At 12 months, mean (SD) weight change in kg was –1.60 (5.20) in the low-fat diet group, and –2.30 (5.20) in the other diet group. Mean weight change in the low-fat diet group compared with the other diet group was 0.70 (95% CI –1.16 to 2.56). *Dieters given low-carbohydrate/low-fibre dietary advice tended to lose more weight than those given a higher-carbohydrate/higher-fibre regimen. This pattern was particularly marked among women, and among participants who were under age 40 years or of lower social class. There were no differences between the diet groups in the proportion complaining of hunger but, in general, members of the low-carbohydrate group complained of more problems in dieting.*
Quality and comments	Blinded assessment not done. No details of randomisation or concealment. *Used HTA calculation for 1 and 3 month SDs (so slightly different CIs to those reported in the paper).*

Harvey-Berino 1998 (in CR Pirozzo) RCT	
Aim	To assess whether an energy-restricted diet or fat-restricted diet was more effective at promoting weight loss, improving eating behaviours and reducing barriers to dietary adherence.

Participants	People who were overweight (20 to 40% overweight as defined by the Metropolitan Life Insurance tables). *80 total – 65 F, 15 M. Mean age 38 years (range 25 to 45 years), not reported by group. Mean (SD) BMI (kg/m^2) 29.5 (1.8) for 28 completers low-fat, 29.9 (1.5) for 29 completers low-energy. Numbers allocated to each group not reported.*
Intervention (including details of diet)	Low-fat diet: 22–26 g/day; unrestricted carbohydrates. Given advice on how to follow diet; given counselling on behavioural modification strategies *(stimulus control, problem-solving, social skills, relapse prevention)* and self-management skills and how to increase physical activity; completed exercise and food diary daily; weekly meetings with group for 6 months.
Control	*LED – 1000–1200 kcal/day. Given advice on how to follow diet; given counselling on behavioural modification strategies* (as above) *and self-management skills and how to increase physical activity; completed exercise and food diary daily; weekly meetings with group for 6 months.*
Length of follow-up	18 months
Results	*A*t 6 months, mean (SD) weight change in kg was –5.20 (4.60) in the low-fat group, and –11.80 (4.90) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was 6.60 (95% CI 4.13 to 9.07). *A*t 12 months, mean (SD) weight change in kg was –3.00 (5.00) in the low-fat group, and –8.70 (5.00) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was 5.70 (95% CI 2.86 to 8.54). *A*t 18 months, mean (SD) weight change in kg was –1.80 (5.00) in the low-fat group, and –7.50 (5.00) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was 5.70 (95% CI 2.86 to 8.54). *At 6 months, 21% of the low-fat group and 75% of the low energy group had lost 10% or more of initial bodyweight. This was statistically significant (*p*<0.0001).*
Quality and comments	Blinded assessment unclear. No details of randomisation or concealment. ITT analysis not done.

McManus 2001 (in CR Pirozzo) RCT	
Aim	To evaluate a diet moderate in fat based on the Mediterranean diet compared with a standard low-fat diet for weight loss (both controlled for energy).
Participants	Healthy people who were overweight (BMI between 26.5 and 46 kg/m^2). *101 total – 91 F, 10 M. Mean (SD) age 44 (10) years in the low-fat diet (*n*=51) and 44 (10) years in the other (moderate fat) diet (*n*=50). Mean BMI (SD) in the low-fat diet group 34 (5) and 33 (3) kg/m^2 in the other group.*
Intervention (including details of diet)	Low-fat: 1200–1500 kcal – carbohydrate (60–65% of energy), fat (20% of energy), protein (15–20% of energy) Dietitian gave advice on how to follow diets and specific food recommendations; provided with meal plans and sample menus; teaching modules addressed behavioural modification skills and physical activity; completed daily food diary; weekly meetings with group for 18 months
Control	*Moderate fat: 1200–1500 kcal – carbohydrate 45–50% of energy, fat 35% of energy, protein 15–20% of energy.* *Dietitian gave advice on how to follow diets and specific food recommendations; provided with meal plans and sample menus; teaching modules addressed behavioural modification skills and physical activity; completed daily food diary; weekly meetings with group for 18 months*
Length of follow-up	18 months.

Results	*A*t 6 months, mean (SD) weight change in kg was –5.10 (4.60) in the low-fat group, and –4.90 (4.30) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was –0.20 (95% CI –2.61 to 2.21). *A*t 12 months, mean (SD) weight change in kg was –5.00 (7.30) in the low-fat group, and –4.80 (5.20) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was –0.20 (95% CI –4.63 to 4.23). *A*t 18 months, mean (SD) weight change in kg was 2.90 (7.70) in the low-fat group, and –4.10 (6.50) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was 7.00 (95% CI 3.42 to 10.58). *At 6 months, mean (SD) in WHR was –0.01 (0.04) in the low-fat group, and –0.02 (0.05) in the other diet group. Mean WHR change in the low-fat group compared with the other diet group was 0.01 (95% CI –0.01 to 0.03) (named wrongly in CR).*
Quality and comments	Blinded assessment unclear. No details of concealment. ITT analysis done. *Results at 6 and 12 months for active participants only – at 18 months, for all available participants.*

Pascale 1995 (in CR Pirozzo) RCT	
Aim	To compare the effects of a behavioural intervention focusing on either energy restriction alone or energy plus fat restriction on weight, lipids, and glycaemic control on people with non-insulin-dependent diabetes mellitus (NIDDM) or a family history of diabetes. (Results reported only for people with family history. Exclusion criterion for the review was no serious medical condition, so assumed to exclude those participants with NIDDM?)
Participants	Women who were overweight (20% or more above IBW by Metropolitan Life Insurance tables) with NIDDM or a family history of diabetes. *46 total – all women. Age range 34 to 51 years. Mean (SD) BMI 36.1 (5.6) kg/m^2 low fat, 35.0 (4.4) kg/m^2 other diet (results for completers only). Low-fat group (*n*=23) and other control group (*n*=23).*
Intervention (including details of diet)	Low fat: 1000–1500 kcal/day; low fat (20% total energy) Given advice on how to follow diet; given counselling on behavioural modification strategies and self-management skills and how to increase physical activity; completed exercise and food diary daily; weekly meetings with group for 4 months.
Control	*Other diet: 1000–1500 kcal/day* *Given advice on how to follow diet; given counselling on behavioural modification strategies and self-management skills and how to increase physical activity; completed exercise and food diary daily; weekly meetings with group for 4 months.*
Length of follow-up	12 months.
Results	*NIDDM: At 16 weeks, mean (SD) weight change in kg was –7.70 (3.60) in the low-fat group, and –4.70 (3.90) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was –3.00 (95% CI –5.64 to –0.36).* *NIDDM: A*t 12 months, mean (SD) weight change in kg was –5.20 (7.30) in the low-fat group, and –0.96 (3.70) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was –4.24 (95% CI –8.36 to –0.12). *Family history: At 16 weeks, mean (SD) weight change in kg was –7.40 (4.0) in the low-fat group, and –6.90 (4.70) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was –0.50 (95% CI –3.72 to 2.72).* *Family history: A*t 12 months, mean (SD) weight change in kg was –3.00 (8.40) in the low-fat group, and –3.50 (7.40) in the other diet group. Mean weight change in the low-fat group compared with the other diet group was 0.50 (95% CI –5.26 to 6.26).
Quality and comments	Blinded assessment unclear. No details of concealment. ITT analysis not done.

Other outcomes

Baron 1986 (in CR Pirozzo) RCT	
Results	*No significant differences between groups for changes from baseline were seen at either 1 or 3 months for TC, HDL, LDL, VLDL, TAG, HDL:LDL ratio, or glucose levels.* *The low-fat group decreased whole milk and red meat intake (servings per week) more than the low-carbohydrate group, but this was not significant at 12 months.* *The low-carbohydrate group decreased white bread intake (slices per week) more than the low-fat group, but this was not significant at 12 months. However, both groups increased consumption of brown bread, with the low-fat group eating significantly more (11.1 vs 8.3 slices per week) at 12 months than the low-carbohydrate groups. Similarly, potato intake decreased in both groups, with the low-carbohydrate group eating significantly less (2.6 vs 4.0 servings per week) at 12 months.* *Total cereal fibre increased in the low-fat group and decreased in the low-carbohydrate group, but the difference was not significant at 12 months.* *Total dietary fibre (g per day) also increased in the low-fat group but decreased in the low-carbohydrate group, and the difference was significant at 1, 3 and 12 months.* *Weight loss differed significantly between participating diet clubs, and club membership was a better predictor of weight loss than diet allocation (results not reported).*
Quality and comments	Dietary intake from self-completed questionnaires.

Harvey-Berino 1998 (in CR Pirozzo) RCT	
Results	*At 6 months in both groups, levels of physical activity increased, and % energy as protein intake increased from baseline, but the differences between groups were not statistically significant. However, energy intake decreased more in the low-energy group (*p<*0.05), % carbohydrate intake increased more in the low-fat group (*p<*0.01), and % fat intake decreased more in the low-fat group (*p<*0.01).* *At 6 months in both groups, measures of wellness improved more in the low-energy group (*p=*0.03), but inconvenience of eating outside the home was significantly higher for this group from baseline, whereas the low-fat group reported a lower inconvenience than at baseline. The difference was statistically significant (*p=*0.01). Other measures (distaste for fat, cost, deprivation of favourite foods and family issues) did not differ between the groups.* *Participants in the low-energy group reported a significantly greater positive change in eating behaviours (measured by Eating Behaviour Inventory) than did those in the low-fat group (*p<0*.001).* *People in the low-carbohydrate group consumed significantly less energy, less carbohydrate and the same amount of fat as those in the low fat condition; however, energy and carbohydrate intake were decreasing for low-fat participants by the 12- and 18-month assessments. There were no long-term differences in most measured predictors of dietary adherence.*
Quality and comments	Dietary intake was from 3-day food diaries, which were then reviewed for accuracy and completeness by a nutritionist who was blind to the treatment allocation of the participant. Other factors relating to dietary adherence (wellness, distaste, cost, inconvenience, deprivation and family) were measured using a scale previously developed for the Women's Health Trial.

McManus 2001 (in CR Pirozzo) RCT	
Results	*Total energy intake (kcal) was similar at 6 and 12 months, but at 18 months, the low-fat group consumed less energy than the moderate fat group (1697 vs 1877,* p=*0.08).* *% Energy intake from both total fat and monounsaturated fat was consistently lower in the low-fat diet at 6, 12 and 18 months (*p<*0.05). Although % intake from polyunsaturated fat was significantly lower in the low-fat group at 6 and 12 months (*p<*0.05), the groups were not significantly different at 18 months (*p=*0.06).* *% Energy intake from saturated fatty acids did not differ between the groups at any time (*p>*0.05).* *At 6 months, % energy intake from carbohydrate was lower in the low-fat group (*p=*0.02) but this difference was not maintained at 12 and 18 months (*p<0*.05).* *No differences were seen in the % energy intake from protein between the groups at any time point (*p>*0.05).* *Dietary fibre did not differ between groups except at 18 months, where the low-fat group reported consuming significantly less fibre (g) than the moderate fat group (*p=*0.03).* *Dietary cholesterol did not differ between groups except at 12 months, where the low-fat group reported consuming significantly more cholesterol (mg/1000 kcal) than the moderate fat group (*p=*0.008).* *Only 20% (10/51) of those in the low-fat group were actively participating in the weight loss programme after 18 months compared with 54% (27/50) in the moderate-fat group, (*p<*0.002).*
Quality and comments	Dietary intake assessed by validated questionnaire.

Pascale 1995 (in CR Pirozzo) RCT	
Results	*Significant decreases in glucose, HDL-cholesterol and TC were seen after 16 weeks of treatment among NIDDM participants; these changes were similar in CAL and CAL+FAT groups, but a greater proportion of participants in CAL condition required oral hypoglycaemic medication. At the 1-year follow-up, all parameters had returned to baseline. No significant differences in weight loss or physiological changes were seen between diets for women with a family history of diabetes.*
Quality and comments	Data for people with family history of diabetes only. Dietary intake assessed from 3-day food diaries.

Reported harms

Baron 1986 (in CR Pirozzo) RCT	
Harms	The participants in the low-fat group tended to voice fewer complaints. At 3 months, 6% of the low-carbohydrate group complained about how much the diet was costing compared with 0% of the low-fat group. 23% of the low-carbohydrate group complained of constipation compared with only 3% of the low-fat group. 81% of the low-carbohydrate group thought they would use the diet again compared with 92% of the low-fat group. 22% of all participants complained of fatigue at 3 months, and 31% found dieting difficult due to emotional stress.
Quality and comments	…

Harvey-Berino 1998 (in CR Pirozzo) RCT	
Harms	None reported.
Quality and comments	…

McManus 2001 (in CR Pirozzo) RCT	
Harms	None of those who dropped out cited the diet as the reasons. No other harms reported.
Quality and comments	…

Pascale 1995 (in CR Pirozzo) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Baron 1986 (in CR Pirozzo) RCT	
Country and setting	*UK.* Diet clubs and work places.
Participants (included/excluded)	*Included if weight greater than upper limit of acceptable weight for a medium framed person (Metropolitan Life Insurance tables). Excluded if dieted in last 3 months, within 6 months of childbirth, or still breast-feeding.*
Recruitment	Recruited from diet clubs and employee groups in one geographical area.
Intervention (mode and intensity)	3-month intervention. Contact at baseline, weekly for 3 months, and then at 12 months (14 contacts).
Control (mode and intensity)	*3-month control. As above.*
Delivery of intervention/control (who)	Diet group leaders
Dropout rates	11% overall.
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Harvey-Berino 1998 (in CR Pirozzo) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if aged 25–45 years, 20–40% above IBW. Excluded if smokers, pregnant or lactating, history of chronic disease or psychosis.*
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	6 months. *24 weeks of group treatment sessions.*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	*A trained therapist reviewed the diaries and gave advice on strategies for dietary adherence.*
Dropout rates	40% overall.
Treatment of dropouts (return to baseline, or last measurement?)	Analysis of data for completers only – no missing data

McManus 2001 (in CR Pirozzo) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	Included if aged 18 to 70 years, BMI 26.5 to 46 kg/m^2, non-smokers, free from chronic disease, and willing to attend weekly classes for the study duration.
Recruitment	Letters sent to primary care physicians at a women's hospital. Also announcements posted.
Intervention (mode and intensity)	*18 months – weekly meetings for 18 months (about 78 contacts)*
Control (mode and intensity)	As above

Delivery of intervention/control (who)	One dietitian per group recorded body weight, provided sample menus, ran the weekly meetings, taught behaviour modification techniques. They also ensured that the intensity of the programmes was similar between groups.
Dropout rates	*At 18 months, 80% in the low-fat diet and 50% in the control group.*
Treatment of dropouts (return to baseline, or last measurement?)	Dropouts contacted at the end of the study for measurements. Also last observation carried forward for ITT analysis.

Pascale 1995 (in CR Pirozzo) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if women whose weight 20% or more above IBW, and who had at least one biological parent with type 2 diabetes. No details of exclusions.*
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	4 months intervention with weekly meetings (about 16 contacts), plus baseline and 12 month follow-up.
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	*Trained therapists reviewed food diaries and offered advice on strategies for dietary adherence.*
Dropout rates	33% overall at 12 months.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.3.8 Protein-sparing modified fast compared with 600 kcal/deficit or low-fat diet

Weight loss

Dansinger 2005 RCT	
Aim	To assess adherence rates and the realistic clinical effectiveness of four popular diets (Atkins, Zone, Weight Watchers and Ornish) for weight loss and cardiac risk factor reduction. Dietary components only of the programmes were used (see details of intervention later).
Participants	People who were overweight (BMI between 27 and 24 kg/m^2) who also had at least one metabolic cardiac risk factor. 160 total – 81 F, 79 M. Mean (SD) age 47 (12) years PSMF (*n*=40), 51 (9) years low-fat (*n*=40). Mean (SD) BMI 35 (3.5) kg/m^2 PSMF, 34 (4.5) kg/m^2 low-fat.
Intervention (including details of diet)	*PSMF: aimed for less than 20 g of carbohydrate daily, with a gradual increase to 50 g/day.* *Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2-month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.*

Control	Low fat: aimed for a 40–30–30 balance of percentage energy from carbohydrate, fat and protein, respectively. No further details reported. Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also encouraged to follow the assigned diet to the best of their ability until the 2 month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.
Length of follow-up	*12 months*
Results	*At 2 months, mean (SD) weight change in kg was –3.60 (3.30) in the PSMF group and –3.80 (3.60) in the low-fat group. Mean weight change in the PSMF group compared with low fat was 0.20 (95% CI –1.31 to 1.71).* *At 6 months, mean (SD) weight change in kg was –3.20 (4.90) in the PSMF group and –3.40 (5.70) in the low-fat group. Mean weight change in the PSMF group compared with low fat was 0.20 (95% CI –2.13 to 2.53).* *At 12 months, mean (SD) weight change in kg was –2.10 (4.80) in the PSMF group and –3.20 (6.00) in the low-fat group. Mean weight change in the PSMF group compared with low fat was 1.10 (95% CI –1.28 to 3.48).* *Weight and BMI were significantly lower than baseline for both groups (p≤0.05) but there was no statistically significant difference between the groups.* *In each group, about 25% of participants lost 5% or more of initial body weight, and about 10% lost 10% or more at 12 months.*
Quality and comments	*Atkins categorised as PSMF. Zone diet categorised as low fat (not able to determine energy intake).* *Blinded assessment done. ITT analysis done. Randomisation done by computer-generated sequence, and good allocation concealment.* *See other sections for comparisons of PSMF, LED, low-fat and very-low-fat (Atkins, Weight Watchers, Zone and Ornish respectively).*

Stern 2004 (and Samaha 2003) RCT	
Aim	To compare the effectiveness of a low-carbohydrate diet (categorised as PSMF) and a conventional diet (categorised as low fat) in people who were obese.
Participants	People who were obese (BMI of ≥35 kg/m^2). 132 total – 23 F, 109 M. Mean (SD) 53 (9) years PSMF (*n*=64), 54 (9) years low-fat (*n*=68). Mean (SD) BMI 42.9 (6.6) kg/m^2 PSMF, 42.9 (7.7) kg/m^2 low fat.
Intervention (including details of diet)	*PSMF: instructed to reduce carbohydrate intake to <30 g per day. No instruction on total fat intake was provided. Vegetables and fruit with high ratios of fibre:carbohydrate were recommended.* *Weekly counselling sessions (2 h long) for 4 weeks, followed by 11 (1 h) monthly sessions. Participants received diet overview handout, instructional nutritional labels, sample, menus and recipes, book on 'counting calories' and carbohydrate. No specific exercise was recommended.*
Control	Low fat: instructed to reduce energy intake by 500 kcal per day, with <30% of energy from fat (guidelines of the National Heart, Lung, and Blood Institute). Weekly counselling sessions (2 h long) for 4 weeks, followed by 11 (1 h) monthly sessions. Participants received diet overview handout, instructional nutritional labels, sample, menus and recipes, book on 'counting calories' and carbohydrate. No specific exercise was recommended.
Length of follow-up	*12 months.*

Results	*At 6 months, mean (SD) weight change in kg was –5.70 (8.60) in the PSMF group and –1.80 (3.90) in the low-fat group. Mean weight change in the PSMF group compared with low-fat was –3.90 (95% CI –6.20 to –1.60).* *At 12 months, mean (SD) weight change in kg was –5.10 (8.70) in the PSMF group and –3.10 (8.40) in the low-fat group. Mean weight change in the PSMF group compared with low-fat was –2.00 (95% CI –4.99 to 0.99).* *At 6 months, 14% of the PSMF group lost 10% or more of initial body weight compared with 3% of the low-fat group (*p=*0.02).*
Quality and comments	*Higher prevalence of hypertension in the PSMF group (72 vs 57%,* p=*0.082, NS).* *ITT analysis done. Blinded assessment not clear. Random allocation but no details of concealment.*

Foster 2003 RCT	
Aim	To evaluate the effects of a low-carbohydrate, high-protein, high-fat diet (categorised as PSMF) compared with a high-carbohydrate, low-fat, energy-deficit conventional diet (categorised as low fat) on weight loss and coronary risk factors in people who were obese.
Participants	People who were obese (no definition reported). 63 total – 43 F, 20 M. Mean (SD) age 44.0 (9.4) years PSMF (*n*=33), 44.2 (7.0) years low-fat (*n*=30). Mean (SD) BMI 33.9 (3.8) kg/m^2 PSMF, 34.4 (3.1) kg/m^2 low-fat.
Intervention (including details of diet)	*PSMF: limiting carbohydrate intake without restriction of fat or protein. For first 2 weeks, carbohydrate intake is limited to 20 g/day, but is then gradually increased until a stable and desirable weight is reached.* *Met with registered dietitian to review central components of the diet. Also given copy of Atkins diet programme book. Participants instructed to read the book and follow the diet as described.*
Control	Low fat: 1200 to 1500 kcal/day for women, 1500 to 1800 kcal/day for men, about 60% of energy from carbohydrate, 25% from fat and 15% from protein. Met with registered dietitian to review central components of the diet, and received information on 'calorie counting'. Also given copy of LEARN programme for weight management. Participants instructed to read the manual and follow the diet as described.
Length of follow-up	*12 months*
Results	*At 3 months, mean (SD) weight change in kg was –6.71 (4.94) in the PSMF group and –2.65 (3.64) in the low-fat group. Mean weight change in the PSMF group compared with low fat was –4.06 (95% CI –6.19 to –1.93).* *At 6 months, mean (SD) weight change in kg was –6.91 (6.42) in the PSMF group and –3.15 (5.50) in the low-fat group. Mean weight change in the PSMF group compared with low fat was –3.76 (95% CI –6.70 to –0.82).* *At 12 months, mean (SD) weight change in kg was –4.34 (6.61) in the PSMF group and –2.46 (6.19) in the low-fat group. Mean weight change in the PSMF group compared with low fat was –1.88 (95% CI –5.04 to 1.28).*
Quality and comments	*Used percentages to calculate actual weight losses and other outcomes.* *ITT analysis done. Blinded assessment not reported. Randomisation done but no details of concealment of allocation.*

Other outcomes

Dansinger 2005 RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was –0.11 (0.59) in the PSMF group, and –0.26 (0.90) in the low-fat group. Mean TC change in the PSMF group compared with low fat was 0.15 (95% CI –0.18 to 0.48).* *At 12 months, mean (SD) LDL change in mmol/l was –0.18 (0.62) in the PSMF*

	group, and –0.30 (0.87) in the low-fat group. Mean LDL change in the PSMF group compared with low fat was 0.12 (95% CI –0.21 to 0.45). *At 12 months, mean (SD) HDL change in mmol/l was 0.09 (0.18) in the PSMF group, and 0.08 (0.26) in the low-fat group. Mean HDL change in the PSMF group compared with low fat was 0.01 (95% CI –0.09 to 0.11).* *At 12 months, mean (SD) TAG change in mmol/l was –0.02 (0.94) in the PSMF group, and 0.03 (1.65) in the low-fat group. Mean TAG change in the PSMF group compared with low fat was –0.05 (95% CI –0.64 to 0.54).* *At 12 months, mean (SD) DBP change in mmHg was –1.40 (7.50) in the PSMF group, and –1.20 (9.50) in the low-fat group. Mean DBP change in the PSMF group compared with low fat was –0.20 (95% CI –3.95 to 3.55).* *At 12 months, mean (SD) SBP change in mmHg was 0.20 (12.00) in the PSMF group, and 1.40 (15.00) in the low-fat group. Mean SBP change in the PSMF group compared with low fat was –1.20 (95% CI –7.15 to 4.75).* *At 12 months, mean (SD) FPG change in mmol/l was 0.08 (0.77) in the PSMF group, and –0.23 (1.00) in the low-fat group. Mean FPG change in the PSMF group compared with low fat was 0.31 (95% CI –0.08 to 0.70).* *At 12 months, the mean energy reductions from baseline (*p≤*0.05) were 138 for PSMF and 251 for low fat. These were not significantly different between groups.* *Group mean adherence scores according to diet records and self-assessment decreased over time, and to a similar extent in all groups. About 25% of each group sustained a mean adherence level of at least 6/10, which 'appeared to delineate a clinically meaningful adherence level'.* *Amount of weight loss was associated with self-reported dietary adherence level (*r=*0.60;* p<*0.001) but not with diet type (*r=*0.07;* p=*0.40).*
Quality and comments	Converted mg/dl to mmol/l (see paper for conversion rates and values used). Dietary intake was assessed from 3-day diet records at 1, 2, 6 and 12 months.

Stern 2004 (and Samaha 2003) RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was 0.16 (1.11) in the PSMF group, and –0.21 (0.91) in the low-fat group. Mean TC change in the PSMF group compared with low fat was 0.37 (95% CI –0.06 to 0.80).* *At 12 months, mean (SD) LDL change in mmol/l was 0.18 (0.91) in the PSMF group, and –0.10 (0.75) in the low-fat group. Mean LDL change in the PSMF group compared with low fat was 0.28 (95% CI –0.07 to 0.63).* *At 12 months, mean (SD) HDL change in mmol/l was –0.03 (0.18) in the PSMF group, and –0.13 (0.16) in the low-fat group. Mean HDL change in the PSMF group compared with low fat was 0.10 (95% CI 0.03 to 0.17).* *At 12 months, mean (SD) TAG change in mmol/l was –0.65 (1.78) in the PSMF group, and 0.05 (0.96) in the low-fat group. Mean TAG change in the PSMF group compared with low fat was –0.70 (95% CI –1.30 to –0.10).* *At 12 months, mean (SD) DBP change in mmHg was 3.00 (15.00) in the PSMF group, and 1.00 (10.00) in the low-fat group. Mean DBP change in the PSMF group compared with low fat was 2.00 (95% CI –3.35 to 7.35).* *At 12 months, mean (SD) SBP change in mmHg was 1.00 (19.00) in the PSMF group, and 2.00 (15.00) in the low-fat group. Mean SBP change in the PSMF group compared with low-fat was –1.00 (95% CI –8.18 to 6.18).* *FPG was not reported for the group as a whole, but for people with or without diabetes. There were no significant changes for either population between each group.* *No significant differences were seen between groups at 12 months for changes in intake of energy, protein, fat, fibre, saturated fat or dietary cholesterol.* *No significant differences were seen in macronutrient content between any of the groups.* *Dietary intake of carbohydrate decreased significantly more in PSMF group (–131 vs –22 g,* p=*0.011) as did dietary sodium (–633 vs 451 mg,* p=*0.05).*
Quality and	Dietary intake from 24 h dietary recall assessed using a previously validated

comments	instrument (Karvetti 1985).

Foster 2003 RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was 0.01 (0.50) in the PSMF group, and –0.14 (0.40) in the low-fat group. Mean TC change in the PSMF group compared with low-fat was 0.15 (95% CI –0.07 to 0.37).* *At 12 months, mean (SD) LDL change in mmol/l was 0.01 (0.55) in the PSMF group, and –0.10 (0.37) in the low-fat group. Mean LDL change in the PSMF group compared with low-fat was 0.11 (95% CI –0.12 to 0.34).* *At 12 months, mean (SD) HDL change in mmol/l was 0.13 (0.23) in the PSMF group, and 0.02 (0.14) in the low-fat group. Mean HDL change in the PSMF group compared with low-fat was 0.11 (95% CI 0.02 to 0.20).* *At 12 months, mean (SD) TAG change in mmol/l was –0.25 (0.34) in the PSMF group, and 0.01 (0.52) in the low-fat group. Mean TAG change in the PSMF group compared with low-fat was –0.26 (95% CI –0.48 to –0.04).* *At 12 months, mean (SD) DBP change in mmHg was –2.76 (9.25) in the PSMF group, and –2.95 (10.24) in the low-fat group. Mean DBP change in the PSMF group compared with low-fat was 0.19 (95% CI –4.65 to 5.03).* *At 12 months, mean (SD) SBP change in mmHg was –1.21 (11.33) in the PSMF group, and 2.10 (14.55) in the low-fat group. Mean SBP change in the PSMF group compared with low-fat was –3.31 (95% CI –9.79 to 3.17).*
Quality and comments	…

Reported harms

Dansinger 2005 RCT	
Harms	Common reasons for discontinuation were that the assigned diet was too hard to follow, or not yielding enough weight loss. No diet-related or adverse events or serious adverse effects were found.
Quality and comments	Reasons for discontinuation not reported by group but overall only.

Stern 2004 (and Samaha 2003) RCT	
Harms	Changes in serum creatinine concentration did not differ significantly between groups. Blood urea nitrogen increased more in the PSMF group (0.4 vs –0.5 mmol/l, p=0.007). Changes in uric acid levels were not clinically significant but were statistically significant (17 vs –12 mmol/l, p=0.05). One participant in the PSMF group was hospitalised with non-cardiac chest pain during the study. Two participants died in the PSMF group (complications of hyperosmolar coma, severe ischaemic cardiomyopathy).
Quality and comments	…

Foster 2003 RCT	
Harms	In the first 3 months, there was a higher percentage of people in the PSMG group who tested positive for urinary ketones (at 3 months, about 43% PSMF vs 4% low-fat, p>0.003). After 3 months, no significant difference was seen between the groups.
Quality and comments	…

Generalisability

Dansinger 2005 RCT	
Country and setting	USA. Enrolled at an academic medical centre.
Participants (included/excluded)	Included if adults of any age who were overweight (BMI between 27 and 42 kg/m^2) and having at least one of the following metabolic cardiac risk factors: FPG ≥6.1 mmol/l, TC ≥5.2 mmol/l, LDL ≥3.4 mmol/l, HDL ≤1.0 mmol/l, TAG ≥1.7 mmol/l, SBP ≥145 mmHg, DBP ≥90 mmHg, or current use of oral medication to treat hypertension, diabetes, dyslipidaemia. Excluded if unstable chronic illness, insulin therapy, urinary microalbumin of more than two times normal, serum creatinine ≥123.8 µmol/l, clinically significant abnormalities of liver or thyroid test results, weight loss medication or pregnancy.
Recruitment	Newspaper advertisements and TV publicity (local news coverage).
Intervention (mode and intensity)	*Four classes lasting 1 h during the first 2 months. Assessed at baseline, 2, 6 and 12 months (additional dietary assessment at 1 month).*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Team consisted of dietitian and physician who facilitated the meetings.
Dropout rates	*48% PSMF and 35% low-fat at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Weight and cardiac risk factors, baseline values carried forward. Dietary intake, baseline or subsequent values used.

Stern 2004 (and Samaha 2003) RCT	
Country and setting	USA. Outpatient practices of a Veterans Affairs Medical Centre.
Participants (included/excluded)	Included if aged ≥18 years, BMI >35 kg/m^2. Excluded if serum creatinine >133 µmol/l, hepatic disease, severe life-limiting medical illness, inability to self monitor glucose levels, active use of weight loss programme or weight loss medication.
Recruitment	No details.
Intervention (mode and intensity)	*Weekly counselling sessions (2 h long) for 4 weeks, followed by 11 (1 h) monthly sessions.*
Control (mode and intensity)	As above.
Delivery of intervention/control (who)	*Sessions led by experts in nutritional counselling.*
Dropout rates	*31% PSMF and 37% low-fat at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Missing weight data was collected from medical records. In the ITT analysis, baseline data was carried forward.

Foster 2003 RCT	
Country and setting	USA (assumed). No details reported.
Participants (included/excluded)	No inclusion criteria reported, other than 'obese persons'. Excluded if clinically significant illness (including type 2 diabetes), taking lipid-lowering drugs, pregnant or lactating, taking medications that affected body weight.
Recruitment	No details.
Intervention (mode and intensity)	*Met with dietitian before study started. Assessed at weeks 2, 4, 8, 12, 16, 20, 26, 34, 24 and 52.*
Control (mode and intensity)	As above.

Delivery of intervention/control (who)	Dietitian instructed on diet.
Dropout rates	*39% PSMF and 43% low-fat at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Baseline values carried forward in cases of missing data.

1.3.9 Protein-sparing modified fast compared with low-energy diet

Weight loss

Wadden 1989 (in HTA) RCT	
Aim	To compare the effectiveness of VLED alone, behaviour therapy (BT) alone, and VLED plus BT on weight control.
Participants	People who were overweight (25 kg or more above IBW from the Metropolitan Life Insurance tables) *76 total – all women (completers only – men excluded from analysis due to small numbers). Mean age (SE) 42.1 (1.1) years. Mean (SE) BMI 39.4 (0.8) kg/m^2. Numbers allocated to each group unclear.*
Intervention (including details of diet)	1000–1200 kcal/day for month 1, months 2 + 3 400–500 kcal/day PSMF consisting of three servings of lean meat, fish or fowl and to avoid all other food with the exception of non-energy beverages and bouillon, requested to drink at least 1.5 litres water per day, daily supplements 3 g each of potassium, sodium chloride and 800 mg calcium; month 4 refeeding to conventional foods, firstly fruit and vegetables then bread and cereal then fats. Participants were encouraged to increase physical activity by walking and using the stairs; diet records kept throughout active treatment; paid US$40 which was refunded after the 1-year follow-up visit.
Control	*1000–1200 kcal/day diet of participants choosing for 25 weeks, taught traditional behavioural methods of weight control which included recording eating behaviour, controlling stimuli related to eating, slowing rate of consumption, increasing lifestyle activity, nutrition education, modifying self-defeating thoughts and emotions, social support, reinforcing changes in eating and exercise behaviour.* I*n months 5 + 6 an additional group was prescribed 1000–1200 kcal/day diet, extensive training in behaviour therapy throughout months 4, 5 + 6 addressed weight maintenance and included relapse prevention training and strategies for handling weight regain.* *Both groups were encouraged to increase physical activity by walking and using the stairs; diet records kept throughout active treatment; paid $10 for each visit and deposited $40 which was refunded after the 1 year follow-up visit.*
Length of follow-up	64 to 66 months

Results	*At 6 months, mean (SD) weight change in kg was –16.80 (6.68) in the PSMF group, and –13.00 (6.57) in the LED group. Mean weight change in the PSMF group compared with LED was –3.80 (95% CI –7.41 to –0.19).* At 12 months, mean (SD) weight change in kg was –10.60 (8.00) in the PSMF group, and –6.60 (8.91) in the LED group. Mean weight change in the PSMF group compared with LED was –4.00 (95% CI –8.87 to 0.87). At 36 months, mean (SD) weight change in kg was –5.11 (8.28) in the PSMF group, and –3.54 (6.26) in the LED group. Mean weight change in the PSMF group compared with LED was –1.57 (95% CI –6.79 to 3.65). At 60 months, mean (SD) weight change in kg was 2.90 (11.26) in the PSMF group, and 2.70 (6.97) in the LED group. Mean weight change in the PSMF group compared with LED was 0.20 (95% CI –5.68 to 6.08). *At the end of the active treatment (6 months), 96.8% of the PSMF and 95.5% of the LED group had lost 5 kg or more, and 90.3% and 63.5% respectively had lost 10 kg or more.* *At 12 months, 72.0% of the PSMF and 54.5% of the LED group had lost 5 kg or more, and 52.0% and 22.7% respectively had lost ≥10 kg.* *At 60 months, 27.3% of the PSMF and 13.3% of the LED group had lost 5 kg or more, and 9.1% and 0.0% respectively had lost ≥10 kg.*
Quality and comments	Two cohorts differed significantly in age at baseline (43.9 vs 39.5 years). 2 kg added to all self-reported weights, 3 and 5 year weight outcomes recalculated for participants who had additional weight loss treatment in years 1–5 post-treatment, self-reported weight at time of seeking additional therapy was subtracted from pre-treatment weights, significant difference in whole sample from uncorrected changes (p<0.002 at 3 years, p<0.005 at 5 years post-treatment). Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. *More than 90% of participants reported a chronic history of obesity and multiple cycles of weight loss and regain.*

Wadden 1994 (in HTA) RCT	
Aim	To determine the effect of maintenance therapy in maintaining an initial weight loss achieved by a VLED (based on PSMF) compared with initial weight loss using a LED
Participants	Women who were overweight (25 kg or more above IBW from the Metropolitan Life Insurance tables) 49 total – all women. Mean (SD) age 36.82 (8.87) years PSMF group (n=28), 42.86 (10.12) years LED group (n=21). Mean (SD) BMI 40.01 (5.73) kg/m^2 PSMF, 38.80 (5.39) LED.
Intervention (including details of diet)	Week 1 advised regarding 1200 kcal/day, weeks 2–17 420 kcal/day liquid formula PSMF (70 g protein, 30 g carbohydrate, 2 g fat) and 2 litres non-energy fluids daily and avoidance of all other foods; week 18 conventional foods gradually reintroduced to 100 kcal/day by week 23, weeks 24–78 1200 kcal/day. All participants received behaviour therapy consisting of keeping an eating record, stimulus control, modifying cognitions, eliciting social support (materials presented in different order for group b for initial 52 weeks); then during weeks 53–78 'upkeep' skills such as weight graphing and biography, preparing low fat meals, continuing to exercise, relapse prevention, risk avoidance and reversing small weight gains; all participants received same exercise programme consisting of 10–20 min three times per week at 40–60% maximum heart rate gradually increased to 20–40 min three to five times per week at 60–70% maximum heart rate by week 52.

Control	*1200 kcal/day BEDD for first 52 weeks, 15–20% protein, 30% fat and remainder carbohydrate, energy intake then adjusted for weeks 53–78 depending on participants desired weight change (minimum 1200 kcal/day).* *All participants received behaviour therapy consisting of keeping an eating record, stimulus control, modifying cognitions, eliciting social support (materials presented in different order for group b for initial 52 weeks); then during weeks 53–78 'upkeep' skills such as weight graphing and biography, preparing low-fat meals, continuing to exercise, relapse prevention, risk avoidance and reversing small weight gains; all participants received same exercise programme consisting of 10–20 min three times per week at 40–60% maximum heart rate gradually increased to 20–40 min three to five times per week at 60–70% maximum heart rate by week 52*
Length of follow-up	78 weeks
Results	*At 1 week, mean (SD) weight change in kg was –0.67 (1.54) in the PSMF group, and –1.45 (1.05) in the LED group. Mean weight change in the PSMF group compared with LED was 0.78 (95% CI 0.05 to 1.51).* *At 5 weeks, mean (SD) weight change in kg was –8.51 (2.37) in the PSMF group, and –4.05 (2.47) in the LED group. Mean weight change in the PSMF group compared with LED was –4.46 (95% CI –5.83 to –3.09).* *At 9 weeks, mean (SD) weight change in kg was –13.29 (4.02) in the PSMF group, and –5.44 (3.61) in the LED group. Mean weight change in the PSMF group compared with LED was –7.85 (95% CI –10.00 to –5.71).* *(Not able to calculate for weeks 13 and 17 as no details of numbers of participants)* *At 6 months, mean (SD) weight change in kg was –21.45 (9.63) in the PSMF group, and –11.86 (7.89) in the LED group. Mean weight change in the PSMF group compared with LED was –9.59 (95% CI –14.86 to –4.32).* At 12 months, mean (SD) weight change in kg was –17.33 (9.86) in the PSMF group, and –14.43 (9.46) in the LED group. Mean weight change in the PSMF group compared with LED was –2.90 (95% CI –8.94 to 3.14). At 18 months, mean (SD) weight change in kg was –10.94 (9.97) in the PSMF group, and –12.18 (8.23) in the LED group. Mean weight change in the PSMF group compared with LED was 1.24 (95% CI –4.63 to 7.11). *At 6 months, 96% of the PSMF group lost ≥5 kg, 85% ≥10 kg and 58% ≥20 kg.* *At 12 months, 87% of the PSMF group lost ≥5 kg, 78% ≥10 kg and 35% ≥20 kg.* *At 18 months, 71% of the PSMF group lost ≥5 kg, 52% ≥10 kg and 19% ≥20 kg.* *At 6 months, 82% of the LED group lost ≥5 kg, 59% ≥10 kg and 18% ≥20 kg.* *At 12 months, 88% of the LED group lost ≥5 kg, 59% ≥10 kg and 18% ≥20 kg.* *At 18 months, 94% of the LED group lost ≥5 kg, 44% ≥10 kg and 19% ≥20 kg.* *At week 17, the PSMF group had lost significantly more fat free mass than the LED group (*p *0.001), but this difference was not maintained at week 48.*
Quality and comments	Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. VLED group over selected to allow for greater attrition.

Pavlou 1989 1 (in HTA) RCT	
Aim	To determine the role of exercise in relation to the type of diet, rate of weight loss and defined exercise experience on long-term maintenance

Participants	Healthy men (no weight inclusion criteria). *160 total (for complete study) – all men. Mean (SD) age 45.1 (10.00) years PSMF, 41.5 (7.59) years LED (Pavlou 1ca). Mean (SD) age 49.6 (8.40) years PSMF, 42.9 (6.63) years LED (Pavlou 1db). Mean (SD) age 41.8 (10.44) years PSMF, 41.5 (7.59) years LED (Pavlou 1ea). Mean (SD) age 41.8 (7.57) years PSMF, 42.9 (6.63) years LED (Pavlou 1fb).* *Mean BMI (kg/m^2) 32.07 PSMF, 32.54 LED (Pavlou 1ca). Mean BMI 31.5 PSMF, 32.4 LED (Pavlou 1db). Mean BMI 30.13 PSMF, 32.54 LED (Pavlou 1ea). Mean BMI 34.82 PSMF, 32.4 LED (Pavlou 1fb).* *Data for completers only (16 PSMF vs 10 LED, 16 PSMF vs 11 LED, 10 PSMF vs 10 LED, 13 PSMF vs 11 LED respectively completed at 18 months post-treatment). No details of allocation to each group.*
Intervention (including details of diet)	All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts. PSMF (groups c and d): ketogenic diet of meat, fish and fowl used as only dietary source to provide equivalent of 1.2 g high biological value protein per kg of IBW or 1000 kcal/day, no carbohydrate and all fat ingested came from meat, fish and fowl; 2.8 g potassium chloride daily. PSMF (groups e and f): DPC-70; assumed PSMF 420 kcal/day diet of powdered protein–carbohydrate mix derived from calcium caseinate, egg albumin and fructose dissolved in water or other non-energy liquid, fat content zero, fortified with vitamins and minerals to meet US Recommended Daily Allowance, mix five packets per day in 850 g (30 oz) of non-energy liquid and consume no other nutrients; 2.8 g potassium chloride daily. For groups allocated to exercise (Pavlou 1ca, Pavlou 1ea) 90 min supervised exercise programme three times per week from baseline to week 8 which consisted of 35–60 min of aerobic activity e.g. walk–jog–run (70–85% maximum heart rate), callisthenics and relaxation techniques For groups allocated to no exercise (Pavlou 1db, Pavlou 1fb) participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks.
Control	*All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts.* *LED: BEDD where 1000 kcal/day selected from usual four food groups in quantities thought to meet basic requirements* *For groups allocated to exercise (Pavlou 1ca, Pavlou 1ea) 90 min supervised exercise programme three times per week from baseline to week 8 which consisted of 35–60 min of aerobic activity e.g. walk–jog–run (70–85% maximum heart rate), callisthenics and relaxation techniques.* *For groups allocated to no exercise (Pavlou 1db, Pavlou 1fb) participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks.*
Length of follow-up	*86 weeks.*

Results	Only 18-month outcomes reported. Published figures showed results over the initial 12 weeks, but difficult to determine exact numbers from graphs. *Food-based PSMF and supervised exercise: at 18 months, mean (SD) weight change in kg was –8.64 (8.36) in the PSMF group, and –9.19 (8.52) in the LED group. Mean weight change in the PSMF group compared with LED was 0.55 (95% CI –7.97 to 9.07).* *Food-based PSMF and no additional exercise: at 18 months, mean (SD) weight change in kg was –1.13 (6.23) in the PSMF group, and –3.57 (6.93) in the LED group. Mean weight change in the PSMF group compared with LED was 2.44 (95% CI –4.36 to 9.24).* *Meal replacement PSMF and supervised exercise: at 18 months, mean (SD) weight change in kg was –9.68 (8.65) in the PSMF group, and –9.19 (8.52) in the LED group. Mean weight change in the PSMF group compared with LED was –0.49 (95% CI –9.31 to 8.33).* *Meal replacement PSMF and no additional exercise: at 18 months, mean (SD) weight change in kg was –0.93 (6.18) in the PSMF group, and –3.57 (6.93) in the LED group. Mean weight change in the PSMF group compared with LED was 2.64 (95% CI –4.10 to 9.38).*
Quality and comments	*HTA reported results for four groups. Pavlou 1ca – PSMF (food) and exercise vs LED and exercise, Pavlou 1db – PSMF (food) vs LED, Pavlou 1ea – PSMF (meal replacement) and exercise vs LED and exercise, and Pavlou 1fb – PSMF (meal replacement) vs LED.* Blinded assessment not done. Possible ITT analysis. Random allocation but no description of concealment. Weight data derived from graph and SDs calculated. *Have recalculated using halved sample size…*

Pavlou 1989 2 (in HTA) RCT	
Aim	To determine the role of exercise in relation to the type of diet, rate of weight loss and defined exercise experience on long-term maintenance
Participants	Healthy men (no weight inclusion criteria). *24 total – all men. Mean (SD) age 48.1 (4.65) years PSMF no exercise, 44.8 (7.84) years LED no exercise, 46.1 (5.14) years PSMF with exercise, 49.2 (6.48) years LED with exercise. Mean BMI (kg/m^2) 30.4 PSMF no exercise, 31.92 LED no exercise, 31.11 PSMF with exercise, 31.75 LED with exercise. Data for completers only. No details of numbers allocated.*
Intervention (including details of diet)	All participants attended weekly educational sessions up to week 12 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 12, non-energy liquids including coffee were allowed in unrestricted amounts. PSMF: ketogenic diet of meat, fish and fowl used as only dietary source to provide equivalent of 1.2 high biological value protein per kg of IBW or 1000 kcal/day, no carbohydrate and all fat ingested came from meat fish and fowl; 2.8 g potassium chloride daily Exercise: 90 min supervised exercise programme three times per week from baseline to week 12 which consisted of 35–60 min of aerobic activity e.g. walk–jog–run (70–85% maximum heart rate), callisthenics and relaxation techniques
Control	*All participants attended weekly educational sessions up to week 12 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 12, non-energy liquids including coffee were allowed in unrestricted amounts.* *BEDD where 1000 kcal/day selected from usual four food groups in quantities thought to meet basic requirements.* *No exercise: participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks*
Length of follow-up	168 weeks

Results	*Only 18- and 36-month outcomes reported. Published values showed results over the initial 12 weeks, but difficult to determine exact numbers from graphs.* Food-based PSMF and supervised exercise: at 18 months, mean (SD) weight change in kg was –14.04 (9.89) in the PSMF group, and –11.83 (9.26) in the LED group. Mean weight change in the PSMF group compared with LED was –2.21 (95% CI –14.09 to 9.67). Food-based PSMF and no additional exercise: at 18 months, mean (SD) weight change in kg was –7.29 (7.98) in the PSMF group, and –5.75 (7.54) in the LED group. Mean weight change in the PSMF group compared with LED was –1.54 (95% CI –10.78 to 7.70). Food-based PSMF and supervised exercise: at 36 months, mean (SD) weight change in kg was –13.00 (3.83) in the PSMF group, and –10.67 (8.93) in the LED group. Mean weight change in the PSMF group compared with LED was –2.33 (95% CI –10.85 to 6.19). Food-based PSMF and no additional exercise: at 36 months, mean (SD) weight change in kg was –3.83 (7.10) in the PSMF group, and –3.25 (6.83) in the LED group. Mean weight change in the PSMF group compared with LED was –0.58 (95% CI –8.86 to 7.70).
Quality and comments	*HTA reported results for two groups. Pavlou 2a – PSMF (food) vs LED, Pavlou 2b – PSMF (food) and exercise vs LED and exercise.* Blinded assessment not done. Possible ITT analysis. Random allocation but no description of concealment. Weight data derived from graph and SDs calculated.

Wing 1991 (in HTA) RCT	
Aim	To determine whether a combination of VLED (categorised as PSMF in HTA) plus behaviour modification would promote better short-term and long-term glycaemic control in people who were obese and had type 2 diabetes than behaviour modification alone.
Participants	People with type 2 diabetes who were overweight (30% or more above IBW from Metropolitan Life Insurance tables). *36 total – 26 F, 10 M. Mean (SD) age 50.6 (7.7) years PSMF, 51.9 (9.9) years LED. Mean (SD) BMI (kg/m^2) 37.34 (4.7) PSMF, 38.1 (5.7) LED. Data for completers only – initial allocation 17 to PSMF and 19 to LED.*
Intervention (including details of diet)	PSMF (food-based with option of meal replacement): month 1 same as LED then weeks 5–12 given 400 kcal/day PSMF consisting of lean meat, fish, fowl and choice of Optifast 70 for occasional meals, week 9 other foods gradually reintroduced and kcal increased so by week 17=1000–1500 kcal/day diet until week 72, participants on insulin started VLED in hospital where insulin withdrawn or sharply reduced; vitamin and mineral daily supplements. All participants given instructions to diet, exercise and behaviour modification emphasised in particular; advised to increase walking and given weekly exercise goals starting at 50 kcal/week (the equivalent of 0.5 mile walk for a 67.5 kg person) increased to 1000 kcal/week (approximately 10 miles walking per week); participants self-monitored their energy intake and exercise daily throughout the programme, stimulus control techniques, including strategies for removing food cues from the environment, slowing the rate of eating, and separating eating from other activities; also taught techniques for modifying cognitions, for relapse prevention and for self-reinforcement; all participants deposited $150 at start which was earned back weekly for meeting homework goals.

Control	*LED: 1000–1500 kcal/day (depending on initial weight) until week 72 unless IBW achieved; information regarding energy content of protein, carbohydrate and fat given and participants advised to increase complex carbohydrate and decrease fat intake, food choices unlimited, in line with American Diabetic Association recommendation* *All participants given instructions to diet, exercise and behaviour modification emphasised in particular; advised to increase walking and given weekly exercise goals starting at 50 kcal/week (the equivalent of 0.5 mile walk for a 67.5 kg person) increased to 1000 kcal/week (approximately 10 miles walking per week); participants self-monitored their energy intake and exercise daily throughout the programme, stimulus control techniques, including strategies for removing food cues from the environment, slowing the rate of eating, and separating eating from other activities; also taught techniques for modifying cognitions, for relapse prevention and for self-reinforcement; all participants deposited $150 at start which was earned back weekly for meeting homework goals.*
Length of follow-up	72 weeks
Results	At 5 months, mean (SD) weight change in kg was –18.60 (11.18) in the PSMF group, and –10.10 (8.77) in the LED group. Mean weight change in the PSMF group compared with LED was –8.50 (95% CI –15.33 to –1.67). *At 18 months, mean (SD) weight change in kg was –8.60 (9.20) in the PSMF group, and –6.80 (6.90) in the LED group. Mean weight change in the PSMF group compared with LED was –1.80 (95% CI –7.33 to 3.73).*
Quality and comments	Author confirmed main study and sub-study publications, mean change in risk outcomes at 72 weeks calculated from actual values, SDs also calculated. Blinded assessment not done. Possible ITT analysis. Random allocation but no description of concealment. Used HTA SD calculation.

Torgerson 1997 (in HTA) and Lantz 2003 RCT	
Aim	To determine whether 12 initial weeks on a VLED (categorised as PSMF) included in a 2-year support programme is associated with better long-term weight loss maintenance than a dietary and behavioural support programmes alone.
Participants	People who were obese (BMI >32 kg/m^2) *113 total – 74 F, 39 M. Mean (SD) age 47.3 (6.7) years PSMF (n=58), 46.9 (5.8) years LED (n=55). Mean (SD) BMI (kg/m^2) 40.2 (3.3) PSMF, 40.5 (4.3) LED.*
Intervention (including details of diet)	PSMF: Modifast PSMF 456–608 kcal/day for 12 weeks then individualised hypoenergetic diet of 1200–1400 kcal/day (women) or 1400–1800 kcal/day (men) consisting of 55% energy as carbohydrate, 15–20% protein, 25–30% fat up to 2 years. All participants were asked to complete food records before each 6 monthly visit, all received behavioural support programme which included nutrition education and lifestyle advice, risk avoidance and coping strategies, cooking groups, physical activity groups offered such as swimming and physical training.
Control	*LED: individualised hypoenergetic diet of 1200–1400 kcal/day (women) or 1400–1800 kcal/day (men) consisting of 55% energy as carbohydrate, 15–20% protein, 25–30% fat, for 2 years* *All participants were asked to complete food records before each 6 monthly visit, all received behavioural support programme which included nutrition education and lifestyle advice, risk avoidance and coping strategies, cooking groups, physical activity groups offered such as swimming and physical training.*
Length of follow-up	*4 years*

Results	Only 24- and 48-month outcomes reported. *At 24 months, mean (SD) weight change in kg was –9.20 (13.00) in the PSMF group, and –6.20 (8.70) in the LED group. Mean weight change in the PSMF group compared with LED was –3.00 (95% CI –7.06 to 1.06).* At 48 months, mean (SD) weight change in kg was –7.60 (12.20) in the PSMF group, and –6.30 (8.50) in the LED group. Mean weight change in the PSMF group compared with LED was –1.30 (95% CI –6.81 to 4.21). Examination of selected demographic, psychosocial and dietary characteristics showed that the VLED-approach was more effective than the supportive strategy alone in men and possibly in individuals sharing household with only one person.

Weight loss at 24 months (about from graph)	**<5%**		**5–10%**		**>10%**	
Completers only	PSMF	LED	PSMF	LED	PSMF	**LED**
Women	55%	53%	26%	15%	17%	**28%**
Men	**26%**	**61%**	**38%**	**17%**	**32%**	**17%**

Quality and comments	Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. *PSMF only for 12 weeks of 24-month intervention. 48-month results for completers only.*

Wing 1994 (in HTA) RCT	
Aim	To evaluate a year-long behavioural weight control programme used with and without an intermittent VLED in the treatment of type 2 diabetes
Participants	People with NIDDM who were overweight (>30% or >18 kg above IBW, Metropolitan Life Insurance tables). *93 total – 60 F, 33 (kg/m^2) 37.9 (6.3). 38 allocated to PSMF and 41 to LED.*
Intervention (including details of diet)	PSMF (food or meal replacement): PSMF 500 kcal/day either as liquid supplement (Optifast) or lean meat, fish or fowl for weeks 0–12 and weeks 24–36; other foods gradually reintroduced over following 4 weeks to consume 1000–1200 kcal/d at weeks 13–23 and weeks 37–50. All participants kept self-monitoring records which were reviewed at weekly group meetings along with detailed discussion on nutrition which included focusing on reducing fat content and increasing intake of complex carbohydrate and fibre; exercise which stressed walking or behavioural techniques which included stimulus control, goal setting and self-monitoring of intake and exercise, preplanning, relapse prevention and modifying cognitions; included role playing and individual discussion and questions; all participants encouraged to increase walking to 2 miles per day 5 days per week; all participants kept 3 day food diaries at baseline, 6 months and 12 months; all diabetes medications discontinued at start and algorithm used to determine if and when to restart medication; all participants given vitamin/mineral supplements throughout study; all participants deposited $150 which was refunded in full for reaching behavioural goals and attending assessments at baseline, 6 months and 50 weeks.

Control	*LED: 1000–1200 kcal/day consisting of <30% energy intake from fat from baseline to week 50.* *All participants kept self-monitoring records which were reviewed at weekly group meetings along with detailed discussion on nutrition which included focusing on reducing fat content and increasing intake of complex carbohydrate and fibre; exercise which stressed walking or behavioural techniques which included stimulus control, goal setting and self-monitoring of intake and exercise, preplanning, relapse prevention and modifying cognitions; included role playing and individual discussion and questions; all participants encouraged to increase walking to 2 miles per day 5 days per week; all participants kept 3 day food diaries at baseline, 6 months and 12 months; all diabetes medications discontinued at start and algorithm used to determine if and when to restart medication; all participants given vitamin/mineral supplements throughout study; all participants deposited $150 which was refunded in full for reaching behavioural goals and attending assessments at baseline, 6 months and 50 weeks.*
Length of follow-up	102 weeks.
Results	*Shorter time periods reported graphically only.* *At 12 months, mean (SD) weight change in kg was –14.20 (10.30) in the PSMF group, and –10.5 (11.60) in the LED group. Mean weight change in the PSMF group compared with LED was –3.70 (95% CI –8.55 to 1.15).* *At 12 months 47% of the PSMF lost ≥15 kg compared with 22% of the LED group (*p<*0.05). 32% of the PSMF lost ≥20 kg compared with 15% of the LED group (*p=*0.07).* *Women in the PSMG group lost significantly more weight at 12 months than did the LED participants (14.1 vs 8.6 kg,* p<*0.023). Men had comparable losses between the groups (15.4 and 15.5kg). The percentage of women losing ≥15 kg or at least 5 BMI units was significantly greater in the PSMF group (*p<*0.01 for both comparisons). The proportion of men achieving these two goals was similar in each group.* At 24 months, mean (SD) weight change in kg was –7.20 (8.00) in the PSMF group, and –5.70 (7.90) in the LED group. Mean weight change in the PSMF group compared with LED was –1.50 (95% CI –5.15 to 2.15).
Quality and comments	Blinded assessment not reported. ITT analysis not done. Random allocation but no description of concealment. Author confirmed study and sub study reports. *Added 12 month outcomes*

Dansinger 2005 RCT	
Aim	To assess adherence rates and the realistic clinical effectiveness of four popular diets (Atkins, Zone, Weight Watchers and Ornish) for weight loss and cardiac risk factor reduction. Dietary components only of the programmes were used (see details of intervention later).
Participants	People who were overweight (BMI between 27 and 24 kg/m^2) who also had at least one metabolic cardiac risk factor. 160 total – 81 F, 79 M. Mean (SD) age 47 (12) years PSMF (*n*=40), 49 (10) years low-fat (*n*=40). Mean (SD) BMI (kg/m^2) 35 (3.5) PSMF, 35 (3.8) low-fat.

Intervention (including details of diet)	*PSMF: aimed for <20 g of carbohydrate daily, with a gradual increase to 50 g/day. Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2-month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.*
Control	LED: number of daily points determined by current weight. Each point was roughly 50 kcal, and most participants aimed for 24 to 32 points daily (1200 to 1500 kcal). Lists provided by Weight Watchers determined point values of common foods. Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2-month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.
Length of follow-up	*12 months*
Results	*At 2 months, mean (SD) weight change in kg was –3.60 (3.30) in the PSMF group and –3.50 (3.80) in the LED group. Mean weight change in the PSMF group compared with LED was –0.10 (95% CI –1.66 to 1.46).* *At 6 months, mean (SD) weight change in kg was –3.20 (4.90) in the PSMF group and –3.50 (5.60) in the LED group. Mean weight change in the PSMF group compared with LED was 0.30 (95% CI –2.01 to 2.61).* *At 12 months, mean (SD) weight change in kg was –2.10 (4.80) in the PSMF group and –3.00 (4.90) in the LED group. Mean weight change in the PSMF group compared with LED was 0.90 (95% CI –1.23 to 3.03).* *Weight and BMI were significantly lower than baseline for both groups (p≤0.05) but there was no statistically significant difference between the groups.* *In each group, about 25% of participants lost 5% or more of initial body weight, and about 10% lost 10% or more at 12 months.*
Quality and comments	*Atkins categorised as PSMF. Weight Watchers diet categorised as LED.* *Blinded assessment done. ITT analysis done. Randomisation done by computer generated sequence, and good allocation concealment.* *See other sections for comparisons of PSMF, LED, low-fat, and very-low-fat (Atkins, Weight Watchers, Zone and Ornish respectively).*

Other outcomes

Wadden 1989 (in HTA) RCT	
Results	*No other outcomes reported.*
Quality and comments	…

Wadden 1994 (in HTA) RCT	
Results	*Participants in both groups scored lower (*p*<0.03) on the Beck Depression*

	Inventory over time (i.e. improved) but there was no significant difference between the two groups. *Also, participants in both groups scored lower (*p*<0.01) on the Binge Eating Scale over time (i.e. improved at weeks 26 and 52) and change from baseline was significantly different for participants in the LED compared with those in the PSMF week 52 (*p*<0.02) but not at week 26.*
Quality and comments	…

Pavlou 1989 1 (in HTA) RCT	
Results	*Only VO_{2max} reported by different diet groups.*
Quality and comments	…

Pavlou 1989 2 (in HTA) RCT	
Results	*Only VO_{2max} at 8 weeks reported by different diet groups.*
Quality and comments	…

Wing 1991 (in HTA) RCT	
Results	*At 18 months, mean (SD) TC change in mmol/l was 0.29 (1.08) in the PSMF group and 0.31 (1.08) in the LED group. Mean TC change in the intervention group compared with control was –0.02 (95% CI –0.76 to 0.72).* *At 18 months, mean (SD) HDL change in mmol/l was 0.22 (0.29) in the PSMF group and 0.13 (0.29) in the LED group. Mean HDL change in the intervention group compared with control was 0.09 (95% CI –0.11 to 0.29).* *At 18 months, mean (SD) TAG change in mmol/l was –0.13 (0.96) in the PSMF group and –0.29 (0.96) in the LED group. Mean TAG change in the intervention group compared with control was 0.16 (95% CI –0.50 to 0.82).* *At 18 months, mean (SD) HbA_{1c} % change was –1.20 (2.58) in the PSMF group and 1.40 (2.58) in the LED group. Mean HbA_{1c} % change in the intervention group compared with control was –2.60 (95% CI –4.36 to –0.84).* *At 18 months, mean (SD) FPG change in mmol/l was –3.80 (3.77) in the PSMF group and 0.70 (3.77) in the LED group. Mean FPG change in the intervention group compared with control was –4.50 (95% CI –7.07 to –1.93).* The PSMF group reported consuming significantly less energy from baseline than the LED group through the treatment period (*p*<0.001), but these data were not available for the 18 month follow-up. The PSMG group increased levels of physical activity significantly from pre- to post-treatment (*p*<0.02) compared with the LD group but these were not maintained at the 18 month point. From the Eating Behaviour Inventory, both groups reported increased use of behaviour modification strategies from pre- to post-treatment (*p*<0.0001) but these were not maintained at the 18 month follow-up.
Quality and comments	Data on dietary intake from daily diaries throughout the study.

Torgerson 1997 (in HTA) and Lantz 2003 RCT	
Results	*High initial hunger-score was associated with attrition, irrespective of treatment.*
Quality and comments	…

Wing 1994 (in HTA) RCT	
Results	*At 12 months, the PSMF group showed an increase in levels of TC compared with a decrease in the LED group (*p*=0.058).* *Other lipid changes were similar in the two groups at 12 months, with significant increases in HDL (*p*<0.001) and decreases in TAG (*p*<0.001).* *Both SBP and DBP decreased significantly in both groups (*p*<0.001), but the*

	*decrease in DBP in the PSMF group was greater (*p=*0.03).* *Also, both groups showed similar decreases in levels of HbA_1, FPG and fasting insulin at 12 months (*p<*0.001).* At 24 months, mean (SD) HbA_{1c} % change was 0.07 (2.22) in the PSMF group, and 0.24 (2.40) in the LED group. Mean HbA_{1c} % change in the intervention group compared with control was –0.17 (95% CI –1.23 to 0.89). At 24 months, mean (SD) FPG change in mmol/l was –1.22 (4.56) in the PSMF group, and 0.39 (4.67) in the LED group. Mean FPG change in the intervention group compared with control was –1.61 (95% CI –3.73 to 0.51). *Attendance rates decreased similarly over time in both groups, but was highly related to weight loss (*p<*0.0001 for both groups).*
Quality and comments	…

Dansinger 2005 RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was –0.11 (0.59) in the PSMF group and –0.21 (0.62) in the LED group. Mean TC change in the PSMF group compared with LED was 0.10 (95% CI –0.17 to 0.37).* *At 12 months, mean (SD) LDL change in mmol/l was –0.18 (0.62) in the PSMF group and –0.24 (0.69) in the LED group. Mean LDL change in the PSMF group compared with LED was 0.06 (95% CI –0.23 to 0.35).* *At 12 months, mean (SD) HDL change in mmol/l was 0.09 (0.18) in the PSMF group and 0.09 (0.25) in the LED group. Mean HDL change in the PSMF group compared with LED was 0.00 (95% CI –0.10 to 0.10).* *At 12 months, mean (SD) TAG change in mmol/l was –0.02 (0.94) in the PSMF group and –0.14 (0.69) in the LED group. Mean TAG change in the PSMF group compared with LED was 0.12 (95% CI –0.24 to 0.48).* *At 12 months, mean (SD) DBP change in mmHg was –1.40 (7.50) in the PSMF group and –1.70 (6.40) in the LED group. Mean DBP change in the PSMF group compared with LED was 0.30 (95% CI –2.76 to 3.36).* *At 12 months, mean (SD) SBP change in mmHg was 0.20 (12.00) in the PSMF group and –2.70 (13.00) in the LED group. Mean SBP change in the PSMF group compared with LED was 2.90 (95% CI –2.58 to 8.38).* *At 12 months, mean (SD) FPG change in mmol/l was 0.08 (0.77) in the PSMF group and –0.26 (1.06) in the LED group. Mean FPG change in the PSMF group compared with LED was 0.34 (95% CI –0.07 to 0.75).* *At 12 months, the mean energy reductions from baseline (*p≤*0.05) were 138 for PSMF and 244 for LED. These were not significantly different between groups.* *No significant differences were seen in macronutrient content between any of the groups.* *Group mean adherence scores according to diet records and self-assessment decreased over time, and to a similar extent in all groups. About 25% of each group sustained a mean adherence level of at least 6/10, which 'appeared to delineate a clinically meaningful adherence level'.*
Quality and comments	Converted mg/dl to mmol/l (see paper for conversion rates and values used). Dietary intake was assessed from 3-day diet records at 1, 2, 6 and 12 months.

Reported harms

Wadden 1989 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wadden 1994 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Pavlou 1989 1 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Pavlou 1989 2 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wing 1991 (in HTA) RCT	
Harms	During the first 4 months of the treatment, both groups were asked about difficulties with coldness, constipation, dry skin, diarrhoea, dizziness, vomiting or weakness. There were no differences between the groups or over time for any participant reporting these (as either mild, moderate, or severe symptoms). No values were reported. ECGs showed no negative effects of the PSMF – in two participants, non-specific ST-T wave changes noted at baseline resolved over the study period. Increased levels of uric acid were seen in the PSMF group (p<0.007), but clinical symptoms of gout did not develop. One participant experienced levels of uric acid <594 µmol/l, which responded to treatment. In addition, levels of alkaline phosphatase decreased (p<0.002) in the PSMF group but no other changes were significant.
Quality and comments	…

Torgerson 1997 (in HTA) and Lantz 2003 RCT	
Harms	No serious adverse effects of a VLED were seen and no serious or unexpected laboratory aberrations in the blood chemistry profiles or ECGs appeared.
Quality and comments	…

Wing 1994 (in HTA) RCT	
Harms	Commonly reported side effects of the PSMF were cold intolerance, constipation, and hair loss. These all resolved when the PSMF was stopped. No numbers were reported. Both groups reported significant improvements in depressive symptomatology (Beck Depression Inventory) over the 12 months (p<0.001), but there was no difference between the groups.
Quality and comments	…

Dansinger 2005 RCT	
Harms	Common reasons for discontinuation were that the assigned diet was too hard to follow, or not yielding enough weight loss. No diet-related or adverse events or serious adverse effects were found.
Quality and comments	Reasons for discontinuation not reported by group but overall only.

Generalisability

Wadden 1989 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if 25 kg or more above IBW (Metropolitan Life Insurance tables).* *Excluded if recent MI or evidence of cardiac abnormalities; history of cerebrovascular, kidney or liver disease; cancer, type 1 diabetes, severe psychiatric illness, pregnancy, contraindications to treatment by VLED (assessed at screening), participants agreed not to participate in additional weight loss treatment before follow-up at 1 year post-treatment.*
Recruitment	N/R.
Intervention (mode and intensity)	16 weeks, contacted 25 times (90 min each week for 16 weeks then months 1, 2, 3, 6, 9 and 12 post-treatment, 3 years and 5 years post-treatment)
Control (mode and intensity)	*25 weeks, contacted 39 times (90 min each week for 25 weeks then 11 post-treatment visits every other week for first 2 months then once a month for next 4 months then every other month for last 6 months, 3 years and 5 years post-treatment)*
Delivery of intervention/control (who)	All participants were treated by doctoral level clinical psychologists.
Dropout rates	Unclear, but 68/76 were assessed at 12 months, 50/76 at 36 months, and 55/76 at 60 months.
Treatment of dropouts (return to baseline, or last measurement?)	Data for completers only.

Wadden 1994 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included women who were overweight (BMI ≥25 kg/m^2). $300 refunded at 6 monthly intervals.* *Excluded if myocardial infarction, cardiac problems, cerebrovascular disease, kidney or liver disease, cancer, type 1 diabetes, bulimia nervosa, psychiatric illness.*
Recruitment	Newspaper advertisements, then medical examination for eligibility.
Intervention (mode and intensity)	18 months, contacted 66 times (baseline then 90 min small group sessions weekly for first 52 weeks, then biweekly for weeks 53–78)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	*Behavioural sessions conducted by either a doctoral-level clinical psychologist or a psychology graduate student. Food and nutrition education delivered by a dietitian.*
Dropout rates	25% PSMF and 24% LED at 78 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	N/R – only complete data used?

Pavlou 1989 1 (in HTA) RCT	
Country and setting	USA. Workplace.
Participants (included/excluded)	*Included men, aged 26–52 years, euthyroid, free from any physical, psychological or metabolic impairment.* *Exclusion criteria not stated.*
Recruitment	Men were recruited from the Boston Police Department and the Metropolitan District Commission. No further details reported.

Intervention (mode and intensity)	8 weeks plus 18 months post-treatment follow-up (weekly from baseline to week 8 then at 8 months and 18 months post-treatment)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	No details.
Dropout rates	31% overall at 18 months post-treatment.
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Pavlou 1989 2 (in HTA) RCT	
Country and setting	USA. Workplace
Participants (included/excluded)	*Included men aged 26–52 years, euthyroid, free from any physical, psychological or metabolic impairment.* *No details of exclusion.*
Recruitment	Men were recruited from the Boston Police Department and the Metropolitan District Commission. No further details reported.
Intervention (mode and intensity)	12 weeks plus 36 months post-treatment follow-up, contacted 16 times (weekly from baseline to week 12 then at 6, 8 and 18 months post-treatment)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	No details.
Dropout rates	13% overall at 36 months post-treatment
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Wing 1991 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if aged 35–70 years, 30% or more IBW (Metropolitan Life Insurance tables), type 2 diabetes* *Excluded if liver disease, renal disease, heart disease.*
Recruitment	N/R
Intervention (mode and intensity)	72 weeks, contacted 25 times (weekly from baseline to week 20 then at weeks 24, 28, 46 and 72)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Groups led by team of therapists. Medication changes were made by the project physician.
Dropout rates	0% PSMF and 16% LED at 72 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Torgerson 1997 (in HTA) and Lantz 2003 RCT	
Country and setting	*Sweden. Outpatient clinics of two county hospitals.*
Participants (included/excluded)	*Recruited if aged 37–60 years, obese (non-surgery arm of SOS study) Exclusion criteria not stated.*
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	2 years, contacted 31 times (baseline then at 1, 2, 4, 6, 8, 12, 13, 14, 16, 18 and 20 weeks then monthly). *After 4 years, averaged 38 visits.*
Control (mode and intensity)	*2 years, contacted 28 times (baseline then at 1, 2, 4, 6 and 8 weeks then monthly).* After 4 years, averaged 38 visits.
Delivery of intervention/control (who)	Individual nutritional counselling, support, and further education on nutrition and lifestyle were delivered by a dietitian. The physician performed the physical examination and evaluation of risk factors and counselling.

Dropout rates	50% PSMF and 53% LED at 4 years.
Treatment of dropouts (return to baseline, or last measurement?)	LOCF.

Wing 1994 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if aged 30–70 years, >30% or >18 kg IBW (based on Metropolitan Life Insurance Tables) and NIDDM (criteria according to National Diabetes Data Group).* *Excluded if had health problems that would interfere with the use of VLCDs.*
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	50 weeks plus follow-up at 1 year later (102 weeks in total), contacted 5two times (weekly in groups of approximately 15)
Control (mode and intensity)	*As above.*
Delivery of intervention/control (who)	Meetings conducted by a multi-disciplinary team of therapists (behavioural therapist, health educator, nutritionist, physician). Also seen by project physician every other week.
Dropout rates	20% PSMF and 21% LED at 102 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	N/R.

Dansinger 2005 RCT	
Country and setting	USA. Enrolled at an academic medical centre.
Participants (included/excluded)	Included if adults of any age who were overweight (BMI between 27 and 42 kg/m^2) and having at least one of the following metabolic cardiac risk factors: FPG ≥6.1 mmol/l, TC ≥5.2 mmol/l, LDL ≥3.4 mmol/l, HDL ≤1.0 mmol/l, TAG ≥1.7 mmol/l, SBP ≥145 mmHg, DBP ≥90 mmHg, or current use of oral medication to treat hypertension, diabetes, dyslipidaemia. Excluded if unstable chronic illness, insulin therapy, urinary microalbumin of more than two times normal, serum creatinine ≥123.8 µmol/l, clinically significant abnormalities of liver or thyroid test results, weight loss medication or pregnancy.
Recruitment	Newspaper advertisements and TV publicity (local news coverage).
Intervention (mode and intensity)	*Four classes lasting 1 h during the first 2 months. Assessed at baseline, 2, 6 and 12 months (additional dietary assessment at 1 month).*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Team consisted of dietitian and physician who facilitated the meetings.
Dropout rates	*48% PSMF and 35% LED at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Weight and cardiac risk factors, baseline values carried forward. Dietary intake, baseline or subsequent values used.

1.3.10 Protein-sparing modified fast compared with very-low-energy diet

Weight loss

Pavlou 1989 1 (in HTA) RCT	
Aim	To determine the role of exercise in relation to the type of diet, rate of weight loss and defined exercise experience on long-term maintenance
Participants	Healthy men (no weight inclusion criteria). *160 total (for complete study) – all men. Mean (SD) age 45.1 (10.00) years PSMF, 41.8 (10.44) years VLED (Pavlou 1ce). Mean (SD) age 49.6 (8.40) years PSMF, 41.8 (7.57) years VLED (Pavlou 1df). Mean (SD) age 45.1 (10.00) years PSMF, 46.1 (9.33) years VLED (Pavlou 1cg). Mean (SD) age 49.6 (8.40) years PSMF, 44.5 (9.6) years VLED (Pavlou 1dh)..* *Mean BMI (kg/m^2) 32.07 PSMF, 30.13 VLED (Pavlou 1ce). Mean BMI 31.5 PSMF, 34.82 VLED (Pavlou 1df). Mean BMI 32.07 PSMF, 31.89 VLED (Pavlou 1cg). Mean BMI 31.5 PSMF, 33.78 VLED (Pavlou 1dh).* *Data for completers only (16 PSMF vs 10 VLED, 16 PSMF vs 13 VLED, 16 PSMF vs 18 VLED, 16 PSMF vs 16 VLED respectively completed at 18 months post-treatment). No details of allocation to each group.*
Intervention (including details of diet)	All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts. PSMF (groups c and d): ketogenic diet of meat, fish and fowl used as only dietary source to provide equivalent of 1.2 g high biological value protein per kg of IBW or 1000 kcal/day, no carbohydrate and all fat ingested came from meat, fish and fowl; 2.8 g potassium chloride daily For groups allocated to exercise (Pavlou 1ce, Pavlou 1cg) 90 min supervised exercise programme three times per week from baseline to week 8 which consisted of 35–60 min of aerobic activity e.g. walk–jog–run (70–85% maximum heart rate), callisthenics and relaxation techniques For groups allocated to no exercise (Pavlou 1df, Pavlou 1dh) participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks
Control	*All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts.* *VLED using PSMF (groups e and f): DPC-70; assumed PSMF 420 kcal/day diet of powdered protein–carbohydrate mix derived from calcium caseinate, egg albumin and fructose dissolved in water or other non-energy liquid, fat content zero, fortified with vitamins and minerals to meet US Recommended Daily Allowance, mix five packets per day in 850 g (30oz) of non-energy liquid and consume no other nutrients; 2.8 g potassium chloride daily.* *VLED (groups g and h): DPC 800; assumed VLED 800 kcal/day diet provided in powdered form to be consumed similarly to DPC-70, provided a complete mixture of nutrients and similar nutritionally to BEDD except for less energy.* *For groups allocated to exercise (Pavlou 1ce, Pavlou 1cg) 90 min supervised exercise programme three times per week from baseline to week 8 which consisted of 35–60 min of aerobic activity e.g. walk–jog–run (70–85% maximum heart rate), callisthenics and relaxation techniques* *For groups allocated to no exercise (Pavlou 1df, Pavlou 1dh) participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks*
Length of follow-up	86 weeks.

Results	Only 18-month outcomes reported. Published values showed results over the initial 12 weeks, but difficult to determine exact numbers from graphs. PSMF vs 420 kcal VLED and supervised exercise: at 18 months, mean (SD) weight change in kg was –8.64 (8.36) in the PSMF group, and –9.68 (8.65) in the VLED group. Mean weight change in the PSMF group compared with VLED was 1.04 (95% CI –6.85 to 8.93). PSMF vs 420 kcal VLED and no additional exercise: at 18 months, mean (SD) weight change in kg was –1.13 (6.23) in the PSMF group, and –0.93 (6.18) in the VLED group. Mean weight change in the PSMF group compared with VLED was 3.76 (95% CI –3.97 to 11.49). PSMF vs 800 kcal VLED and supervised exercise: at 18 months, mean (SD) weight change in kg was –8.64 (8.36) in the PSMF group, and –12.40 (9.42) in the VLED group. Mean weight change in the PSMF group compared with VLED was –0.20 (95% CI –5.38 to 4.98). PSMF vs 800 kcal VLED and no additional exercise: at 18 months, mean (SD) weight change in kg was –1.13 (6.23) in the PSMF group, and –3.45 (6.89) in the VLED group. Mean weight change in the PSMF group compared with VLED was 2.32 (95% CI –3.16 to 7.80).
Quality and comments	*HTA reported results for four groups. Pavlou 1ce – PSMF (food) and exercise vs VLED (420 kcal) and exercise, Pavlou 1df – PSMF (food) vs VLED (420 kcal), Pavlou 1cg – PSMF and exercise vs VLED (800 kcal) and exercise, and Pavlou 1dh - PSMF vs VLED (800 kcal).* Blinded assessment not done. Possible ITT analysis. Random allocation but no description of concealment. Weight data derived from graph and SDs calculated. *Recalculated values presented.*

Other outcomes

Pavlou 1989 1 (in HTA) RCT	
Results	*No other outcomes by different diet groups were reported.*
Quality and comments	…

Reported harms

Pavlou 1989 1 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Pavlou 1989 1 (in HTA) RCT	
Country and setting	USA. Workplace.
Participants (included/excluded)	*Included men, aged 26–52 years, euthyroid, free from any physical, psychological or metabolic impairment.* *Exclusion criteria not stated.*
Recruitment	Men were recruited from the Boston Police Department and the Metropolitan District Commission. No further details reported.
Intervention (mode and intensity)	8 weeks plus 18 months post-treatment follow-up (weekly from baseline to week 8 then at 8 months and 18 months post-treatment)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	No details.
Dropout rates	31% overall at 18 months post-treatment.

Treatment of dropouts (return to baseline, or last measurement?)	N/R

1.3.11 Low-fat diet compared with very-low-fat diet

Weight loss

Dansinger 2005 RCT	
Aim	To assess adherence rates and the realistic clinical effectiveness of four popular diets (Atkins, Zone, Weight Watchers and Ornish) for weight loss and cardiac risk factor reduction. Dietary components only of the programmes were used (see details of intervention later).
Participants	People who were overweight (BMI between 27 and 24 kg/m^2) who also had at least one metabolic cardiac risk factor. 160 total – 81 F, 79 M. Mean (SD) age 51 (9) years low-fat (*n*=40), 49 (12) years very-low-fat (*n*=40). Mean (SD) BMI (kg/m^2) 34 (4.5) low-fat, 35 (3.9) very-low-fat.
Intervention (including details of diet)	*Low fat: aimed for a 40–30–30 balance of % energy from carbohydrate, fat and protein respectively. No further details reported.* *Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2-month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.*
Control	Very low fat: aimed for a vegetarian diet containing 10% of energy from fat. No further details reported. Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2-month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.
Length of follow-up	*12 months*

Results	*At 2 months, mean (SD) weight change in kg was –3.80 (3.60) in the low-fat group and –3.60 (3.40) in the very-low-fat group. Mean weight change in the low-fat group compared with very-low-fat was –0.20 (95% CI –1.73 to 1.33).* *At 6 months, mean (SD) weight change in kg was –3.40 (5.70) in the low-fat group and –3.60 (6.70) in the very low-fat group. Mean weight change in the low-fat group compared with very-low-fat was 0.20 (95% CI –2.53 to 2.93).* *At 12 months, mean (SD) weight change in kg was –3.20 (6.00) in the low-fat group and –3.30 (7.30) in the very-low-fat group. Mean weight change in the low-fat group compared with very-low-fat was 0.10 (95% CI –2.83 to 3.03).* *Weight and BMI were significantly lower than baseline for both groups (p≤0.05) but there was no statistically significant difference between the groups.* *In each group, about 25% of participants lost 5% or more of initial body weight, and about 10% lost 10% or more at 12 months.*
Quality and comments	*Zone categorised as low-fat. Ornish diet categorised as very-low-fat.* *Blinded assessment done. ITT analysis done. Randomisation done by computer generated sequence, and good allocation concealment.* *See other sections for comparisons of PSMF, LED, low-fat and very-low-fat (Atkins, Weight Watchers, Zone and Ornish respectively).*

Other outcomes

Dansinger 2005 RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was –0.26 (0.90) in the low-fat group, and –0.28 (0.54) in the very-low-fat group. Mean TC change in the low-fat group compared with very-low-fat was 0.02 (95% CI –0.31 to 0.35).* *At 12 months, mean (SD) LDL change in mmol/l was –0.30 (0.87) in the low-fat group, and –0.32 (0.49) in the very-low-fat group. Mean LDL change in the low-fat group compared with very-low-fat was 0.02 (95% CI –0.29 to 0.33).* *At 12 months, mean (SD) HDL change in mmol/l was 0.08 (0.26) in the low-fat group, and –0.01 (0.17) in the very-low-fat group. Mean HDL change in the low-fat group compared with very-low-fat was 0.09 (95% CI –0.01 to 0.19).* *At 12 months, mean (SD) TAG change in mmol/l was 0.03 (1.65) in the low-fat group, and 0.06 (0.40) in the very-low-fat group. Mean TAG change in the low-fat group compared with very-low-fat was –0.30 (95% CI –0.56 to 0.50).* *At 12 months, mean (SD) DBP change in mmHg was –1.20 (9.50) in the low-fat group, and 0.20 (4.60) in the very-low-fat group. Mean DBP change in the low-fat group compared with very-low-fat was –1.40 (95% CI –4.67 to 1.87).* *At 12 months, mean (SD) SBP change in mmHg was 1.40 (15.00) in the low-fat group, and 0.50 (7.70) in the very-low-fat group. Mean SBP change in the low-fat group compared with very-low-fat was 0.90 (95% CI –4.33 to 6.13).* *At 12 months, mean (SD) FPG change in mmol/l was –0.23 (1.00) in the low-fat group, and –0.23 (1.67) in the very-low-fat group. Mean FPG change in the low-fat group compared with very-low-fat was 0.00 (95% CI –0.60 to 0.60).* *At 12 months, the mean energy reductions from baseline (p≤0.05) were 251 for low-fat and 192 for very-low-fat. These were not significantly different between groups.* *No significant differences were seen in macronutrient content between any of the groups.* *Group mean adherence scores according to diet records and self-assessment decreased over time, and to a similar extent in all groups. About 25% of each group sustained a mean adherence level of at least 6/10, which 'appeared to delineate a clinically meaningful adherence level'.*
Quality and comments	Converted mg/dl to mmol/l (see paper for conversion rates and values used). Dietary intake was assessed from 3-day diet records at 1, 2, 6 and 12 months.

Reported harms

Dansinger 2005 RCT	
Harms	Common reasons for discontinuation were that the assigned diet was too hard to follow, or not yielding enough weight loss. No diet-related or adverse events or serious adverse effects were found.
Quality and comments	Reasons for discontinuation not reported by group but overall only.

Generalisability

Dansinger 2005 RCT	
Country and setting	USA. Enrolled at an academic medical centre.
Participants (included/excluded)	Included if adults of any age who were overweight (BMI between 27 and 42 kg/m^2) and having at least one of the following metabolic cardiac risk factors: FPG ≥6.1 mmol/l, TC ≥5.2 mmol/l, LDL ≥3.4 mmol/l, HDL ≤1.0 mmol/l, TAG ≥1.7 mmol/l, SBP ≥145 mmHg, DBP ≥90 mmHg, or current use of oral medication to treat hypertension, diabetes, dyslipidaemia. Excluded if unstable chronic illness, insulin therapy, urinary microalbumin of more than two times normal, serum creatinine ≥123.8 µmol/l, clinically significant abnormalities of liver or thyroid test results, weight loss medication or pregnancy.
Recruitment	Newspaper advertisements and TV publicity (local news coverage).
Intervention (mode and intensity)	*Four classes lasting 1 h during the first 2 months. Assessed at baseline, 2, 6 and 12 months (additional dietary assessment at 1 month).*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Team consisted of dietitian and physician who facilitated the meetings.
Dropout rates	*35% low-fat and 50% very-low-fat at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Weight and cardiac risk factors, baseline values carried forward. Dietary intake, baseline or subsequent values used.

1.3.12 Low-energy-diet compared with very-low-fat diet

Weight loss

Dansinger 2005 RCT	
Aim	To assess adherence rates and the realistic clinical effectiveness of four popular diets (Atkins, Zone, Weight Watchers and Ornish) for weight loss and cardiac risk factor reduction. Dietary components only of the programmes were used (see details of intervention later).
Participants	People who were overweight (BMI between 27 and 24 kg/m^2) who also had at least one metabolic cardiac risk factor. 160 total – 81 F, 79 M. Mean (SD) age 49 (10) years LED (*n*=40), 49 (12) years very-low-fat (*n*=40). Mean (SD) BMI (kg/m^2) 35 (3.8) LED, 35 (3.9) very-low-fat.

Intervention (including details of diet)	*LED: number of daily points determined by current weight. Each point was about 50 kcal, and most participants aimed for 24 to 32 points daily (1200 to 1500 kcal). Lists provided by Weight Watchers determined point values of common foods.* *Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2-month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.*
Control	Very-low-fat: aimed for a vegetarian diet containing 10% of energy from fat. No further details reported. Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2-month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.
Length of follow-up	*12 months*
Results	*At 2 months, mean (SD) weight change in kg was –3.50 (3.80) in the LED group and –3.60 (3.40) in the very-low-fat group. Mean weight change in the LED group compared with very low-fat was 0.10 (95% CI –1.48 to 1.68).* *At 6 months, mean (SD) weight change in kg was –3.50 (5.60) in the LED group and –3.60 (6.70) in the very-low-fat group. Mean weight change in the LED group compared with very low-fat was 0.10 (95% CI –2.61 to 2.81).* *At 12 months, mean (SD) weight change in kg was –3.00 (4.90) in the LED group and –3.30 (7.30) in the very-low-fat group. Mean weight change in the LED group compared with very low-fat was 0.30 (95% CI –2.42 to 3.02).* *Weight and BMI were significantly lower than baseline for both groups (p≤0.05) but there was no statistically significant difference between the groups.* *In each group, about 25% of participants lost 5% or more of initial body weight, and about 10% lost 10% or more at 12 months.*
Quality and comments	*Weight Watchers categorised as LED. Ornish diet categorised as very-low-fat.* *Blinded assessment done. ITT analysis done. Randomisation done by computer generated sequence, and good allocation concealment.* *See other sections for comparisons of PSMF, LED, low-fat, and very-low-fat (Atkins, Weight Watchers, Zone and Ornish respectively).*

Other outcomes

Dansinger 2005 RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was –0.21 (0.62) in the LED group, and –0.28 (0.54) in the very-low-fat group. Mean TC change in the LED group compared with very-low-fat was 0.07 (95% CI –0.18 to 0.32).*

	At 12 months, mean (SD) LDL change in mmol/l was –0.24 (0.69) in the LED group, and –0.32 (0.49) in the very low-fat group. Mean LDL change in the LED group compared with very-low-fat was 0.08 (95% CI –0.18 to 0.34). *At 12 months, mean (SD) HDL change in mmol/l was 0.09 (0.25) in the LED group, and –0.01 (0.17) in the very low-fat group. Mean HDL change in the LED group compared with very-low-fat was 0.10 (95% CI 0.01 to 0.19).* *At 12 months, mean (SD) TAG change in mmol/l was –0.14 (0.69) in the LED group, and 0.06 (0.40) in the very low-fat group. Mean TAG change in the LED group compared with very-low-fat was –0.20 (95% CI –0.45 to 0.05).* *At 12 months, mean (SD) DBP change in mmHg was –1.70 (6.40) in the LED group, and 0.20 (4.60) in the very low-fat group. Mean DBP change in the LED group compared with very-low-fat was –1.90 (95% CI –4.34 to 0.54).* *At 12 months, mean (SD) SBP change in mmHg was –2.70 (13.00) in the LED group, and 0.50 (7.70) in the very low-fat group. Mean SBP change in the LED group compared with very-low-fat was –3.20 (95% CI –7.88 to 1.48).* *At 12 months, mean (SD) FPG change in mmol/l was –0.26 (1.06) in the LED group, and –0.23 (1.67) in the very-low-fat group. Mean FPG change in the LED group compared with very-low-fat was –0.03 (95% CI –0.64 to 0.48).* *At 12 months, the mean energy reductions from baseline (p≤0.05) were 244 for LED and 192 for very-low-fat. These were not significantly different between groups.* *No significant differences were seen in macronutrient content between any of the groups.* *Group mean adherence scores according to diet records and self-assessment decreased over time, and to a similar extent in all groups. About 25% of each group sustained a mean adherence level of at least 6/10, which 'appeared to delineate a clinically meaningful adherence level'.*
Quality and comments	Converted mg/dl to mmol/l (see paper for conversion rates and values used). Dietary intake was assessed from 3-day diet records at 1, 2, 6 and 12 months.

Reported harms

Dansinger 2005 RCT	
Harms	Common reasons for discontinuation were that the assigned diet was too hard to follow, or not yielding enough weight loss. No diet-related or adverse events or serious adverse effects were found.
Quality and comments	Reasons for discontinuation not reported by group but overall only.

Generalisability

Dansinger 2005 RCT	
Country and setting	USA. Enrolled at an academic medical centre.
Participants (included/excluded)	Included if adults of any age who were overweight (BMI between 27 and 42 kg/m^2) and having at least one of the following metabolic cardiac risk factors: FPG ≥6.1 mmol/l, TC ≥5.2 mmol/l, LDL ≥3.4 mmol/l, HDL ≤1.0 mmol/l, TAG ≥1.7 mmol/l, SBP ≥145 mmHg, DBP ≥90 mmHg, or current use of oral medication to treat hypertension, diabetes, dyslipidaemia. Excluded if unstable chronic illness, insulin therapy, urinary microalbumin of more than two times normal, serum creatinine ≥123.8 µmol/l, clinically significant abnormalities of liver or thyroid test results, weight loss medication or pregnancy.
Recruitment	Newspaper advertisements and TV publicity (local news coverage).
Intervention (mode and intensity)	*Four classes lasting 1 h during the first 2 months. Assessed at baseline, 2, 6, and 12 months (additional dietary assessment at 1 month).*

Control (mode and intensity)	As above
Delivery of intervention/control (who)	Team consisted of dietitian and physician who facilitated the meetings.
Dropout rates	*35% LED and 50% very-low-fat diet at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Weight and cardiac risk factors, baseline values carried forward. Dietary intake, baseline or subsequent values used.

1.3.13 Protein-sparing modified fast compared with very-low-fat diet

Weight loss

Dansinger 2005 RCT	
Aim	To assess adherence rates and the realistic clinical effectiveness of four popular diets (Atkins, Zone, Weight Watchers, and Ornish) for weight loss and cardiac risk factor reduction. Dietary components only of the programmes were used (see details of intervention later).
Participants	People who were overweight (BMI between 27 and 24) who also had at least one metabolic cardiac risk factor. 160 total – 81F, 79M. Mean (SD) age 47 (12) years PSMF (*n*=40), 49 (12) years very-low-fat (*n*=40). Mean (SD) BMI 35 (3.5) PSMF, 35 (3.9) very-low-fat.
Intervention (including details of diet)	*PSMF: aimed for less than 20 g of carbohydrate daily, with a gradual increase to 50 g/day.* *Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also, encouraged to follow the assigned diet to the best of their ability until the 2 month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.*
Control	Very-low-fat: aimed for a vegetarian diet containing 10% of energy from fat. No further details reported. Participants met in groups of about ten people, where a dietitian and physician administered diet-specific advice. Meetings were held on four occasions for 1 h during the first 2 months of the study. At the first meeting, the diet assignment was revealed and corresponding rationale, written materials, and official diet cookbook. Subsequent meetings aimed to maximise adherence by reinforcing positive dietary changes and addressing barriers to adherence. Recommendations on supplements, exercise and external support were standardised across all groups. All participants were encouraged to take a daily multivitamin, do at least 60 min exercise per week, and to avoid commercial support services. Also encouraged to follow the assigned diet to the best of their ability until the 2 month assessment, after which encouraged to follow assigned diet according to own self-determined interest level.
Length of follow-up	*12 months*

Results	*At 2 months, mean (SD) weight change in kg was –3.60 (3.30) in the PSMF group and –3.60 (3.40) in the very low-fat group. Mean weight change in the PSMF group compared with very-low-fat was 0.00 (95% CI –1.47 to 1.47).* *At 6 months, mean (SD) weight change in kg was –3.20 (4.90) in the PSMF group and –3.60 (6.70) in the very low-fat group. Mean weight change in the PSMF group compared with very-low-fat was 0.40 (95% CI –2.17 to 2.97).* *At 12 months, mean (SD) weight change in kg was –2.10 (4.80) in the PSMF group and –3.30 (7.30) in the very low-fat group. Mean weight change in the PSMF group compared with very-low-fat was 1.20 (95% CI –1.51 to 3.91).* *Weight and BMI were significantly lower than baseline for both groups (p≤0.05) but there was no statistically significant difference between the groups.* *In each group, about 25% of participants lost 5% or more of initial body weight, and about 10% lost 10% or more at 12 months.*
Quality and comments	*Atkins categorised as PSMF. Ornish diet categorised as very-low-fat.* *Blinded assessment done. ITT analysis done. Randomisation done by computer-generated sequence, and good allocation concealment.* *See other sections for comparisons of PSMF, LED, low fat, and very-low-fat (Atkins, Weight Watchers, Zone and Ornish respectively).*

Other outcomes

Dansinger 2005 RCT	
Results	*Only reported values at 12 months.* *At 12 months, mean (SD) TC change in mmol/l was –0.11 (0.59) in the PSMF group, and –0.28 (0.54) in the very-low-fat group. Mean TC change in the PSMF group compared with very-low-fat was 0.17 (95% CI –0.08 to 0.42).* *At 12 months, mean (SD) LDL change in mmol/l was –0.18 (0.62) in the PSMF group, and –0.32 (0.49) in the very low-fat group. Mean LDL change in the PSMF group compared with very-low-fat was 0.14 (95% CI –0.10 to 0.38).* *At 12 months, mean (SD) HDL change in mmol/l was 0.09 (0.18) in the PSMF group, and –0.01 (0.17) in the very low-fat group. Mean HDL change in the PSMF group compared with very-low-fat was 0.10 (95% CI 0.02 to 0.18).* *At 12 months, mean (SD) TAG change in mmol/l was 0.02 (0.94) in the PSMF group, and 0.06 (0.40) in the very-low-fat group. Mean TAG change in the PSMF group compared with very-low-fat was –0.08 (95% CI –0.40 to 0.24).* *At 12 months, mean (SD) DBP change in mmHg was –1.40 (7.50) in the PSMF group, and 0.20 (4.60) in the very low-fat group. Mean DBP change in the PSMF group compared with very-low-fat was –1.60 (95% CI –4.33 to 1.33).* *At 12 months, mean (SD) SBP change in mmHg was 0.20 (12.00) in the PSMF group, and 0.50 (7.70) in the very low-fat group. Mean SBP change in the PSMF group compared with very-low-fat was –0.30 (95% CI –4.72 to 4.12).* *At 12 months, mean (SD) FPG change in mmol/l was 0.08 (0.77) in the PSMF group, and –0.23 (1.67) in the very low-fat group. Mean FPG change in the PSMF group compared with very-low-fat was 0.31 (95% CI –0.26 to 0.88).* *At 12 months, the mean energy reductions from baseline (*p≤*0.05) were 138 for PSMF and 192 for very-low-fat. These were not significantly different between groups.* *No significant differences were seen in macronutrient content between any of the groups.* *Group mean adherence scores according to diet records and self-assessment decreased over time, and to a similar extent in all groups. About 25% of each group sustained a mean adherence level of at least 6/10, which 'appeared to delineate a clinically meaningful adherence level'.*
Quality and comments	Converted mg/dl to mmol/l (see paper for conversion rates and figures used). Dietary intake was assessed from 3-day diet records at 1, 2, 6 and 12 months.

Reported harms

Dansinger 2005 RCT	
Harms	Common reasons for discontinuation were that the assigned diet was too hard to follow, or not yielding enough weight loss. No diet-related or adverse events or serious adverse effects were found.
Quality and comments	Reasons for discontinuation not reported by group but overall only.

Generalisability

Dansinger 2005 RCT	
Country and setting	USA. Enrolled at an academic medical centre.
Participants (included/excluded)	Included if adults of any age who were overweight (BMI between 27 and 42 kg/m^2) and having at least one of the following metabolic cardiac risk factors: FPG ≥6.1 mmol/l, TC ≥5.2 mmol/l, LD L≥3.4 mmol/l, HDL ≤1.0 mmol/l, TAG ≥1.7 mmol/l, SBP ≥145 mmHg, DBP ≥90 mmHg, or current use of oral medication to treat hypertension, diabetes, dyslipidaemia. Excluded if unstable chronic illness, insulin therapy, urinary microalbumin of more than two times normal, serum creatinine ≥123.8 µmol/l, clinically significant abnormalities of liver or thyroid test results, weight loss medication or pregnancy.
Recruitment	Newspaper advertisements and TV publicity (local news coverage).
Intervention (mode and intensity)	*Four classes lasting 1 h during the first 2 months. Assessed at baseline, 2, 6 and 12 months (additional dietary assessment at 1 month).*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Team consisted of dietitian and physician who facilitated the meetings.
Dropout rates	*48% PSMF and 50% very-low-fat at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Weight and cardiac risk factors, baseline values carried forward. Dietary intake, baseline or subsequent values used.

1.3.14 Low-glycaemic-index (high-protein) diet compared with high-glycaemic-index (standard-protein) diet

Weight loss

Brinkworth 2004 RCT	
Aim	To compare the long-term compliance and effects of two low-fat diets differing in carbohydrate:protein ratio on body composition and biomarkers of CVD in obese people with hyperinsulinaemia.
Participants	People who were overweight (27<BMI (kg/m^2)<43) with a fasting serum insulin >12 mU/l. Total 58 – 45 F, 13 M. Mean age (SD) 52.0 (2.6) years high-protein (HP) (*n*=21), 51.5 (1.6) years standard-protein (SP) (*n*=22). Mean (SD) BMI (kg/m^2) 34.6 (0.9) HP, 33.6 (0.8) SP. Results for completers only.

Intervention (including details of diet)	*HP: 30% energy from protein (about 110 g/ day), 40% of energy from carbohydrate (about 140 g/day) and 30% from fat (about 50 g/day) in the energy restriction phase (about 1500 kcal/day for 12 weeks). During the next 4 weeks, the energy balance phase energy intake was increased to about 2000 kcal/day with the same macronutrient balance (extra 21 g protein).* *Met with a dietitian prior to the study and every 2 weeks up to week 16 for 15–30 min to discuss dietary issues.* *During the following 12 months, participants asked to continue the same dietary pattern, but were not provided with any foodstuffs or dietary counselling.*
Control	SP: 15% energy from protein (about 60 g/day), 55% of energy from carbohydrate (about 200 g/day) and 30% from fat (about 50 g/day) in the energy restriction phase (about 1500 kcal/day for 12 weeks). During the next 4 weeks, the energy balance phase energy intake was increased to about 2000 kcal/day with the same macronutrient balance (extra 7 g protein). Met with a dietitian prior to the study and every 2 weeks up to week 16 for 15–30 min to discuss dietary issues. During the following 12 months, participants asked to continue the same dietary pattern, but were not provided with any foodstuffs or dietary counselling.
Length of follow-up	*68 weeks (16 weeks plus 52)*
Results	*At 16 weeks, mean (SD) weight change in kg was –8.70 (3.21) in the HP group and –9.10 (3.28) in the SP group. Mean weight change in the HP group compared with SP was 0.40 (95% CI –1.54 to 2.34).* *At 68 weeks, mean (SD) weight change in kg was –4.10 (5.96) in the HP group and –2.90 (3.75) in the SP group. Mean weight change in the HP group compared with SP was –1.20 (95% CI –4.19 to 1.79).* *Other time points were shown graphically, but values were not reported.*
Quality and comments	*Blinded assessment not reported. ITT analysis done for completers.* *Randomisation done but no details of process or allocation concealment.*

Due 2004 RCT	
Aim	To evaluate the effects of a fat-reduced HP diet compared with a fat-reduced medium-protein (MP) diet.
Participants	Adults who were overweight (BMI 25–35). Total 50 – 38F 12M. Mean age 39.8 (95% CI 35.8 to 43.8) years HP (*n*=25), 39.4 (95% CI 35.3 to 43.6) years SP (*n*=25). Mean BMI (kg/m^2) 30.0 (95% CI 29.1 to 30.9) HP, 30.8 (95% CI 29.9 to 31.6) SP.
Intervention (including details of diet)	*Diet: HP (25% energy from protein). Energy from fat <30%. Macronutrient composition strictly controlled, but energy intake was ad libitum.* *Instructed not to change physical activity or smoking habits.* *For first 6 months, food provided from study shop only. Dietitian advised on items to ensure that diet adhered to.* *Counselling every 2 weeks from months 6 to 12. No details of content.*
Control	As above, except diet was MP (12% energy from protein).
Length of follow-up	*24 months*

Results	*At 6 months, mean (SD) weight change in kg was –9.40 (8.58) in the HP group and –5.90 (7.58) in the MP group. Mean weight change in the HP group compared with MP was –3.50 (95% CI –8.18 to 1.18).* *At 12 months, mean (SD) weight change in kg was –6.20 (7.67) in the HP group and –4.30 (7.13) in the MP group. Mean weight change in the HP group compared with MP was –1.90 (95% CI –6.45 to 2.65).* *At 24 months, mean (SD) weight change in kg was –6.40 (7.73) in the HP group and –3.20 (6.82) in the MP group. Mean weight change in the HP group compared with MP was –3.40 (95% CI –10.52 to 3.72).* *WC and WHR were significantly reduced in the HP group at 6 months and 12 months.*

	>5 kg		***>10 kg***	
	HP	***MP***	***HP***	***MP***
6 months	*78%*	*61% (NS)*	*39%*	***13% (p<0.05)***
12 months	*57%*	*50% (NS)*	*17%*	***0% (p=0.009)***
24 months	***55%***	***50% (NS)***	***18%***	***0% (NS)***

Quality and comments	*Blinded assessment not reported. ITT analysis unclear (last observation carried forwards [LOCF]) where done, and stated that results were similar). Randomisation done but no details of process or allocation concealment. Used HTA formula for weight SDs.*

Other outcomes

Brinkworth 2004 RCT	
Results	*Both diets significantly increased HDL-cholesterol concentrations (p<0.001) and decreased fasting insulin, insulin resistance, intracellular adhesion molecule-1 and C-reactive protein levels (p<0.05). Protein intake was significantly greater in HP during the initial 16 weeks (p<0.001), but decreased in HP and increased in SP during 52-week follow-up, with no difference between groups at week 68, indicating poor long-term dietary adherence behaviour to both dietary patterns. DBP fell significantly in the male participants from week 16 to 68, but not for females. However, at 68 weeks, there was no difference between men and women for DBP.*
Quality and comments	…

Due 2004 RCT	
Results	*No significant differences at baseline for dietary intake. Significantly higher % energy from protein was seen in the HP group from 6–12 months (p<0.0001). Conversely, % energy from carbohydrate was significantly lower in the HP group from 6–12 months (p≤0.0005).* *Only significant differences were seen in total energy intake at 6 months (lower in the HP group) and % energy from fat remained similar at all time points.* *No significant differences seen for lipids, glucose, TAG or insulin between the two groups.*
Quality and comments	Dietary records from 6 months onwards – up to 6 months, from shop records.

Reported harms

Brinkworth 2004 RCT	
Harms	The HP diet appeared to have no significant effect on either renal function or bone mineral content.
Quality and	…

comments	

Due 2004 RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Brinkworth 2004 RCT	
Country and setting	Australia. Outpatient clinics.
Participants (included/excluded)	Included if aged between 20 and 65 years, Had a fasting serum insulin >12 µmol/l, and BMI between 27 and 43 kg/m^2. Excluded if type 2 diabetes, history of clinically significant illness (liver, unstable cardiovascular, respiratory, gastrointestinal (GI), malignancy), pregnant or lactating.
Recruitment	Advertisements
Intervention (mode and intensity)	*Seen every 2 weeks for 16 weeks*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Dietitian
Dropout rates	*28% HP, 24% SP at 68 weeks*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only. ITT used last-observation carried forward.

Due 2004 RCT	
Country and setting	Denmark. University department.
Participants (included/excluded)	Included if aged 18 to 65 years, BMI 25–35 kg/m^2. No exclusion criteria reported.
Recruitment	No details
Intervention (mode and intensity)	*After 6 months of food provision, seen every 2 weeks for counselling for months 6–12*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Dietitian assisted in food selection. Also dietitian involvement in BT sessions.
Dropout rates	*8% HP and 28% MP at 12 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only

1.4 Behavioural interventions (with or without diet)

1.4.1 Diet and behaviour therapy vs usual care

Weight loss

Munsch 2003 RCT	
Aim	To evaluate the effectiveness of a cognitive BT group therapy programme for the treatment of obesity

Participants	People who were overweight (BMI ≥30 kg/m^2). Total 70 – 52 F, 18 M. Mean age (SD) 49 (12) years F, 45 (14) years M diet+BT (*n*=53), 49 (10) years F, 49 (10) years M usual care (*n*=17). Mean (SD) BMI (kg/m^2) 35.7 (5.6) F, 36.8 (5.2) M diet+BT, 34.0 (3.0) F, 33.4 (2.5) M usual care.
Intervention	*Diet: no details other than 'long term change over to a balanced, fat-reduced nutrition'. Classified as 600 kcal/deficit or low fat.* *BT: self-monitoring, strategies to control eating behaviour, problem analysis and self-observation, alteration of cognitive patterns, social competence, relapse prevention. Adapted from LEARN manual.*
Comparison	Usual care: non-specific comments on weight loss.
Length of follow-up	*12 months*
Results	*At 16 weeks, mean weight change (SD) was –3.80 (6.99) kg in the diet and BT group compared with –0.70 (6.11) kg in the usual care group. Mean weight change in the intervention group compared with usual care was –3.10 (95% CI –7.17 to 0.97).* *At 12 months, mean weight change (SD) was –4.70 (7.25) kg in the diet and BT group compared with –0.40 (6.01) kg in the usual care group. Mean weight change in the intervention group compared with usual care was –4.30 (95% CI –9.02 to 0.42).*
Quality and comments	*Results for GP group only reported (clinic group not randomised). Used HTA formula for SDs.* *Blinded assessment not reported. ITT analysis not done. Random allocation but no description of concealment.* *Study reported significant differences between the two groups at 12 months – not seen in analysis?*

Other outcomes

Munsch 2003 RCT	
Results	*In regard to psychological factors the treatment group showed an increased sense of control over eating behaviour, and feelings of distractibility and hunger were reduced after treatment and at follow-up (*p*<0.05). The diet and BT group showed statistically relevant increases in feelings of attractiveness regarding their body and shape (*p*<0.05).*
Quality and comments	…

Harms

Munsch 2003 RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Munsch 2003 RCT	
Country and setting	Switzerland. GP surgeries
Participants (included/excluded)	Included if BMI ≥30 kg/m^2. Excluded if severe mental disorders, insulin dependent diabetes, hypothyroidism, terminal illness.
Recruitment	From patients and advertisements.
Randomisation	N/R.
Intervention (mode and intensity)	*16 weekly meetings (90 min)*
Duration of active intervention	16 weeks

Comparison (mode and intensity)	Usual care
Delivery of intervention/comparison (who)	Specially trained GPs and tutors.
Dropout rates	*23% diet and BT, 53% usual care at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.4.2 Diet and behaviour therapy vs information

Weight loss

Messier 2004 RCT	
Aim	To determine whether long-term exercise and dietary weight loss are more effective, either separately or in combination, than usual care in improving physical function, pain, mobility in older overweight/obese adults with osteoarthritis (OA)
Participants	People with osteoarthritis, aged ≥60 years who were overweight (BMI ≥28 kg/m^2) Total 316 – 227 F, 89 M. Mean (SD) age years 68 (6.34) years diet+BT (*n*=82), 69 (0.88) years information (*n*=78). Mean (SD) BMI (kg/m^2) 34.5 (5.43) diet+BT, 34.2 (5.30) information.
Intervention	*Diet: to produce and maintain an average weight loss of 5% during the 18-month intervention period. Classified as a 600 kcal/day deficit/LED diet* *BT: self-monitoring, goal setting, cognitive restructuring, problem-solving, and environmental management*
Control	The group met monthly for 1 h for the first 3 months. A health educator, who scheduled videotaped presentations and physician talks on topics concerning OA, obesity and exercise, organised the healthy lifestyle programme. Patients were advised to follow the American College of Rheumatology and European League Against Rheumatism recommendations for weight loss and exercise as treatments for OA. Question-and-answer sessions followed each presentation. Monthly phone contact was maintained during months 4–6, followed by contact every other month during months 7–18. During phone contact, information on pain, medication use, illnesses, and hospitalisation was obtained.
Length of follow-up	*18 months*
Results	*At 18 months, mean (SD) weight change in kg was –4.61 (7.22) in the diet and BT group, and –1.10 (6.23) in the information group. Mean weight change in the intervention group compared with information was –3.51 (95% CI –5.60 to –1.42).*
Quality and comments	*ITT analysis done. Blinded assessment done. Good concealment of allocation. SDs calculated using HTA formula.*

Other outcomes

Messier 2004 RCT	
Results	*The diet and BT group was not significantly different from the healthy lifestyle group for any of the functional or mobility measures.*
Quality and comments	…

Reported harms

Messier 2004 RCT	
Harms	Two deaths occurred, but were unrelated to the interventions. One participant

Quality and comments	tripped and sustained a laceration to his head. No details of allocation. …

Generalisability

Messier 2004 RCT	
Country and setting	USA. Older Americans Independence Centre.
Participants (included/excluded)	Included if aged ≥60 years, calculated BMI ≥28 kg/m^2, knee pain on most days of the month, sedentary activity pattern with <20 min of formal exercise once weekly for the past 6 months, self-reported difficulty in at least one of the following activities ascribed to knee pain: walking one-quarter of a mile (three to four city blocks), climbing stairs, bending, stooping, kneeling (e.g., to pick up clothes), shopping, house cleaning or other self-care activities, getting in and out of bed, standing up from a chair, lifting and carrying groceries, or getting in and out of the bath, radiographic evidence of grade I–III tibiofemoral or patellofemoral OA based on weight-bearing anteroposterior and sunrise view radiographs, and willingness to undergo testing and intervention procedures. Excluded if serious medical condition that prevented safe participation in an exercise programme, including symptomatic heart or vascular disease (angina, peripheral vascular disease, congestive heart failure), severe hypertension, recent stroke, chronic obstructive pulmonary disease, severe insulin-dependent diabetes mellitus, psychiatric disease, renal disease, liver disease, active cancer other than skin cancer, and anaemia, a Mini-Mental State Examination score of <24, inability to finish the 18-month study or unlikely to be compliant, inability to walk without a cane or other assistive device, participation in another research study, reported alcohol consumption of >14 drinks per week, ST segment depression of at least 2 mm at an exercise level of 4 metabolic equivalent tasks (METS) or less, hypotension, or complex arrhythmias during a graded exercise test, inability to complete the protocol, in the opinion of the clinical staff, because of frailty, illness, or other reasons.
Recruitment	Mass mailings to age-eligible persons within the target area, targeted mailings to employees of the university and medical centre, presentations to various groups of older adults, mass media advertisements and placement of posters (with pull-off reply cards attached) in strategic locations. Also, strategies were developed to enhance recruitment among racial minorities, including advertisements and interviews on minority-run radio stations, newspaper ads in predominantly African American publications, letters to churches attended mainly by minorities, and inserts in these church bulletins. Initial screening for major eligibility criteria was via telephone.
Intervention (mode and intensity)	*One introductory individual session was followed by 16 weekly sessions (three group sessions and one individual session each month).*
Duration of active intervention	18 months
Control (mode and intensity)	Group met monthly for 1 h for the first 3 months. Monthly phone contact was maintained during months 4–6, followed by contact every other month during months 7–18.
Delivery of intervention/control (who)	Diet and BT: N/R Information: health educator, who scheduled videotaped presentations and physician talks on topics concerning OA, obesity and exercise, organised the healthy lifestyle programme.
Dropout rates	*23% activity, 14% information at 24 months*

Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.4.3 Active diet, and behaviour therapy vs passive (information-based) diet and behaviour therapy

Weight loss

Cousins 1992 (in HTA) RCT	
Aim	To assess the effectiveness of a culturally sensitive, family-based weight-loss programme for cardiovascular risk reduction in obese Mexican American women
Participants	Women who were overweight (20 to 100% above IBW). *168 total – all women. Mean (SD) age 33.6 (6.4) years individual group (*n=*32), 33.8 (6.1) years family group (*n=*27), 33.8 (7.0) years control (*n=*27). Mean (SD) BMI* (kg/m^2) *31.7 (5.0) individual group, 30.3 (4.5) family group, 31.6 (4.9) control.*
Intervention	All participants received *Cuidando el Corazon*, a bilingual manual consisting of a low-fat eating plan and behaviour modification strategies; aimed at diet of 1200 kcal (women) 30% of energy from fat (10% unsaturated fat), 20% from protein, 50% from carbohydrate, <300 mg cholesterol/day, advised regarding moderate sodium intake, cookbook of recipes for fat-modified traditional Mexican foods, behaviour modification strategies such as maintaining weight loss, problem-solving and preventing relapse were described in simple terms and manual translated into Spanish. Individual group: individualised instruction by bilingual dietitian on nutrition, feedback on food records and behaviour modification techniques, group exercise, food tasting, cooking demonstrations; last 6 months group leaders focused on preventing or minimising relapse and emphasised problem-solving approach to problems of low-fat eating and exercise, where participants could enlist support of the group; taught using techniques specifically for adults with limited literacy skills. Family group: same sessions as individual group except that spouses encouraged to attend sessions (separate classes for children); manual modified to include information on partner support and to encourage family changes in eating and exercise behaviours.
Control	*All participants received* Cuidando el Corazon*, a bilingual manual consisting of a low-fat eating plan and behaviour modification strategies; aimed at diet of 1200 kcal (women) 30% energy as fat (10% unsaturated fat), 20% as protein, 50% as carbohydrate, <300 mg cholesterol/day, advised regarding moderate sodium intake, cookbook of recipes for fat-modified traditional Mexican foods, behaviour modification strategies such as maintaining weight loss, problem-solving and preventing relapse were described in simple terms and manual translated into Spanish.*
Length of follow-up	12 months

Results	*At 3 months, mean weight change (SD) was –2.60 (6.65) kg in the individual group compared with –0.90 (6.17) kg in the information group. Mean weight change in the individual group compared with the information group was –1.70 (95% CI –5.77 to 2.37).* *At 6 months, mean weight change (SD) was –3.30 (6.85) kg in the individual group compared with –0.20 (5.97) kg in the information group. Mean weight change in the individual group compared with the information group was –3.10 (95% CI –7.12 to 0.92).* *At 12 months, mean weight change (SD) was –2.10 (6.51) kg in the individual group compared with –0.70 (6.11) kg in the information group. Mean weight change in the individual group compared with the information group was –1.40 (95% CI –5.41 to 2.61).* *At 3 months, mean weight change (SD) was –3.00 (6.76) kg in the family group compared with –0.90 (6.17) kg in the information group. Mean weight change in the family group compared with the information group was –2.10 (95% CI –6.22 to 2.02).* *At 6 months, mean weight change (SD) was –4.50 (7.19) kg in the family group compared with –0.20 (5.97) kg in the information group. Mean weight change in the family group compared with the information group was –4.30 (95% CI –8.44 to –0.16).* *At 12 months, mean weight change (SD) was –3.80 (6.99) kg in the family group compared with–0.70 (6.11) kg in the information group. Mean weight change in the family group compared with the information group was –3.10 (95% CI –7.25 to 1.05).*
Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Mean change in weight at 12 months calculated from actual values, and SDs also calculated. Halved control groups for analysis

Wing 1998 (in HTA) RCT	
Aim	To assess the effect of lifestyle intervention over 2 years on changes in weight, CHD risk factors, and incidence of diabetes in overweight adults with a parental history of diabetes
Participants	Adults aged 40 to 55 years who did not have diabetes, and were overweight (30 to 100% of IBW). *154 total – 122 F, 32 M. Mean (SD) age 45.0 (4.7) years diet (*n=*37), 45.3 (4.9) control (*n=*40). Mean (SD) BMI (kg/m^2) 36.1 (4.1) diet, 36.0 (5.4) control.*
Intervention	Diet: 800–1000 kcal/day weeks 1–8 then adjusted to 1200–1500 kcal/day by week 16, food diaries reviewed and feedback given, meal plans and shopping lists, behavioural or nutritional topic given at each session.
Control	*Participants received LEARN behavioural manual with information on healthy eating, exercise and behavioural strategies; participants encouraged to lose weight and exercise on their own, only participated in the assessments*
Length of follow-up	24 months
Results	*At 6 months, mean weight change (SD) was –9.10 (6.40) kg in the diet and BT group compared with –1.50 (2.70) kg in the control group. Mean weight change in the intervention group compared with control was –7.60 (95% CI –9.92 to –5.28).* At 12 months, mean weight change (SD) was –5.50 (6.90) kg in the diet and BT group compared with –0.30 (4.50) kg in the control group. Mean weight change in the intervention group compared with control was –5.20 (95% CI –8.07 to –2.33). At 24 months, mean weight change (SD) was –2.10 (7.60) kg in the diet and BT group compared with –0.30 (4.50) kg in the control group. Mean weight change in the intervention group compared with control was –1.80 (95% CI –4.77 to 1.17)
Quality and comments	Author confirmed main study and sub-study results. Blinded assessment done. ITT analysis done. Random allocation but no description of concealment.

Other outcomes

Cousins 1992 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Wing 1998 (in HTA) RCT	
Results	*At 6 months, mean (SD) TC change in mmol/l was –0.49 (0.71) in the diet group, and 0.12 (0.50) in the control group. Mean TC change in the diet group compared with control was –0.61 (95% CI –0.90 to –0.32).* *At 6 months, mean (SD) LDL change in mmol/l was –0.32 (0.60) in the diet group, and 0.08 (0.46) in the control group. Mean LDL change in the diet group compared with control was –0.40 (95% CI –0.65 to –0.15).* *At 6 months, mean (SD) HDL change in mmol/l was –0.10 (0.17) in the diet group, and –0.02 (0.11) in the control group. Mean HDL change in the diet group compared with control was –0.08 (95% CI –0.15 to –0.01).* *At 6 months, mean (SD) TAG change in mmol/l was –0.30 (1.45) in the diet group, and 0.29(0.32) in the control group. Mean TAG change in the diet group compared with control was –0.59 (95% CI –1.08 to –0.10).* *At 6 months, mean (SD) DBP change in mmHg was –6.20 (6.90) in the diet group, and –2.20 (8.00) in the control group. Mean DBP change in the diet group compared with control was –4.00 (95% CI –7.59 to –0.41).* *At 6 months, mean (SD) SBP change in mmHg was –10.20 (9.20) in the diet group, and –2.00 (10.50) in the control group. Mean SBP change in the diet group compared with control was –8.20 (95% CI –12.95 to –3.45).* *At 6 months, mean (SD) FPG change in mmol/l was –0.20 (0.40) in the diet group, and 0.10 (0.50) in the control group. Mean FPG change in the diet group compared with control was –0.30 (95% CI –0.52 to –0.08).* *At 6 months, mean (SD) change in %HbA_{1c} was 0.10 (0.50) in the diet group, and 0.20 (0.40) in the control group. Mean %HbA_{1c} change in the diet group compared with control was –0.10 (95% CI –0.32 to 0.12).* At 12 months, mean (SD) TC change in mmol/l was 0.26 (0.76) in the diet group, and 0.39 (0.70) in the control group. Mean TC change in the diet group compared with control was –0.13 (95% CI –0.49 to 0.23). At 12 months, mean (SD) LDL change in mmol/l was 0.12 (0.73) in the diet group, and 0.24 (0.66) in the control group. Mean LDL change in the diet group compared with control was –0.12 (95% CI –0.47 to 0.23). At 12 months, mean (SD) HDL change in mmol/l was 0.10 (0.16) in the diet group, and 0.08 (0.16) in the control group. Mean HDL change in the diet group compared with control was 0.02 (95% CI –0.06 to 0.10). At 12 months, mean (SD) TAG change in mmol/l was 0.55 (3.77) in the diet group, and 0.40 (1.25) in the control group. Mean TAG change in the diet group compared with control was 0.15 (95% CI –1.21 to 1.51). At 12 months, mean (SD) DBP change in mmHg was 3.40 (8.10) in the diet group, and 4.90 (8.20) in the control group. Mean DBP change in the diet group compared with control was –1.50 (95% CI –5.57 to 2.57). At 12 months, mean (SD) SBP change in mmHg was 1.30 (8.30) in the diet group, and 1.10 (9.60) in the control group. Mean SBP change in the diet group compared with control was 0.20 (95% CI –4.30 to 4.70). At 12 months, mean (SD) FPG change in mmol/l was 0.20 (0.80) in the diet group, and 0.00 (0.60) in the control group. Mean FPG change in the diet group compared with control was 0.20 (95% CI –0.15 to 0.55). At 24 months, mean (SD) TC change in mmol/l was –0.12 (0.61) in the diet group, and 0.18 (0.53) in the control group. Mean TC change in the diet group compared with control was –0.30 (95% CI –0.58 to –0.02). At 24 months, mean (SD) LDL change in mmol/l was –0.16 (0.63) in the diet

	group, and 0.03 (0.46) in the control group. Mean LDL change in the diet group compared with control was –0.19 (95% CI –0.45 to 0.07). At 24 months, mean (SD) HDL change in mmol/l was 0.02 (0.20) in the diet group, and 0.04 (0.24) in the control group. Mean HDL change in the diet group compared with control was –0.02 (95% CI –0.13 to 0.09). At 24 months, mean (SD) TAG change in mmol/l was 0.19 (2.42) in the diet group, and 0.52 (1.14) in the control group. Mean TAG change in the diet group compared with control was –0.33 (95% CI –1.23 to 0.57). At 24 months, mean (SD) DBP change in mmHg was 3.00 (7.80) in the diet group, and 2.00 (8.00) in the control group. Mean DBP change in the diet group compared with control was 1.00 (95% CI –2.82 to 4.82). At 24 months, mean (SD) SBP change in mmHg was –0.80 (9.40) in the diet group, and –1.50 (12.00) in the control group. Mean SBP change in the diet group compared with control was 0.70 (95% CI –4.55 to 5.95). At 24 months, mean (SD) FPG change in mmol/l was 0.30 (1.00) in the diet group, and 0.20 (0.40) in the control group. Mean FPG change in the diet group compared with control was 0.10 (95% CI –0.26 to 0.46). At 24 months, mean (SD) change in %HbA_{1c} was –0.10 (0.50) in the diet group, and –0.10 (0.30) in the control group. Mean %HbA_{1c} change in the diet group compared with control was 0.00 (95% CI –0.20 to 0.20). *At 6, 12 and 24 months, the diet group reported significant decreases from baseline in energy intake and percentage of energy from fat. Smaller, often non-significant decreases were also seen in the control group.* *At 24 months, the relative risk (of weight loss of 4.5 kg compared with no weight loss) of developing diabetes in the diet group was about 0.88 and about 0.89 in the control group. For people with impaired glucose tolerance (IGT), the relative risks were about 0.96 and 0.88 respectively.*
Quality and comments	Dietary intake assessed using self-completed questionnaires and 3-day food diaries.

Reported harms

Cousins 1992 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wing 1998 (in HTA) RCT	
Harms	7% in the control group and 30.3% of the diet group developed diabetes during the 24-month study. The development of diabetes was associated with increased initial IGT.
Quality and comments	…

Generalisability

Cousins 1992 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if Mexican American women, ?married, aged 18–45 years, 20–100% above IBW.* *Excluded if hypertension (DBP ≥115 mmHg), diabetes (fasting plasma glucose ≥140 mg/dl), chronic illness with diet or exercise recommendations different from those in the study.*
Recruitment	Media promotion, personal contacts in the local community (mainly churches and health agencies).

Intervention (mode and intensity)	12 months, contacted 37 times (baseline then weekly group sessions for initial 24 weeks then 6 monthly sessions up to month 12)
Control (mode and intensity)	*Unclear but presumed contacted only at baseline and at 12 months*
Delivery of intervention/control (who)	Classes taught by bilingual registered dietitians.
Dropout rates	49% overall at 12 months.
Treatment of dropouts (return to baseline, or last measurement?)	*Data for completers only.*

Wing 1998 (in HTA) RCT	
Country and setting	USA. No further details –university hospital?
Participants (included/excluded)	Included if aged 40–55 years, non-diabetic (confirmed by oral glucose tolerance test [OGTT]), 1 or 2 biological parents with type 2 diabetes, 30–100% above IBW. Excluded if diagnosis of diabetes.
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*2 years, contacted approximately 52 times (baseline, weekly for first 6 months then every 2 weeks for next 6 months then 2 × 6 week course during second year).*
Control (mode and intensity)	Contacted at baseline, 6 months, 1 year and at 2 years.
Delivery of intervention/control (who)	Group meetings were led by a multidisciplinary team, including a behaviour therapist and a registered dietitian.
Dropout rates	*5% diet and 23% control at 24 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

1.4.4 Family vs individual treatment

Weight loss

Cousins 1992 (in HTA) RCT	
Aim	To assess the effectiveness of a culturally sensitive, family-based weight-loss programme for cardiovascular risk reduction in obese Mexican American women
Participants	Women who were overweight (20 to 100% above IBW). *168 total – all women. Mean (SD) age 33.6 (6.4) years individual group (*n=*32), 33.8 (6.1) years family group (*n=*27), 33.8 (7.0) years control (*n=*27). Mean (SD) BMI (kg/m^2) 31.7 (5.0) individual group, 30.3 (4.5) family group, 31.6 (4.9) control.*

Intervention	All participants received *Cuidando el Corazon*, a bilingual manual consisting of a low-fat eating plan and behaviour modification strategies; aimed at diet of 1200 kcal (women) 30% of energy from fat (10% unsaturated fat), 20% from protein, 50% from carbohydrate, <300 mg cholesterol/day, advised regarding moderate sodium intake, cookbook of recipes for fat-modified traditional Mexican foods, behaviour modification strategies such as maintaining weight loss, problem-solving and preventing relapse were described in simple terms and manual translated into Spanish. Individual group: individualised instruction by bilingual dietitian on nutrition, feedback on food records and behaviour modification techniques, group exercise, food tasting, cooking demonstrations; last 6 months group leaders focused on preventing or minimising relapse and emphasised problem-solving approach to problems of low-fat eating and exercise, where participants could enlist support of the group; taught using techniques specifically for adults with limited literacy skills. Family group: same sessions as individual group except that spouses encouraged to attend sessions (separate classes for children); manual modified to include information on partner support and to encourage family changes in eating and exercise behaviours.
Control	*All participants received* Cuidando el Corazon*, a bilingual manual consisting of a low-fat eating plan and behaviour modification strategies; aimed at diet of 1200 kcal (women) 30% of energy from fat (10% unsaturated fat), 20% from protein, 50% from carbohydrate, <300 mg cholesterol/day, advised regarding moderate sodium intake, cookbook of recipes for fat-modified traditional Mexican foods, behaviour modification strategies such as maintaining weight loss, problem-solving and preventing relapse were described in simple terms and manual translated into Spanish.*
Length of follow-up	12 months
Results	*At 3 months, mean weight change (SD) was –3.00 (6.76) kg in the family group compared with –2.60 (6.65) kg in the individual group. Mean weight change in the family group compared with the individual group was –0.40 (95% CI –3.84 to 3.04).* *At 6 months, mean weight change (SD) was –4.50 (7.19) kg in the family group compared with –3.30 (6.85) kg in the individual group. Mean weight change in the family group compared with the individual group was –2.40 (95% CI –6.00 to 1.20).* At 12 months, mean weight change (SD) was –3.80 (6.99) kg in the family group compared with –2.10 (6.51) kg in the individual group. Mean weight change in the family group compared with the individual group was –1.70 (95% CI –5.17 to 1.77).
Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Mean change in weight at 12 months calculated from actual values, and SDs also calculated.

Black 1984 (in HTA) RCT	
Aim	To determine if spouse attendance at treatment sessions and participation in behavioural contracting would produce greater weight losses than other levels of spouse involvement.
Participants	Married women who were overweight (at least 10% overweight) and whose husband was willing to participate and provide support. *36 total – all women. Mean age 35.1 years overall. Mean weight (kg) 77.3 overall. Individual group (*n*=12), passive spouse involvement (*n*=12), active spouse involvement (*n*=12).*

Intervention	All participants received 90 min introductory meeting and signed contract to complete daily food record and record of non-routine physical activity for 2 weeks, 4 behavioural contracts written during 10 weeks focusing on changing eating and exercise habits. Passive spouse involvement: husbands attended as passive observers not encouraged to help their wives, counsellor negotiated and co-signed contracts. Active spouse involvement: husbands attended and actively participated in sessions and contracts specified ways husband could help their wives, spouse negotiated and co-signed contracts.
Control	*All participants received 90 min introductory meeting and signed contract to complete daily food record and record of non-routine physical activity for 2 weeks, 4 behavioural contracts written during 10 weeks focusing on changing eating and exercise habits.* *Individual group: participants attended alone, counsellor negotiated and co-signed contracts.*
Length of follow-up	4 years (only 12-month data reported due to exclusions and small numbers)
Results	*At 10 weeks, mean weight change (SD) was –4.61 (7.22) kg in the active family group compared with –3.71 (6.96) kg in the individual group. Mean weight change in the family group compared with the individual group was –0.90 (95% CI –6.83 to 5.03).* At 12 months, mean weight change (SD) was –7.04 (7.91) kg in the active family group compared with –7.42 (8.01) kg in the individual group. Mean weight change in the family group compared with the individual group was 0.38 (95% CI –6.27 to 7.03).
Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. *SDs calculated using HTA formula. Slight differences in figures from HTA due to conversions and calculation roundings.*

Murphy 1982 (in HTA) RCT	
Aim	To assess the effect of spouse involvement on weight loss and maintenance
Participants	Couples, at least of whom was overweight (20 to 80% over IBW) 75 total – 50 F, 25 M. Mean age 35.3 years individual, one party contracts (*n*=13), 39.7 years individual, two party contracts (*n*=13), 42.3 years family, one party contracts (*n*=13), 47.5 years family, two party contracts (*n*=12), 42.0 years supportive group (*n*=11), 39.1 years waiting list control (*n*=13). Mean BMI 31.50, 32.03, 29.94, 30.49, 31.97, 29.89 kg/m^2 respectively.
Intervention	Individual, one party contracts: received treatment manual which focused on three meals per day and occasional snacks to reduce energy intake (minimum 1000 kcal/day) and increasing energy expenditure through walking; participants attended alone and entered into four contingency contracts regarding energy and nutrition, eating habits, exercise and problem behaviours; participants self-selected rewards and punishments. Individual, two party contracts: received same manual except for contingency contracts, attended alone, both participant and spouse agreed contingency contracts and spouse encouraged to actively participate in assisting with compliance and controlling rewards (mutually rewarding and/or punishing). Family, one party contracts: received identical manual as Individual, one party group, attended with spouse, participant alone responsible for contingency compliance, rewards and punishment Family, two party contracts: received identical manual to Individual, two party group, both participant and spouse attended sessions and both took part in contingency contracts. Supportive: attended alone, did not receive manual or enter into contingency contracts, group support format with therapist acting as facilitator, discussed possible strategies for successful weight loss.
Control	*Waiting list control for initial 10 weeks only, no treatment received, weight measured at week 1 and week 10.*

Length of follow-up	4 years
Results	*At 10 weeks, mean weight change (SD) was –8.16 (8.23) kg in the family, one party contracts group compared with –7.08 (7.92) kg in the individual, one party contracts group. Mean weight change in the family group compared with the individual group was–1.08 (95% CI –10.14 to 7.98).* *At 10 weeks, mean weight change (SD) was –7.62 (8.07) kg in the family, two party contracts group compared with –6.85 (7.85) kg in the individual, two party contracts group. Mean weight change in the family group compared with the individual group was –0.77 (95% CI –8.84 to 7.30).* *At 15 weeks, mean weight change (SD) was –9.43 (8.59) kg in the family, one party contracts group compared with –7.98 (8.17) kg in the individual, one party contracts group. Mean weight change in the family group compared with the individual group was –1.45 (95% CI –11.11 to 8.21).* *At 15 weeks, mean weight change (SD) was –9.66 (8.65) kg in the family, two party contracts group compared with –8.30 (8.26) kg in the individual, two party contracts group. Mean weight change in the family group compared with the individual group was –1.36 (95% CI –9.93 to 7.21).* *At 22 weeks, mean weight change (SD) was –10.34 (8.84) kg in the family, one party contracts group compared with –9.39 (8.57) kg in the individual, one party contracts group. Mean weight change in the family group compared with the individual group was –0.95 (95% CI –11.30 to 9.40).* *At 22 weeks, mean weight change (SD) was –10.89 (9.00) kg in the family, two party contracts group compared with –9.25 (8.53) kg in the individual, two party contracts group. Mean weight change in the family group compared with the individual group was –1.64 (95% CI –10.52 to 7.24).* *At 36 weeks, mean weight change (SD) was –6.89 (7.87) kg in the family, one party contracts group compared with –9.53 (8.61) kg in the individual, one party contracts group. Mean weight change in the family group compared with the individual group was 2.64 (95% CI –7.11 to 12.39).* *At 36 weeks, mean weight change (SD) was –8.21 (8.24) kg in the family, two party contracts group compared with –9.53 (8.61) kg in the individual, two party contracts group. Mean weight change in the family group compared with the individual group was1.32 (95% CI –8.39 to 11.03).* At 12 months, mean weight change (SD) was –5.44 (7.46) kg in the family, one party contracts group compared with –3.18 (6.81) kg in the individual, one party contracts group. Mean weight change in the family group compared with the individual group was –2.26 (95% CI –12.16 to 7.64). At 12 months, mean weight change (SD) was –8.75 (8.39) kg in the family, two party contracts group compared with –3.49 (6.90) kg in the individual, two party contracts group. Mean weight change in the family group compared with the individual group was –5.26 (95% CI –13.28 to 2.76). At 24 months, mean weight change (SD) was –3.36 (6.86) kg in the family, one party contracts group compared with –2.59 (6.65) kg in the individual, one party contracts group. Mean weight change in the family group compared with the individual group was –0.77 (95% CI –8.54 to 7.00). At 24 months, mean weight change (SD) was –7.21 (7.96) kg in the family, two party contracts group compared with 2.54 (6.63) kg in the individual, two party contracts group. Mean weight change in the family group compared with the individual group was –9.75 (95% CI –17.14 to –2.36). At 48 months, mean weight change (SD) was 0.73 (6.12) kg in the family, one party contracts group compared with –4.20 (7.10) kg in the individual, one party contracts group. Mean weight change in the family group compared with the individual group was 4.93 (95% CI –3.86 to 13.72). At 48 months, mean weight change (SD) was –2.87 (6.73) kg in the family, two party contracts group compared with 5.67 (7.52) kg in the individual, two party contracts group. Mean weight change in the family group compared with the individual group was –8.54 (95% CI –17.67 to 0.59).

Quality and comments	Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. SDs calculated. *HTA analysis compares ind-1 party vs family-1 party (Murphy 1982a) and ind-2 party vs family-2 party (Murphy 1982b). Again, some slight differences to HTA due to calculations.*

Pearce 1981 (in HTA) RCT	
Aim	To evaluate the effect of spouse training for long-term weight loss.
Participants	Married women who were overweight (at least 9 kg overweight or 20% above IBW Metropolitan Life Insurance norms) *68 total – all women. Mean age 39.0 years overall. Mean weight 87.43 kg overall. 14 women were allocated to the active spouse group and 13 to the individual group.*
Intervention	All participants advised to reduce energy intake to participants pre-treatment weight × 7 in pounds (1350 kcal/day), minimum 1000 kcal/day and advised to increase physical activity if weight not lost. Cooperative (active) spouse group: training in behavioural self-control including self-monitoring, imagery techniques, stimulus control and behaviour management methods. Spouses attended and actively helped wives to lose weight, spouses monitored each other's behaviour. Individual group: training in behavioural self-control including self-monitoring, imagery techniques, stimulus control and behaviour management methods. Spouses not involved and wives attended alone, wife unobtrusively monitored husbands behaviour. Non-participating spouse group: training in behavioural self-control including self-monitoring, imagery techniques, stimulus control and behaviour management methods. Spouse sent letter asking them to detach themselves from wife's weight losing efforts, wife attended alone and self-monitored and unobtrusively monitored husbands behaviour. Non-BT: focus directed at hypothetical and underlying causes of over eating, no training on behavioural techniques, attention diverted from current behaviours to past ones.
Control	*Waiting list control, participants received treatment after initial 10 weeks (therefore data not used for subsequent analyses)*
Length of follow-up	12 months
Results	*At 10 weeks, mean weight change (SD) was –6.50 (2.91) kg in the active spouse group compared with –4.32 (2.45) kg in the individual group. Mean weight change in the family group compared with the individual group was –2.18 (95% CI –4.20 to –0.16).* *At 22 weeks, mean weight change (SD) was –8.18 (4.74) kg in the active spouse group compared with –4.55 (4.31) kg in the individual group. Mean weight change in the family group compared with the individual group was –3.63 (95% CI –7.25 to –0.01).* *At 36 weeks, mean weight change (SD) was –7.47 (5.08) kg in the active spouse group compared with –3.42 (4.37) kg in the individual group. Mean weight change in the family group compared with the individual group was –4.05 (95% CI –7.84 to –0.26).* At 12 months, mean weight change (SD) was –8.25 (5.38) kg in the active spouse group compared with –2.16 (5.97) kg in the individual group. Mean weight change in the family group compared with the individual group was –6.09 (95% CI –10.64 to –1.54).
Quality and comments	Blinded assessment not reported. ITT analysis not done. Random allocation but no description of concealment. Only used active spouse group vs individual group for comparison.

Rosenthal 1980 (in HTA) RCT	
Aim	To compare the effectiveness of different degrees of husband involvement in the wives' weight loss effort.

Participants	Married women who were overweight (10% above IBW). *43 total – all women. Mean age 34.5 years overall. Mean BMI 27.56 kg/m^2 spouse involved throughout (*n=*4 completed), 29.29 some spouse and some individual therapy (*n=*7 completed), 28.80 individual only (*n=*9 completed). Mean BMI for first two groups combined 28.43.*
Intervention	Spouse involved throughout: husband attended all eight session with wives, "Slim chance in a fat world" weight loss programme, husband assigned readings and informed of behavioural ways in which they could help their wives to lose weight; sessions 5 to 8 discussed couples specific situations. Spouse and individual: husband attended first four sessions to learn techniques for helping their wives to lose weight then wives attended alone for following sessions, identical weight loss programme as above.
Control	*Individual only: no husband involvement, identical weight loss programme as above.*
Length of follow-up	186 weeks (30 weeks treatments then 3 year follow-up).
Results	At 186 weeks, mean weight change (SD) was –4.37 (7.15) kg in the active spouse group compared with –3.62 (6.94) kg in the individual group. Mean weight change in the family group compared with the individual group was –0.75 (95% CI –6.95 to 5.45).
Quality and comments	Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. Combined results for spouse throughout and spouse and individual groups. SDs calculated.

Wing 1999 (in HTA) RCT	
Aim	To evaluate the effectiveness of a more comprehensive social support condition on the prevention of weight gain during a 6-month maintenance period.
Participants	Healthy people who were overweight (6.8 to 31.8 kg above IBW). *166 total – 84 F, 82 M. Mean (SD) age 41.8 (9.2) years individual (*n=*38), 43.5 (7.8) years assigned team (*n=*48), 40.6 (8.3) years non-encouraged friends (*n=*40), 43.8 (8.6) years encouraged friends (*n=*40). Mean (SD) BMI (kg/m^2) 30.6 (3.7) individual, 31.8 (3.1) assigned team, 32.1 (3.7) non-encouraged friends, 30.3 (4.0) encouraged friends.*
Intervention	All participants advised to eat no more than 1000 kcal/day with 22 g of fat if weighed less than 90.7 kg at baseline or no more than 1500 kcal/day with 33 g of fat if baseline weight more than 90.7 kg; given grocery lists and meals plans weekly during initial 16 weeks, exercise prescribed in gradual increments up to 100 kcal/week expenditure (equivalent to walking for 2 miles on 5 days per week), food and exercise diaries completed during 16 weeks, behavioural lessons focused on problem-solving, assertion, stimulus control, developing social support, dealing with high risk situations, cognitions and maintenance strategies. Non-encouraged friends: recruited with friends but relationships among and between teams not acknowledged, identical programme as Individual group. Encouraged friends: recruited with four friends whom became natural team and received same social support as assigned team.

Control	*All participants advised to eat no more than 1000 kcal/day with 22 g of fat if weighed less than 90.7 kg at baseline or no more than 1500 kcal/day with 33 g of fat if baseline weight more than 90.7 kg; given grocery lists and meals plans weekly during initial 16 weeks, exercise prescribed in gradual increments up to 100 kcal/week expenditure (equivalent to walking for 2 miles 5 days per week), food and exercise diaries completed during 16 weeks, behavioural lessons focused on problem-solving, assertion, stimulus control, developing social support, dealing with high risk situations, cognitions and maintenance strategies. Individual: recruited alone with no effort to increase communication in group, $25 deposit refunded for attending each follow-up at months 4 and 10. Assigned team: participants assigned to a team of four members and given social support intervention involving intra-group activities such as calling other members of their team to provide support, group assignments and an intra-group competition with team who had largest number of its members retaining their weight loss in full from months 4–7 and months 4–10, jackpot consisted of $25 of each participants deposit.*
Length of follow-up	16 months
Results	*At 4 months, mean weight change (SD) was –8.80 (8.41) kg in the intervention (friends) group compared with –6.70 (7.81) kg in the control (non-friends) group. Mean weight change in the friends group compared with the non-friends group was –2.10 (95% CI –4.57 to 0.37).* *At 10 months, mean weight change (SD) was –8.70 (8.38) kg in the intervention (friends) group compared with –5.80 (7.56) kg in the control (non-friends) group. Mean weight change in the friends group compared with the non-friends group was –2.90 (95% CI –5.33 to –0.47).* At 16 months, mean weight change (SD) was –4.70 (7.25) kg in the intervention (friends) group compared with –3.00 (6.76) kg in the control (non-friends) group. Mean weight change in the friends group compared with the non-friends group was –1.70 (95% CI –3.84 to 0.44).
Quality and comments	Assessed intervention groups and control groups together for analysis. Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. *Friends could include family members. No details of how many friends were family members were given. Also groups of four rather than couples in other trials.* *Added to 18 months summary – not sure why as only 16-month follow-up? SDs calculated using HTA formula.*

Wing 1991b (in HTA) RCT	
Aim	To test the effectiveness of a 'family-based' approach for weight loss in people with type 2 diabetes
Participants	*People with type 1 diabetes who were overweight (20% or more over IBW). 43 total=25 F, 18 M. Mean (SD) age 53.6 (7.7) years spouse (*n=*24), 51.2 (7.3) years individual (*n=*25). Mean (SD) BMI (kg/m^2) 35.68 (5.76) spouse, 36.64 (5.77) individual.*
Intervention	All participants received behavioural weight loss programme consisting of stimulus control, problem-solving, assertion, goal setting and cognitive techniques; participants advised to monitor energy intake to between 1200–1500 kcal/day with a reduction in fat intake and simple carbohydrate and increase in fibre; stepwise goals for walking with final goal to expend 100 kcal/week; deposit refunded according to weight loss and attendance. Spouse participated in all aspects of programme and no distinction made in treatment between participant and spouse, half of therapy sessions focused on social support and behavioural marital therapy literature, e.g. mutual positive reinforcement

Control	*All participants received behavioural weight loss programme consisting of stimulus control, problem-solving, assertion, goal setting and cognitive techniques; participants advised to monitor energy intake to between 1200–1500 kcal/day with a reduction in fat intake and simple carbohydrate and increase in fibre; stepwise goals for walking with final goal to expend 100 kcal/week; deposit refunded according to weight loss and attendance.*
Length of follow-up	72 weeks
Results	*At 5 months (20 weeks), mean weight change (SD) was –8.66 (5.08) kg in the active spouse group compared with –9.03 (8.26) kg in the individual group. Mean weight change in the family group compared with the individual group was 0.37 (95% CI –3.67 to 4.41).* At 18 months (72 weeks), mean weight change (SD) was –3.18 (5.31) kg in the active spouse group compared with –5.26 (10.39) kg in the individual group. Mean weight change in the family group compared with the individual group was 2.08 (95% CI –2.76 to 6.92).
Quality and comments	Blinded assessment not done. ITT analysis possibly done. Random allocation but no description of concealment.

Other outcomes

Cousins 1992 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Black 1984 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Murphy 1982 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Pearce 1981 (in HTA) RCT	
Results	*There was no difference in the daily energy intake or compliance scores between the two groups.*
Quality and comments	Daily records of energy intake and self-reported compliance scores.

Rosenthal 1980 (in HTA) RCT	
Results	*Some outcomes related to the perceptions of the wives and the husbands were reported. These consistently showed that involving husbands in the treatment of women who were overweight enhanced weight loss, but that this effect may not be maintained over time.*
Quality and comments	…

Wing 1999 (in HTA) RCT	
Results	*There was a better attendance for people recruited with friends compared with the other group at 16 months (*p*<0.008).*
Quality and comments	…

Wing 1991b (in HTA) RCT	
Results	*At 20 weeks, mean (SD) %HbA_{1c} change was –1.20 (1.90) in the family group, and –2.10 (2.10) in the individual group. Mean %HbA_{1c} change in the family group compared with the individual group was 0.90 (95% CI –0.30 to 2.10).* At 72 weeks, mean (SD) %HbA_{1c} change was –0.10 (1.90) in the family group, and –0.70 (2.70) in the individual group. Mean %HbA_{1c} change in the family group compared with the individual group was 0.60 (95% CI –0.78 to 1.98). *At 20 weeks, mean (SD) FPG change in mmol/l was –2.78 (2.89) in the family group, and –3.56 (4.61) in the individual group. Mean FPG change in the family group compared with the individual group was 0.78 (95% CI –1.49 to 3.05).* At 72 weeks, mean (SD) FPG change in mmol/l was –0.61 (3.39) in the family group, and –2.00 (4.72) in the individual group. Mean FPG change in the family group compared with the individual group was 1.39 (95% CI –1.04 to 3.82). *Participants in both groups consumed significantly less energy over time, but those in the individual group had a significant greater decrease than those in the spouse group. Other outcomes such as % energy from fat, improved in both groups but were not significantly different between groups.* *There was a significant interaction of gender and treatment, such that women did better when treated with a spouse and men did better when treated individually.*
Quality and comments	Intake and exercise data were self-reported.

Reported harms

Cousins 1992 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Black 1984 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Murphy 1982 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Pearce 1981 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Rosenthal 1980 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wing 1999 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wing 1991b (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Cousins 1992 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if Mexican American women, married?, aged 18–45 years, 20–100% above IBW.* *Excluded if hypertension (DBP ≥115 mmHg), diabetes (fasting plasma glucose ≥140 mg/dl), chronic illness with diet or exercise recommendations different from those in the study.*
Recruitment	Media promotion, personal contacts in the local community (mainly churches and health agencies).
Intervention (mode and intensity)	12 months, contacted 37 times (baseline then weekly group sessions for initial 24 weeks then 6 monthly sessions up to month 12)
Control (mode and intensity)	*Unclear but presumed contacted only at baseline and at 12 months*
Delivery of intervention/control (who)	Classes taught by bilingual registered dietitians.
Dropout rates	49% overall at 12 months.
Treatment of dropouts (return to baseline, or last measurement?)	*Data for completers only.*

Black 1984 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if married women, 10% or greater overweight, husband signed statement if requested to attend, $11 deposit refunded on attendance.* *Excluded if physiological or medical problems that would inhibit weight loss.*
Recruitment	Advertisements in community and university newspaper. Referrals from colleagues.
Intervention (mode and intensity)	10 weeks with follow-up to 4 years, contacted 14 times (90 min introductory baseline visit then 10 weekly visits of 30–90 min duration then at 1, 3 and 4 years post-treatment (218 weeks in total)
Control (mode and intensity)	*As for spouse involvement.*
Delivery of intervention/control (who)	Counsellor was a doctoral candidate in clinical psychology (study author).
Dropout rates	*8% in active group, 17% in passive group, and 8% in individual group at 62 weeks.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Murphy 1982 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	Included married couples, 20–80% above IBW (US Department of Agriculture 1969), spouse willing to attend all treatment sessions, no contra-indications for restricting intake or increasing exercise (decided by physician). No details of exclusions.
Recruitment	Newspaper and radio advertisements, then personal interview.
Intervention (mode and intensity)	*All intervention groups. 10 weeks with follow-up to 4 years post-treatment, contacted 21 times (baseline then 11 × 1.5 h sessions in first 10 weeks then at 12, 15, 18, 22, 29 and 36 weeks, 1 year, 2 years and 4 years post-treatment)*
Control (mode and intensity)	10 weeks, contacted 12 times (baseline then 11 × 1.5 h sessions in first 10 weeks)

Delivery of intervention/control (who)	No details.
Dropout rates	*63% ind-1 party, 53% ind-2 party, 64% family-1 party, 50% family-2 party, 60% supportive at 4 years.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Pearce 1981 (in HTA) RCT	
Country and setting	Canada. No further details.
Participants (included/excluded)	Included if women, aged 20–60 years, 9 kg or 20% overweight or more (Metropolitan Life Insurance tables), doctors permission, $50 deposit refunded on attendance of nine out of ten sessions and three follow-ups. Excluded if involvement in another weight control programme or psychotherapy, obesity related morbidity such as diabetes, thyroid problems, colitis, ulcers; taking medication which affected waters retention, appetite, metabolism; pregnant or planning pregnancy, unwilling to commit for 15 months or unwilling to pay $50 deposit, husbands unwilling to participate.
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*12 months, contacted 14 times (baseline then weekly for initial 10 weeks then at 3, 6 and 12 months)*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	One male and one female graduate students in clinical psychology (neither of whom were obese) delivered the therapy. The male therapist was experienced (minimum 2 years with experience of BT for weight loss) compared with the female therapist who had just begun her graduate training and had no experience of delivering BT for weight loss. The therapists were trained before delivering the intervention to ensure uniformity of delivery. Also, therapists met each week to provide continued uniformity and resolve any differences or difficulties.
Dropout rates	*14% in the active group, and 8% in the individual group at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R. Results for completers only?

Rosenthal 1980 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	Included if women, ≥10% above IBW (Metropolitan Life Insurance tables 1970), husband and wife both willing to attend meetings every 2 weeks, willing to comply with demands of the weight loss programme, $10 commitment deposit (returned at first follow-up visit), signed medical release form certifying good health, signed form stating will not participate in concurrent obesity therapy. Exclusion criteria not stated.
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*16 weeks active treatment, contacted 11 times (baseline then eight × 75 min group sessions twice monthly, follow-up at 6 weeks post-treatment and 3 years post-treatment)*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Sessions were conducted by two female therapists – no further details.
Dropout rates	*53% overall at 3 years post-treatment.*

Treatment of dropouts (return to baseline, or last measurement?)	N/R – completers only?

Wing 1999 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	Included if aged 25–55 years, 6.8–31.8 kg above IBW, generally good health. Exclusion criteria: not stated
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*16 weeks with follow-up at 16 months, contacted 18 times (baseline then weekly for initial 16 weeks then at 16 months).*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Meetings were led by a behaviour therapist, a nutritionist, or both.
Dropout rates	*46% overall at 16 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Dropouts assumed to return to baseline weight.

Wing 1991b (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	Included if aged 30–65 years, 20 % or more over IBW, FRG ≥140 mg/dl or ≥200 mg d/l at 2 h after oral glucose load and one other value 200mg/dl or more; spouses 15% or more above IBW and 30–70 years; $150 deposit per couple. Exclusion criteria: not stated
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*72 weeks, contacted 21 times (baseline then weekly for first 12 weeks then at weeks 14, 16, 18, 20, 24, 28, 40 and 72)*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	The programme was conducted by a multi-disciplinary team – no details.
Dropout rates	*17% in the spouse group, 23% individual group at 72 weeks.*
Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

1.4.5 Group vs individual treatment

Weight loss

Hakala 1993 (in HTA) RCT	
Aim	To compare group and individual weight reduction programmes in the treatment of severe obesity
Participants	People who were severely overweight (at least 50% overweight according to the Finnish Social Insurance Institution. *60 total – 40 F, 20 M. Mean (SD) age 41 (8) years overall. Mean (SD) BMI (kg/m^2) 43 (5) overall. Thirty allocated to group and 30 to individual counselling arms.*

Intervention	Vitamin supplements recommended if weight loss >10 kg in first 3 months. Group: 2 week inpatient intensive group counselling treatment in groups of 10, consisting of 15 h of nutrition counselling, behaviour modification, 15 h physical activation and training, 12 h occupational therapy and 1 h individual nutrition counselling; also included a lecture and examination by a physician; participants provided with 1200 kcal/day diet of four low fat low sugar meals per day; nutrition education based on a mixed diet, group sessions after initial 2 weeks consisted of weight, group discussion, advice and motivation; participants also given individual appointments with physician and 4 month intervals.
Control	*Vitamin supplements recommended if weight loss >10 kg in first 3 months.* *Individual: counselling consisting of 20 min individual visits with same physician monthly for first 6 months, advised on weight reduction with 1200 kcal/day diet and physical activity, information given systematically in small portions, participants received information leaflets, counselling paid attention to personal characteristics, family relationships and working situation; after 6 months the sessions concentrated on follow-up of body weight changes and health status until end of year 2.*
Length of follow-up	5 years
Results	*Shorter terms results reported by gender only.* At 12 months, mean weight change (SD) was –14.80 (8.90) kg in the group arm compared with –17.00 (10.30) kg in the individual group. Mean weight change in the group arm compared with the individual group was 2.20 (95% CI –2.77 to 7.17). At 24 months, mean weight change (SD) was –4.20 (9.70) kg in the group arm compared with –12.30 (12.90) kg in the individual group. Mean weight change in the group arm compared with the individual group was 8.10 (95% CI 2.19 to 14.01). At 60 months, mean weight change (SD) was –2.40 (12.00) kg in the group arm compared with –6.80 (16.70) kg in the individual group. Mean weight change in the group arm compared with the individual group was 4.40 (95% CI –3.51 to 12.31).
Quality and comments	Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment. Author provided weight outcomes by group (reported by gender in paper). *Self reported weights, with some validation at 60 months.*

Jones 1986 (in HTA) RCT	
Aim	To evaluate the effect of introducing self-monitoring, cue avoidance and group treatment in a conventional NHS weight reduction clinic with no additional resources or staff training.
Participants	Women referred to a secondary care clinic who were judged as suitable by the responsible dietitian. *160 total – all women. Mean (SD) age 50.3 (13.5) years overall. Mean (SD) BMI (kg/m^2) 35.1 (9.2) overall. 17 allocated to group sessions and 21 to individual sessions.*
Intervention	All participants received individualised dietary advice at first session, recommended 1000 kcal/day below energy requirements but not less than 1000 kcal/day; (treatment was extended beyond 17 weeks if further involvement thought to be warranted). Group: four group treatment sessions in small groups of 5–7 for 60 min each
Control	*All participants received individualised dietary advice at first session, recommended 1000 kcal/day below energy requirements but not less than 1000 kcal/day; (treatment was extended beyond 17 weeks if further involvement thought to be warranted).* *Individual: participants seen individually for 10 min each session*
Length of follow-up	*68 weeks*

Results	*At 16 weeks, mean weight change (SD) was –3.95 (3.67) kg in the group arm compared with –4.79 (2.81) kg in the individual group. Mean weight change in the group arm compared with the individual group was 0.84 (95% CI –2.18 to 3.86).* At 18 months, mean weight change (SD) was –2.33 (5.06) kg in the group arm compared with –3.07 (5.34) kg in the individual group. Mean weight change in the group arm compared with the individual group was 0.74 (95% CI –4.21 to 5.69).
Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Only used four (in total) of the eight intervention arms. *Other arms described in relevant sections/reviews.*

Long 1983 (in HTA) RCT	
Aim	To assess the effectiveness of combining behaviour modification with dietetic counselling in a hospital out-patient clinic.
Participants	Women who were overweight (BMI >25 kg/m^2) who were referred to an outpatient obesity clinic. *36 total – all women. Mean (range) age 36.8 (18 to 56) overall. Mean (range) BMI (kg/m^2) 33.5 (28.9 to 49.4) overall. Twelve each allocated to group or individual sessions.*
Intervention	All participants received same advice regarding obesity, health, nutrition and weight reduction, told successful weight loss depended on reducing energy intake and/or increasing physical activity. Group: 12 × 1 h group sessions plus four brief 30 min weigh-in sessions during initial 16 weeks; diet advice same as Individual group and also fostered high expectation of weight loss based on group support. Only average group weight loss reported to group not individual weights.
Control	*All participants received same advice regarding obesity, health, nutrition and weight reduction, told successful weight loss depended on reducing energy intake and/or increasing physical activity.* *Individual: advised regarding high-fibre diet tailored to give 1000–1200 kcal/day, seen individually by dietitian for 45 min initially then 15 × 15 minute sessions during initial 16 weeks, advised on weight reducing diets, nutrition, commercial slimming foods, seasonal topics and weight maintenance*
Length of follow-up	*68 weeks*
Results	*At 16 weeks, mean weight change (SD) was –4.60 (7.22) kg in the group arm compared with –8.30 (8.26) kg in the individual group. Mean weight change in the group arm compared with the individual group was3.70 (95% CI –3.57 to 10.97).* At 18 months (68 weeks), mean weight change (SD) was –0.90 (6.17) kg in the group arm compared with –8.10 (8.21) kg in the individual group. Mean weight change in the group arm compared with the individual group was 7.20 (95% CI –0.41 to 14.81).
Quality and comments	*Slight difference to HTA due to calculations.* Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Only used four (in total) of the eight intervention arms. Median weight change assumed to be similar to mean. SDs calculated.

Straw 1983 (in HTA) RCT	
Aim	To assess the efficacy of individualised behavioural obesity treatment and maintenance procedures.
Participants	Women who were overweight (≥35% body weight as fat). *45 total – all women. Mean age 39.99 (data completers only). Mean (SD) weight 85.16 (13.97) kg group arm (*n=*18), 86.73 (16.52) kg individual (*n=*15).*

Intervention	Participants required to purchase Ferguson's book *Learning to Eat* and to complete all assignments in it; topics included self-monitoring, stimulus control, eating style, problem-solving, activity management and social support. Participants seen in groups of 8–10. Also further randomised (at 10 weeks) to weight check each month where received encouragement or to individual problem-solving where topic determined by participant and discussed for 30 min twice a month then monthly to month 12.
Control	*Participants required to purchase Ferguson's book* Learning to Eat *and to complete all assignments in it; topics included self-monitoring, stimulus control, eating style, problem-solving, activity management and social support.* *Participants seen individually.* *Also further randomised (at 10 weeks) to weight check each month where received encouragement or to individual problem-solving where topic determined by participant and discussed for 30 min twice a month then monthly to month 12.*
Length of follow-up	12 months
Results	Weigh-in maintenance: At 10 weeks, mean weight change (SD) was –3.68 (2.90) kg in the group arm compared with –3.83 (3.14) kg in the individual group. Mean weight change in the group arm compared with the individual group was 0.15 (95% CI –2.74 to 3.04). Individual problem-solving maintenance: At 10 weeks, mean weight change (SD) was –2.59 (3.59) kg in the group arm compared with –4.76 (3.35) kg in the individual group. Mean weight change in the group arm compared with the individual group was 2.17 (95% CI –1.96 to 6.30). Weigh-in maintenance: At 12 months, mean weight change (SD) was –3.98 (7.04) kg in the group arm compared with 1.69 (6.39) kg in the individual group. Mean weight change in the group arm compared with the individual group was –5.67 (95% CI –13.28 to 1.94). Individual problem-solving maintenance: At 12 months, mean weight change (SD) was –4.99 (7.33) kg in the group arm compared with –6.94 (7.88) kg in the individual group. Mean weight change in the group arm compared with the individual group was 1.95 (95% CI –7.48 to 11.38).
Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Mean change in weight calculated from change at week 10 plus change during weeks 11–52, SDs calculated, not all groups used in comparisons. Straw 1983a – weigh-in maintenance; Straw 1983b – individual problem-solving maintenance. *Have used Treatment values from Table 3 as 10-week outcomes?*

Other outcomes

Hakala 1993 (in HTA) RCT

Results

Mean participation rates in the group sessions (GRP) were 69% in the first 12 month follow-up period compared with 86% of appointments being kept in the individual group (IND), and 29% and 69% respectively in the second year.

	Increase or no change (%)	1–10 kg loss (%)	11–20 kg loss (%)	21–30 kg loss (%)	>30 kg loss (%)
3 months GRP (*n*=30)	0	12	78	10	0
3 months IND (*n*=28)	7	33	52	8	0
24 months GRP (*n*=30)	30	45	18	7	0
24 months IND	13	21	40	18	8

	(*n*=28)				
	60 months GRP (*n*=28)	43	33	17	7	0
	60 months IND (*n*=25)	37	37	12	12	2
Quality and comments	…					

Jones 1986 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Long 1983 (in HTA) RCT

Results

	>6.4 kg loss (%)	**>7.25 kg loss (%)**	**>10.88 kg loss (%)**
16 weeks GRP (*n*=10)	30	20	10
16 weeks IND (*n*=8)	75	50	25
68 weeks GRP (*n*=7)	14	14	14
68 weeks IND (*n*=7)	57	57	28

Quality and comments …

Straw 1983 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Reported harms

Hakala 1993 (in HTA) RCT	
Harms	None reported.
Quality and comments	

Jones 1986 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Long 1983 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Straw 1983 (in HTA) RCT	
Harms	Two women were seriously ill with cancer and dropped out. Group status was unclear.
Quality and comments	…

Generalisability

Hakala 1993 (in HTA) RCT	
Country and setting	Finland. Group intervention included a 2 week inpatient treatment period at the Rehabilitation Research Centre. Individual counselling assumed to be office-based but no details of setting.
Participants (included/excluded)	*Included if aged 22–54 years, >50% overweight (Finnish Adult Population 1980), no serious cardiovascular, metabolic or psychiatric disease.* *Excluded if presence of schizophrenia, hypothyroidism, cardiac failure*
Recruitment	Advertisements in local newspaper. The most overweight respondents were invited to participate (*n*=70).
Intervention (mode and intensity)	2 years, contacted 42 times (initial 2-week inpatient stay then weekly for 6 weeks, every other week for 10 months then once a month in year 2 then at 5 years)
Control (mode and intensity)	*2 years, contacted 17 times (baseline, once a month in year 1 and every 4 months in year 2 then at 5 years)*
Delivery of intervention/control (who)	Inpatient programme included nutrition counselling by a nutritionist, and a lecture and examination by a physician. Group sessions were conducted in turn by a nutritionist, a physiotherapist, and an occupational therapist. Individual appointments with a physician also. Individual group had appointments with the same physician throughout. The physician advised on weight reduction using diet and delivered counselling and information (using leaflets).
Dropout rates	0% group and 7% individual at 12 months, 7% group and 17% individual at 5 years.
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Jones 1986 (in HTA) RCT	
Country and setting	UK. NHS outpatient weight reduction clinic (secondary care).
Participants (included/excluded)	*Included if women, aged 18 years or older, judged as suitable by dietitian.* *Excluded if diabetes, pregnancy*
Recruitment	Consecutive referrals to a district dietetic service from medical practitioners.
Intervention (mode and intensity)	17 weeks with follow-up 12 months later (69 weeks in total) contacted 7 times (baseline then week 1 then 4 more sessions at 4 week intervals then 12 months post-treatment)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Four dietitians, experienced in the dietary treatment of obesity but not behaviour therapy, carried out all the treatments. No additional resources or training were given.
Dropout rates	64% overall at 69 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

Long 1983 (in HTA) RCT	
Country and setting	UK. Outpatient clinic.

Participants (included/excluded)	*Included women, aged 18–60 years, BMI >25 kg/m^2* *Excluded if expectant mothers, diabetes, pre-operative patients, begun weight loss as inpatients, recent dramatic weight reduction.* *Fourteen indicated onset of weight gain in childhood or adolescence, and 15 attributed the weight gain to pregnancy. All had attempted at least one formal weight control method in addition to unsupervised dieting (Weight Watchers mentioned most frequently). Twenty-five reported having at least one overweight parent.*
Recruitment	Consecutive referrals deemed 'suitable' by the responsible dietitian.
Intervention (mode and intensity)	16 weeks with follow-up to 1 year post-treatment, contacted 20 times (baseline then weekly for 16 weeks then at 3, 6 and 12 months post-treatment)
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	Four qualified dietitians and one clinical psychologist served as therapists. No therapist had extensive experience of group therapy. Groups were run by a male/female therapist team, whilst individuals were seen by a female dietitian.
Dropout rates	42% in both groups at 68 weeks
Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

Straw 1983 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included women, 35% or more of body weight as fat (skinfold thickness calliper)* *Excluded if serious physical or emotional problems, problems which required a special diet such as diabetes or hypoglycaemia, severely limited physical activity, endocrine disorder, Beck Depression Inventory score of ≥20, schedule did not allow random assignment*
Recruitment	Newspaper announcements.
Intervention (mode and intensity)	In treatment phase, 10 weeks, contacted 11 times (baseline then 1 h weekly for 10 weeks) Weigh-in maintenance: contacted 9 times (monthly from week 11 to 12 months) IPS: 42 weeks, contacted 12 times (30 min twice monthly from week 11 for 3 months then monthly to 12 months)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	All treatments administered by clinical psychology students under supervision (first author).
Dropout rates	18% overall at 12 months
Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

1.4.6 Different levels of intensity of behaviour therapy and diet

Weight loss

Melin 2003 RCT	
Aim	To compare two group treatment programmes for people who were obese.
Participants	People who were obese (attending an obesity clinic – no cut-off defined). Total 43 – 39 F, 4 M. Mean (SD) age 40.7 years intervention group (*n*=22), 39.4 years standard group (*n*=21).
Intervention	*Intensive BT: continuous intensive treatment (self-monitoring, relapse situations, eating behaviour) with planned group meetings. Possibility to repeat self-monitoring, and obtain more information and education on nutrition, food habits and strategies to control eating behaviour.* *Diet: VLED 25 days total, 3 days over which reduced energy from 800 kcal to 200 kcal/day (liquid every 2 h – water, herbal tea, fruit/vegetable juice) for 19 days, then increased to 800 kcal/day over 3 days. Alternating with 600 kcal/day deficit diet.*
Comparison	Standard BT: as above, but met less often, had less contact, fewer repetitions of self-monitoring and less counselling. Diet: as above
Length of follow-up	*48 months*
Results	*At 3 months, mean weight change (SD) was –8.30 (2.64) kg in the intensive group compared with –10.00 (2.75) kg in the standard group. Mean weight change in the intensive group compared with the standard group was 1.70 (95% CI –0.17 to 3.57).* *At 6 months, mean weight change (SD) was –10.60 (2.64) kg in the intensive group compared with –12.30 (2.75) kg in the standard group. Mean weight change in the intensive group compared with the standard group was 1.70 (95% CI –0.17 to 3.57).* *At 12 months, mean weight change (SD) was –7.58 (4.04) kg in the intensive group compared with –6.40 (4.49) kg in the standard group. Mean weight change in the intensive group compared with the standard group was –1.18 (95% CI –4.16 to 1.80).* *At 24 months, mean weight change (SD) was –6.80 (5.77) kg in the intensive group compared with –8.60 (6.20) kg in the standard group. Mean weight change in the intensive group compared with the standard group was 1.80 (95% CI –2.37 to 5.97).* *No significant difference was seen for weight loss between high and low attenders.*
Quality and comments	*Calculated SDs from SEMs. Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Results for completers only.*

Other outcomes

Melin 2003 RCT	
Results	*At 3 months, mean (SD) FPG change in mmol/l was –0.35 (1.44) in the intensive group, and –0.90 (1.51) in the standard group. Mean FPG change in the intensive group compared with standard was 0.55 (95% CI –0.48 to 1.58).* *At 6 months, mean (SD) FPG change in mmol/l was –0.20 (0.87) in the intensive group, and –0.60 (0.93) in the standard group. Mean FPG change in the intensive group compared with standard was 0.40 (95% CI –0.23 to 1.03).* *At 12 months, mean (SD) FPG change in mmol/l was –0.20 (1.15) in the intensive group, and –0.90 (1.32) in the standard group. Mean FPG change in the intensive group compared with standard was 0.70 (95% CI –0.16 to 1.56).*

	At 24 months, mean (SD) FPG change in mmol/l was 0.08 (0.99) in the intensive group, and –0.50 (1.01) in the standard group. Mean FPG change in the intensive group compared with standard was 0.58 (95% CI –0.11 to 1.27). *At 3 months, mean (SD) SBP change in mmHg was –6.90 (27.42) in the intensive group, and -2.40 (37.88) in the standard group. Mean SBP change in the intensive group compared with standard was –4.50 (95% CI –27.68 to 18.68).* *At 6 months, mean (SD) SBP change in mmHg was –8.10 (10.72) in the intensive group, and –2.10 (11.23) in the standard group. Mean SBP change in the intensive group compared with standard was –6.00 (95% CI –13.63 to 1.63).* *At 12 months, mean (SD) SBP change in mmHg was –5.00 (12.37) in the intensive group, and –0.40 (13.94) in the standard group. Mean SBP change in the intensive group compared with standard was –4.60 (95% CI –13.78 to 4.58).* *At 24 months, mean (SD) SBP change in mmHg was –9.80 (17.11) in the intensive group, and 2.20 (15.10) in the standard group. Mean SBP change in the intensive group compared with standard was –12.00 (95% CI –23.16 to –0.84).* *At 3 months, mean (SD) DBP change in mmHg was –3.50 (13.19) in the intensive group, and –7.20 (18.20) in the standard group. Mean DBP change in the intensive group compared with standard was 3.70 (95% CI –7.44 to 14.84).* *At 6 months, mean (SD) DBP change in mmHg was –5.20 (8.04) in the intensive group, and –5.00 (8.40) in the standard group. Mean DBP change in the intensive group compared with standard was –0.20 (95% CI –5.92 to 5.52).* *At 12 months, mean (SD) DBP change in mmHg was –2.40 (8.25) in the intensive group, and –3.30 (8.91) in the standard group. Mean DBP change in the intensive group compared with standard was 0.90 (95% CI –5.08 to 6.88).* *At 24 months, mean (SD) DBP change in mmHg was –6.60 (8.25) in the intensive group, and 1.30 (8.44) in the standard group. Mean DBP change in the intensive group compared with standard was –7.90 (95% CI –13.70 to –2.10).*
Quality and comments	Only DBP at 24months noted as significantly different in published paper.

Harms

Melin 2003 RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Melin 2003 RCT	
Country and setting	Sweden. Secondary care obesity clinic.
Participants (included/excluded)	N/R, other than patients referred to the obesity clinic.
Recruitment	Referrals
Randomisation	N/R
Intervention (mode and intensity)	*Meetings every 2 weeks for 12 months, then 6 meetings during second year. During VLED period, meetings twice per week.*
Duration of active intervention	24 months
Comparison (mode and intensity)	Meetings every 3 months for 24 months. During VLED period, meetings twice per week.
Delivery of intervention/comparison (who)	Dietitian and psychologist.
Dropout rates	*23% intervention group, 29% standard group at 24 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.4.7 Diet and behaviour therapy vs diet

Weight loss

Wadden 1989 (in HTA) RCT	
Aim	To compare the effectiveness of VLED alone, behaviour therapy alone, and VLED plus BT on weight control.
Participants	People who were overweight (≥25 kg above IBW from the Metropolitan Life Insurance tables) *76 total – all women (completers only – men excluded from analysis due to small numbers). Mean age (SE) 42.1 (1.1) years. Mean (SE) BMI (kg/m^2) 39.4 (0.8). Numbers allocated to each group unclear.*
Intervention (including details of diet)	1000–1200 kcal/day for month 1, months 2 + 3 400–500 kcal/day PSMF consisting of three servings of lean meat, fish or fowl and to avoid all other food with the exception of non-energy beverages and bouillon, requested to drink at least 1.5 l water per day, daily supplements 3 g each of potassium, sodium chloride and 800 mg calcium; month 4 refeeding to conventional foods, firstly fruit and vegetables then bread and cereal then fats. In addition months 5 + 6 prescribed 1000–1200 kcal/day diet, extensive training in behaviour therapy throughout (taught traditional behavioural methods of weight control which included recording eating behaviour, controlling stimuli related to eating, slowing rate of consumption, increasing lifestyle activity, nutrition education, modifying self-defeating thoughts and emotions, social support, reinforcing changes in eating and exercise behaviour;); months 4, 5 + 6 addressed weight maintenance and included relapse prevention training and strategies for handling weight regain. Also encouraged to increase physical activity by walking and using the stairs; diet records kept throughout active treatment; paid $10 for each visit and deposited $40 which was refunded after the 1-year follow-up visit.
Control	*1000–1200 kcal/day for month 1, months 2 + 3 400–500 kcal/day PSMF consisting of three servings of lean meat, fish or fowl and to avoid all other food with the exception of non-energy beverages and bouillon, requested to drink at least 1.5 litre of water per day, daily supplements 3 g each of potassium, sodium chloride and 800 mg calcium; month 4 refeeding to conventional foods, firstly fruit and vegetables then bread and cereal then fats.* *Also encouraged to increase physical activity by walking and using the stairs; diet records kept throughout active treatment; paid $10 for each visit and deposited $40 which was refunded after the 1 year follow-up visit.*
Length of follow-up	64 to 66 months
Results	*At 6 months, mean (SD) weight change in kg was –16.80 (6.68) in the diet and BT group, and –13.10 (4.80) in the diet group. Mean weight change in the diet and BT group compared with diet was –3.70 (95% CI –6.76 to –0.64).* At 12 months, mean (SD) weight change in kg was –12.89 (8.91) in the diet and BT group, and –4.70 (7.31) in the diet group. Mean weight change in the diet and BT group compared with diet was –8.19 (95% CI –13.64 to –2.74). At 36 months, mean (SD) weight change in kg was –5.11 (8.28) in the diet and BT group, and –2.20 (8.50) in the diet group. Mean weight change in the diet and BT group compared with diet was –2.91 (95% CI –8.60 to 2.78). At 60 months, mean (SD) weight change in kg was 2.90 (11.26) in the diet and BT group, and 1.00 (6.79) in the diet group. Mean weight change in the diet and BT group compared with diet was 1.90 (95% CI –3.75 to 7.55). *At the end of the active treatment (6 months), 96.8% of the diet and BT group and 95.6% of the diet group had lost 5kg or more, and 90.3% and 73.9% respectively had lost 10 kg or more.* *At 12 months, 72.0% of the diet and BT group and 52.4% of the diet group had lost 5 kg or more, and 52.0% and 14.3% respectively had lost 10 kg or more.* *At 60 months, 27.3% of the diet and BT group and 11.1% of the diet group had lost 5 kg or more, and 9.1% and 11.1% respectively had lost 10 kg or more.*

Quality and comments	Two cohorts differed significantly in age at baseline (43.9. vs 39.5 years). 2 kg added to all self-reported weights, 3 and 5 year weight outcomes recalculated for participants who had additional weight loss treatment in years 1–5 post-treatment, self-reported weight at time of seeking additional therapy was subtracted from pre-treatment weights, significant difference in whole sample from uncorrected changes (p<0.002 at 3 years, p<0.005 at 5 years post-treatment). Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. *More than 90% of participants reported a chronic history of obesity and multiple cycles of weight loss and regain.*

Jones 1986 (in HTA) RCT	
Aim	To evaluate the effect of introducing self-monitoring, cue avoidance, and group treatment in a conventional NHS weight reduction clinic with no additional resources or staff training.
Participants	Women referred to a secondary care clinic who were judged as suitable by the responsible dietitian. *160 total – all women. Mean (SD) age 50.3 (13.5) years overall. Mean (SD) BMI (kg/m^2) 35.1 (9.2) overall. 17 allocated to group sessions and 21 to individual sessions.*
Intervention	All participants received individualised dietary advice at first session, recommended 1000 kcal/day below energy requirements but not less than 1000 kcal/day (treatment was extended beyond 17 weeks if further involvement thought to be warranted). Diet and BT (group Jones 1986c): participants received leaflet at each four sessions regarding cue avoidance and food management, seen in group format. The recommendations and their implementation were discussed during visits with the dietitian. Diet and BT (individual Jones 1986d): participants received leaflet at each four sessions regarding cue avoidance and food management, seen individually. The recommendations and their implementation were discussed during visits with the dietitian.
Control	*All participants received individualised dietary advice at first session, recommended 1000 kcal/day below energy requirements but not less than 1000 kcal/day; (treatment was extended beyond 17 weeks if further involvement thought to be warranted).* *Four group treatment sessions in small groups of 5–7 for 60 min each or participants seen individually for 10 min each session.*
Length of follow-up	*68 weeks*
Results	*Group: At 16 weeks, mean weight change (SD) was –8.74 (2.35) kg in the diet and BT arm compared with –3.95 (3.67) kg in the diet group. Mean weight change in the diet and BT arm compared with the diet group was –4.79 (95% CI –7.75 to –1.83).* Group: At 12 months, mean weight change (SD) was –7.79 (5.21) kg in the diet and BT arm compared with –2.33 (5.06) kg in the diet group. Mean weight change in the diet and BT arm compared with the diet group was –5.46 (95% CI –10.67 to –0.25). *Individual: At 16 weeks, mean weight change (SD) was –4.52 (3.66) kg in the diet and BT arm compared with –4.79 (2.81) kg in the diet group. Mean weight change in the diet and BT arm compared with the diet group was 0.27 (95% CI –2.74 to 3.28).* Individual: At 12 months, mean weight change (SD) was –5.06 (7.91) kg in the diet and BT arm compared with –3.07 (5.34) kg in the diet group. Mean weight change in the diet and BT arm compared with the diet group was –4.18 (95% CI –8.32 to –0.04).

Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Only used four (in total) of the eight intervention arms. *Other arms described in relevant sections/reviews.*

Long 1983 (in HTA) RCT	
Aim	To assess the effectiveness of combining behaviour modification with dietetic counselling in a hospital outpatient clinic.
Participants	Women who were overweight (BMI >25 kg/m^2) who were referred to an outpatient obesity clinic. *36 total – all women. Mean (range) age 36.8 (18 to 56) overall. Mean (range) BMI (kg/m^2) 33.5 (28.9 to 49.4) overall. Twelve each allocated to group or individual sessions.*
Intervention	All participants received same advice regarding obesity, health, nutrition and weight reduction, told successful weight loss depended on reducing energy intake and/or increasing physical activity. Twelve × 90 min sessions held weekly for first 16 weeks with dietitian and clinical psychologist plus four brief weigh in sessions; first 15–20 min of each group session participants given same diet advice as other group; participants discussed application of behavioural strategies based on learning principles following each of 12 didactic sessions including self-monitoring, stimulus control, slowing rate of eating, generating social support, exercise, dietary planning, pre-planning, individual problem-solving, assertiveness and cognitive restructuring. Only average group weight loss reported to group not individual weights.
Control	*All participants received same advice regarding obesity, health, nutrition and weight reduction, told successful weight loss depended on reducing energy intake and/or increasing physical activity.* *Twelve × 1 h group sessions plus four brief 30 min weigh in sessions during initial 16 weeks; diet advice same as Individual group and also fostered high expectation of weight loss based on group support. Only average group weight loss reported to group not individual weights.*
Length of follow-up	*68 weeks*
Results	*At 16 weeks, mean weight change (SD) was –6.90 (7.87) kg in the diet and BT arm compared with –4.60 (7.22) kg in the diet group. Mean weight change in the diet and BT arm compared with the diet group was –2.30 (95% CI –8.92 to 4.32).* At 12 months, mean weight change (SD) was –7.70 (8.09) kg in the diet and BT arm compared with –0.90 (6.17) kg in the diet group. Mean weight change in the diet and BT arm compared with the diet group was –6.80 (95% CI –13.79 to 0.19).
Quality and comments	*Slight difference to HTA due to calculations.* Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. Only used four (in total) of the eight intervention arms. Median weight change assumed to be similar to mean. SDs calculated.

Other outcomes

Wadden 1989 (in HTA) RCT	
Results	*No other outcomes reported.*
Quality and comments	…

Jones 1986 (in HTA) RCT	
Results	*None reported.*
Quality and comments	…

Long 1983 (in HTA) RCT				
Results		**>6.4 kg loss (%)**	**>7.25 kg loss (%)**	**>10.88 kg loss (%)**
	16 weeks diet+BT (*n*=10)	70	50	10
	16 weeks D (n=10)	30	20	10
	68 weeks diet+BT (*n*=9)	55	55	33
	68 weeks diet only (*n*=7)	14	14	14
Quality and comments	…			

Reported harms

Wadden 1989 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Jones 1986 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Long 1983 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Wadden 1989 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	*Included if ≥25 kg above IBW (Metropolitan Life Insurance tables). Excluded if recent MI or evidence of cardiac abnormalities; history of cerebrovascular, kidney or liver disease; cancer, type 1 diabetes, severe psychiatric illness, pregnancy, contraindications to treatment by VLED (assessed at screening), participants agreed not to participate in additional weight loss treatment before follow-up at 1 year post-treatment.*
Recruitment	N/R
Intervention (mode and intensity)	25 weeks, contacted 39 times (90 min each week for 25 weeks then 11 post-treatment visits every other week for first 2 months then once a month for next 4 months then every other month for last 6 months, 3 years and 5 years post-treatment)
Control (mode and intensity)	*16 weeks, contacted 25 times (90minutes each week for 16 weeks then months 1, 2, 3, 6, 9 and 12 post-treatment, 3 years and 5 years post-treatment).*
Delivery of intervention/control (who)	All participants were treated by doctoral level clinical psychologists.
Dropout rates	Unclear, but 68/76 were assessed at 12 months, 50/76 at 36 months and 55/76 at 60 months.

Treatment of dropouts (return to baseline, or last measurement?)	Data for completers only.

Jones 1986 (in HTA) RCT	
Country and setting	UK. NHS outpatient weight reduction clinic (secondary care).
Participants (included/excluded)	*Included if women, aged ≥18 years, judged as suitable by dietitian. Excluded if diabetes, pregnancy*
Recruitment	Consecutive referrals to a district dietetic service from medical practitioners.
Intervention (mode and intensity)	17 weeks with follow-up 12 months later (69 weeks in total) contacted 7 times (baseline then week 1 then 4 more sessions at 4 week intervals then 12 months post-treatment)
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Four dietitians, experienced in the dietary treatment of obesity but not behaviour therapy, carried out all the treatments. No additional resources or training were given.
Dropout rates	64% overall at 69 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

Long 1983 (in HTA) RCT	
Country and setting	UK. Outpatient clinic.
Participants (included/excluded)	*Included women, aged 18–60 years, BMI >25 kg/m^2* *Excluded if expectant mothers, diabetes, pre-operative patients, begun weight loss as inpatients, recent dramatic weight reduction.* *Fourteen indicated onset of weight gain in childhood or adolescence, and 15 attributed the weight gain to pregnancy. All had attempted at least one formal weight control method in addition to unsupervised dieting (Weight Watchers mentioned most frequently). Twenty-five reported having at least one overweight parent.*
Recruitment	Consecutive referrals deemed 'suitable' by the responsible dietitian.
Intervention (mode and intensity)	16 weeks with follow-up to 1 year post-treatment, contacted 20 times (baseline then weekly for 16 weeks then at 3, 6 and 12 months post-treatment)
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	Four qualified dietitians and one clinical psychologist served as therapists. No therapist had extensive experience of group therapy. Groups were run by a male/female therapist team, whilst individuals were seen by a female dietitian.
Dropout rates	25% in diet and BT, 42% in diet group at 68 weeks
Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

1.4.8 Comparison of different behavioural treatments

Weight loss

Perri 2001 RCT	
Aim	To compare extended programmes of relapse prevention or problem-solving with no contact (after completion of a 20 week BT programme).
Participants	Women who were obese (BMI 27–40 kg/m^2).
Intervention	*Initial BT programme: self-monitoring, goal setting, stimulus control* *Initial diet: 1200 kcal/day with low fat (<25% of energy intake)* *Initial activity: home-based walking for 30 min/day 5 days/week.* *Relapse prevention (RP): anticipating, avoiding, coping with lapses (including six sessions on problem-solving techniques)*
Comparison	As above for initial programme Problem-solving: used five-stage problem-solving method in group to solve individuals problems
Length of follow-up	*17 months*
Results	*At 5 months, mean (SD) weight change in kg was –8.41 (4.55) in the BT and RP group, and –9.28 (5.21) in the BT and problem-solving group (PS). Mean weight change in the BT and RP group compared with BT and PS was 0.87 (95% CI –2.05 to 3.79).* *At 11 months, mean (SD) weight change in kg was –9.11 (8.49) in the BT and relapse prevention group, and –11.33 (9.12) in the BT and PS group. Mean weight change in the BT and RP group compared with BT and PS was 2.22 (95% CI –3.05 to 7.49).* *At 17 months, mean (SD) weight change in kg was –5.85 (6.39) in the BT and RP group, and –10.82 (8.65) in the BT and PS group. Mean weight change in the BT and RP group compared with BT and PS was 4.97 (95% CI 0.46 to 9.48).*
Quality and comments	Blinded assessment not reported. ITT analysis done but not reported. Random allocation but no description of concealment. *Ten men were recruited, but results for women only – data excluded.* *Also control group (no contact). Results only reported for different extended therapies. Used HTS formula for weight change at 11 months. Results reported as NS between RP and PS but appears to be significant in analysis?*

Change	***RP* (n=22)**	***PS* (n=34)**
Lost ≥10%	*21.4%*	***35.3%***
Lost 5–9.9%	*21.4%*	***17.6%***
Lost 0–4.9%	*42.9%*	***38.2%***
Gained weight	***14.3%***	***8.8%***

Other outcomes

Perri 2001 RCT	
Results	*No other outcome reported.*
Quality and comments	RP and PS groups only.

Harms

Perri 2001 RCT	
Harms	None reported.
Quality and comments	

Generalisability

Perri 2001 RCT	
Country and setting	USA. Not clear.
Participants (included/excluded)	Included if BMI between 27 and 40 kg/m^2, aged 12 to 60 years and had physician approval. No exclusions reported.
Recruitment	Newspaper advertisements.
Randomisation	N/R
Intervention (mode and intensity)	*Initial programme: weekly 2 h sessions for 20 weeks.* *RP: 12 months of biweekly sessions.*
Duration of active intervention	17 months
Comparison (mode and intensity)	*Initial programme: weekly 2 h sessions for 20 weeks.* PS: 12 months of biweekly sessions.
Delivery of intervention/comparison (who)	Clinical psychology graduates for initial BT. Group leaders for RP and PS with experience in conducting BT for obesity.
Dropout rates	*15% for initial programme, then 29% RP and 34% PS at 17 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5 Physical activity interventions (alone or in combination with diet or behaviour therapy)

1.5.1 Physical activity vs control (no treatment)

Weight loss

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Aim	The primary aim of the trial was to compare the isolated and combined effects of the diet and exercise on the variables fibrinogen, fibrinolytic capacity, coagulation factor VII and platelet volume. Secondary aims were the effects on other coagulation and fibrinolytic components and activities; lipids and lipoproteins; fatty acids; glucose and insulin response to a glucose load; clinical, physiological and anthropometric variables; and quality of life
Participants	*Men and women aged 41 to 50 years who were overweight (BMI >24 kg/m^2) and sedentary.* *219 total – 21 F, 198 M. Mean (SD) age 44.9 (2.5) years. Mean (SD) BMI (*kg/m^2*) 29.54 (3.89) diet group (*n*=55), 28.56 (3.22) exercise group (*n*=54), 28.57 (3.47) diet and exercise group (*n*=67), 28.30 (3.15) control group (*n*=43).*
Intervention	For initial 8 weeks the intensity and duration of supervised endurance workouts increased progressively then maintained at three times per week for 1 h each session at 60–80% maximum heart rate as assessed at baseline using treadmill; 60% of each workout was aerobic, 25% circuit training and 15% fast walking/jogging; attendance measured and exercise log book kept. Advised to stop smoking.
Control	*Told not to change lifestyle and that after 12 months would receive dietary advice and supervised physical training. Advised to stop smoking.*
Length of follow-up	12 months
Results	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –0.9 (4.20) in the activity group, and 1.10 (2.62) in the control group. Mean weight change in the intervention group compared with control was –2.00 (95% CI –3.41 to –0.52).
Quality and comments	TC and LDL levels significantly lower in the exercise and the diet and exercise groups (p<0.05). ITT not done. Only blood analyses blinded. Discrepancy between results in published papers. Good concealment of allocation.

Pritchard 1997 (in Shaw CR) RCT	
Aim	To compare the effects of two weight loss interventions, diet or exercise, on changes in bone, fat and lean tissue
Participants	*Healthy men aged 35 to 55 years who were overweight (BMI 26 to 35 kg/m^2). 66 total – all men. Mean age (SD) 44.9 (6.5) years in the activity group (*n*=22), 42.3 (4.5) years in the control group (*n*=20). Mean BMI (SD) (kg/m^2) 29.2 (2.8) in the activity group, 28.6 (2.8) in the control. Data for 12-month completers only (*n*=58 overall).*

Intervention	Participants selected their own unsupervised aerobic exercise regimen of at least three sessions of 30 min each week at 65–75% maximum heart rate; initial heart rate over 33 h normal activity which included the selected exercise used to determine personal heart rate target zone; eleven participants walked, two jogged, two alternated jogging and swimming, three attended the gym and three rode exercise bikes, participants exercised 3–7 sessions per week, advised to avoid change in food intake, completion of daily adherence calendar, at 13 months dietary intervention was added (See Diet review for detail of diet intervention)
Control	*Attended monthly weight monitoring sessions where counselled to follow usual food and exercise habits. Told participants that they would be able to enter the weight loss study at the end of the study. Both diet and physical activity interventions were added at 13 months.*
Length of follow-up	18 months
Results	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –2.60 (3.00) in the activity group, and 0.30 (2.40) in the control group. Mean weight change in the intervention group compared with control was –2.90 (95% CI –4.68 to –1.12).
Quality and comments	ITT analysis done. Blinded assessment not done. Real possibility of disclosure of allocation, although some attempt made at concealment. Author provided unpublished report. Data up to 12 months only used. Discrepancy in data between reports.

Wood 1988 (in Shaw CR) RCT	
Aim	To determine the influence of two methods for losing fat weight on the levels of plasma lipids and lipoproteins in overweight sedentary men – decreasing energy intake without increasing exercise (diet), and increasing energy expenditure without altering energy intake (exercise, primarily running)
Participants	*Men aged 30 to 59 years, overweight (120 to 160% IBW) and no regular exercise for past 3 months.* *155 M. Mean (SD) age 44.2 (8.2) years diet group (*n=*51), 44.1 (7.8) years activity group (*n=*52), 45.2 (7.2) years control (*n=*52). Mean (SD) weight 93.0 (8.8) kg diet group, 94.1 (8.6) activity group, and 95.4 (10.6) control. (Results for 131 assessed participants).* Noted in HTA as highest mean reported weight (kg)
Intervention	Participants received supervised exercise training session to promote increase in energy expenditure and body fat loss of one-third, consisting of 1 h three times per week including callisthenics, walking, jogging and principally running at 60–80% peak heart rate (according to treadmill test results), advised to increase routine physical activity plus two more sessions per week unsupervised exercise; activity logs kept and advised not to change diet including composition, weight stabilisation last 6 weeks.
Control	*Advised not to make any changes in diet, including composition, exercise or body weight, offered weight loss programme of diet and exercise at end of study.*
Length of follow-up	24 months
Results	*At 7 months, mean (SD) weight change in kg was –3.00 (2.80) in the activity group, and 0.20 (2.50) in the control group. Mean weight change in the intervention group compared with control was –3.00 (95% CI –4.30 to –2.10). At 12 months, mean (SD) weight change in kg was –4.00 (3.90) in the activity group, and 0.60 (3.70) in the control group. Mean weight change in the intervention group compared with control was –4.60 (95% CI –6.18 to –3.02).*
Quality and comments	ITT analysis not done. Blinded assessment only in year 2. Random allocation but no description of concealment. Only 12-month outcomes reported in published papers.

Other outcomes

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.20 (0.56) in the activity group, and –0.16 (0.59) in the control group. Mean TC change in the intervention group compared with control was –0.04 (95% CI –0.28 to 0.20). At 12 months, mean (SD) LDL change in mmol/l was –0.13 (0.49) in the activity group, and –0.22 (0.59) in the control group. Mean LDL change in the intervention group compared with control was 0.09 (95% CI –0.13 to 0.31). At 12 months, mean (SD) HDL change in mmol/l was 0.04 (0.14) in the activity group, and 0.02 (0.10) in the control group. Mean HDL change in the intervention group compared with control was 0.02 (95% CI –0.03 to 0.07). At 12 months, mean (SD) TAG change in mmol/l was –0.24 (0.70) in the activity group, and 0.17 (0.92) in the control group. Mean TAG change in the intervention group compared with control was –0.41 (95% CI –0.75 to –0.07). At 12 months, mean (SD) DBP change in mmHg was –2.70 (7.00) in the activity group, and –0.70 (8.52) in the control group. Mean DBP change in the intervention group compared with control was –2.00 (95% CI –5.21 to 1.21). At 12 months, mean (SD) SBP change in mmHg was –2.20 (7.70) in the activity group, and –0.50 (11.15) in the control group. Mean SBP change in the intervention group compared with control was –1.70 (95% CI –5.67 to 2.27). At 12 months, mean (SD) FPG change in mmol/l was –0.09 (0.42) in the activity group, and 0.07 (0.46) in the control group. Mean FPG change in the intervention group compared with control was –0.16 (95% CI –0.34 to 0.02). *The activity group had a significant mean change from baseline in fat intake (as % of energy) of –1.6% (*p<*0.05). No other changes from baseline were significant.* *At 12 months,* VO_{2max} *had increased by 4.0 ml/kg per min, which was significantly different to the control group (*p<*0.05). No values were reported for the control group.*
Quality and comments	Dietary intake assessed through a validated food-frequency questionnaire. Activity was supervised, and home activity was recorded (no details). Also participants interviewed at 12 months about changes in activity habits.

Pritchard 1997 (in Shaw CR) RCT	
Results	*At 12 months, significant differences from baseline were seen in the activity group compared with control for index of activity (+15.6 vs +6.4%) and energy expenditure (+14.6 vs +6.5%) (*p<*0.05). Also there was a significant increase in dietary calcium in the activity group compared with control (+30.3 vs –0.8%;* p<*0.001).* *No significant differences were seen between activity and control for energy intake, % energy as fat or % energy as protein.* *Also at 12 months, no significant differences were seen from baseline between activity and control in bone mineral density, bone mass, or lean mass. Fat mass decreased in the activity group but increased in the control group (–11.0 vs +0.4%) (*p<0.*05).*
Quality and comments	Dietary intake estimated from participants' 3-day food diaries. Activity from 3-day diaries and 24 h activity logs monthly.

Wood 1988 (in Shaw CR) RCT	
Results	*At 7 months, changes in TAG, HDL and* HDL_2 *levels were significantly different to controls (–0.25 vs –0.01,* p≤*0.51, 0.09 vs 0.00* p≤*0.01, 0.06 vs 0.00* p≤*0.01, respectively). Changes in TC, LDL and* HDL_3 *levels were not significantly different between groups.* *At 12 months, mean (SD) TC change in mmol/l was –0.25 (0.64) in the activity group, and –0.23 (0.65) in the control group. Mean TC change in the*

	*intervention group compared with control was –0.02 (95% CI –0.29 to 0.25). At 12 months, mean (SD) LDL change in mmol/l was –0.25 (0.61) in the activity group, and –0.21 (0.67) in the control group. Mean LDL change in the intervention group compared with control was –0.04 (95% CI –0.31 to 0.23). At 12 months, mean (SD) HDL change in mmol/l was 0.11 (0.15) in the activity group, and –0.02 (0.11) in the control group. Mean HDL change in the intervention group compared with control was 0.13 (95% CI 0.08 to 0.18). At 12 months, mean (SD) TAG change in mmol/l was –0.16 (0.53) in the activity group, and 0.08 (0.60) in the control group. Mean TAG change in the intervention group compared with control was –0.24 (95% CI –0.48 to 0.00). At 12 months, mean (SD) DBP change in mmHg was –4.10 (8.00) in the activity group, and –2.60 (8.10) in the control group. Mean DBP change in the intervention group compared with control was –1.50 (95% CI –5.11 to 2.11). At 12 months, mean (SD) SBP change in mmHg was –6.60 (8.40) in the activity group, and –4.10 (8.00) in the control group. Mean SBP change in the intervention group compared with control was –2.50 (95% CI –6.17 to 1.17). *TC ratio/HDL cholesterol ratios were significantly lower in the activity group compared with control at both 7 and 12 months (p≤0.05). At 12 months, the activity group showed significant changes from baseline compared with control for body fat (–3.7% vs –0.9%) (p<0.01), g of fat per day (–2.2 vs 1.4) (p<0.05), and mono-unsaturated fat intake (–1.1 vs 0.5 g/kcal) (p<0.01). No other changes in outcomes were significant (energy per day, saturated fat, polyunsaturated fat, alcohol, calcium, potassium, sodium levels). At 12 months, $\dot{V}O_{2max}$ and treadmill test duration increased significantly in the activity group compared with control (p≤0.001) (treadmill test duration [min] 4.1 vs –2.4 $\dot{V}O_{2max}$, and 0.3 vs –1.6).*
Quality and comments	Dietary intake estimated from participants' 7-day food diaries. Supervised exercise. *In the summary statistics, only the 12-month value is significant?

Reported harms

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Harms	*One death and two cancers (allocation not known).*
Quality and comments	…

Pritchard 1997 (in Shaw CR) RCT	
Harms	Two participants withdrew before completion due to ill health unrelated to the study.
Quality and comments	…

Wood 1988 (in Shaw CR) RCT	
Harms	*One diagnosis of cancer reported in year 2.*
Quality and comments	…

Generalisability

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Country and setting	Norway. Community-based?

Participants (included/excluded)	*Included if aged 41 to 50 years, sedentary (exercise no more than once per week), BMI >24 kg/m^2, DBP 86 to 99 mmHg, TC 5.2 to 7.74 mmol/l, HDL <1.2 mmol/l, fasting serum TAG >1.4 mmol/l. Excluded if overt diabetes or CVD, other disease or drugs that could interfere with test results, treatment with antihypertensive drugs, acetylsalicylic acid, lipid-lowering diet, personal traits unsuitable for inclusion.*
Recruitment	Participants recruited from continuous screening programme of 40-year old men and women in Oslo. No further details reported.
Intervention (mode and intensity)	12 months, contacted 158 times (baseline, three times per week and follow-up at 12 months)
Duration of active intervention	*12 months*
Control (mode and intensity)	*12-month control. Contacted at baseline and 12 months.*
Delivery of intervention/control (who)	N/R other than 'under the guidance of highly qualified instructors'.
Dropout rates	9% in activity group and 0% in control at 12 months (includes five excluded).
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Pritchard 1997 (in Shaw CR) RCT	
Country and setting	Australia. Work-based.
Participants (included/excluded)	*Included men aged 35 to 55 years of age, satisfactory cardiovascular fitness test, BMI 26 to 35 kg/m^2, 110 to 130% of IBW, otherwise healthy.* *No details of exclusion criteria given.*
Recruitment	Volunteers recruited from a national business corporation, previously screened as being overweight in a corporate health programme.
Intervention (mode and intensity)	18 months of intervention. Contacted 19 times (baseline then monthly. Also encouraged to attend bimonthly motivational group breakfasts or lunch meetings with guest speakers or videos relevant to diet, exercise and health issues).
Duration of active intervention	*12 months*
Control (mode and intensity)	12 months of control. 6 months of diet and exercise. Contacted at baseline and weight monitored monthly
Delivery of intervention/control (who)	N/R
Dropout rates	*5% in the activity group and 5% in the control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Wood 1988 (in Shaw CR) RCT	
Country and setting	USA. University clinic.
Participants (included/excluded)	*Included men aged 30 to 59 years, 120 to 160% IBW, no regular exercise for past 3 months, non-smokers, clinically healthy, resting clinic BP <160/100mmHg, plasma cholesterol<8.28mmol/l, plasma TAG<5.65mmol/l, average<4 alcoholic drinks per day, expected to reside in Stanford area for at least 12 months, normal ECG during grade treadmill test.* *Excluded if orthopaedic limitations, medications known to effect BP or plasma lipids.*

Recruitment	Potential participants invited to be screened via mass media. Interviewed by telephone, and scheduled for orientation session if criteria met and still interested.
Intervention (mode and intensity)	First 12 months, no details of frequency of contact. In year 2, monthly mailings, telephone contact of 5 to 10mins each during months 13, 14, 15, 18, 21, 24 (for contact groups). In year 2, contacted twice at 18 and 24 months (no contact groups).
Duration of active intervention	*12 months*
Control (mode and intensity)	Contacted three times in year 1 – baseline and 7, 12 months.
Delivery of intervention/control (who)	Exercise supervised by 'training staff'. No details given.
Dropout rates	2% activity, 6% control in first 12 months. 13% activity 2 (contact) group, 32% in activity 3 (no contact) group at 24 months.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.2 Physical activity vs information

Weight loss

Messier 2004 RCT	
Aim	To determine whether long-term exercise and dietary weight loss are more effective, either separately or in combination, than usual care in improving physical function, pain, mobility in older overweight/obese adults with osteoarthritis
Participants	People with osteoarthritis, aged 60 years and older who were overweight (BMI ≥28 kg/m^2) Total 316 – 227 F, 89 M. Mean (SD) age years 69 (7.16) years activity (*n*=80), 68 (6.34) years BT (*n*=82). Mean (SD) BMI (kg/m^2) 34.2 (5.37) activity, 34.5 (5.43) BT.
Intervention	Three days/week exercise programme consisted of an aerobic phase (15 min), a resistance-training phase (15 min), a second aerobic phase (15 min), and a cool-down phase (15 min). The first 4 months of the 18-month intervention was facility-based. At any time after the first 4 months, participants who wished to exercise at home underwent a 2-month transition phase during which he or she alternated attendance between the facility and the home. Hence, some participants remained in a facility-based programme, others opted for a home-based programme, and some participants chose a combined facility–home-based programme. Provided with an aerobic exercise prescription that included walking within a heart rate range of 50–75% of heart rate reserve. The resistance-training portion of the programme consisted of two sets of 12 repetitions of the following exercises: leg extension, leg curl, heel raise, and step-up. Cuff weights and weighted vests were used to provide resistance. A 1.0–1.5-min rest interval separated each exercise. Following two orientation sessions, participants began the exercise programme using the lowest possible resistance. Resistance was increased after the participant performed two sets of 12 repetitions for two consecutive days. *For participants in the home-based programme, weights were exchanged at the participant's request or after a determination was made during face-to-face or telephone contact to increase the weights. Telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Exercise and attendance logs were used to gather data and monitor progress.*
Control	The group met monthly for 1 h for the first 3 months. A health educator, who scheduled videotaped presentations and physician talks on topics concerning OA, obesity, and exercise, organised the healthy lifestyle programme. Patients were advised to follow the American College of Rheumatology and European League Against Rheumatism recommendations for weight loss and exercise as treatments for OA. Question-and-answer sessions followed each presentation. Monthly phone contact was maintained during months 4–6, followed by contact every other month during months 7–18. During phone contact, information on pain, medication use, illnesses and hospitalisation was obtained.
Length of follow-up	*18 months*
Results	*At 18 months, mean (SD) weight change in kg was –3.46 (6.89) in the activity group, and 1.10 (6.22) in the information group. Mean weight change in the intervention group compared with BT was –4.56 (95% CI –6.61 to –2.51).*
Quality and comments	*ITT analysis done. Blinded assessment done. Good concealment of allocation. SDs calculated*

Other outcomes

Messier 2004 RCT	
Results	*No significant differences were seen for self-reported physical function, motility, or pain (although pain did improve in all groups over time) in the activity group compared with BT only.*
Quality and comments	…

Reported harms

Messier 2004 RCT	
Harms	Two deaths occurred, but were unrelated to the interventions. One participant tripped and sustained a laceration to his head. No details of allocation.
Quality and comments	…

Generalisability

Messier 2004 RCT	
Country and setting	USA. Older Americans Independence Centre.
Participants (included/excluded)	Included if aged ≥60 years, calculated BMI ≥28 kg/m^2, knee pain on most days of the month, sedentary activity pattern with <20 min of formal exercise once weekly for the past 6 months, self-reported difficulty in at least one of the following activities ascribed to knee pain: walking one-quarter of a mile (three to four city blocks), climbing stairs, bending, stooping, kneeling (e.g., to pick up clothes), shopping, house cleaning or other self-care activities, getting in and out of bed, standing up from a chair, lifting and carrying groceries, or getting in and out of the bath, radiographic evidence of grade I–III tibiofemoral or patellofemoral OA based on weight-bearing anteroposterior and sunrise view radiographs, and willingness to undergo testing and intervention procedures. Excluded if serious medical condition that prevented safe participation in an exercise programme, including symptomatic heart or vascular disease (angina, peripheral vascular disease, congestive heart failure), severe hypertension, recent stroke, chronic obstructive pulmonary disease, severe insulin-dependent diabetes mellitus, psychiatric disease, renal disease, liver disease, active cancer other than skin cancer, anaemia, a Mini-Mental State Examination score of <24, inability to finish the 18-month study or unlikely to be compliant, inability to walk without a cane or other assistive device, participation in another research study, reported alcohol consumption of >14 drinks per week, ST segment depression of at least 2 mm at an exercise level of 4 METS or less, hypotension, or complex arrhythmias during a graded exercise test, inability to complete the protocol, in the opinion of the clinical staff, because of frailty, illness, or other reasons.

Recruitment	Mass mailings to age-eligible persons within the target area, targeted mailings to employees of the university and medical centre, presentations to various groups of older adults, mass media advertisement, and placement of posters (with pull-off reply cards attached) in strategic locations. Also, strategies were developed to enhance recruitment among racial minorities, including ads and interviews on minority-run radio stations, newspaper ads in predominantly African American publications, letters to churches attended mainly by minorities, and inserts in these church bulletins. Initial screening for major eligibility criteria was via telephone.
Intervention (mode and intensity)	*Three days/week exercise for 4 months (facility-based), then either home- or facility-based. For participants in the home-based programme, telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Assessment at baseline, 6, 18 months.*
Duration of active intervention	18 months
Control (mode and intensity)	One introductory individual session was followed by 16 weekly sessions (three group sessions and one individual session each month). The transition phase included sessions every other week for 8 weeks (three group sessions and one individual session). The maintenance phase included monthly meetings and phone contacts, alternated every 2 weeks.
Delivery of intervention/control (who)	Exercise: not reported BT: not reported.
Dropout rates	*20% activity, 23% information at 24 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.3 Physical activity vs diet

Weight loss

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Aim	The primary aim of the trial was to compare the isolated and combined effects of the diet and exercise on the variables fibrinogen, fibrinolytic capacity, coagulation factor VII and platelet volume. Secondary aims were the effects on other coagulation and fibrinolytic components and activities; lipids and lipoproteins; fatty acids; glucose and insulin response to a glucose load; clinical, physiological and anthropometric variables; and quality of life
Participants	*Men and women aged 41 to 50 years who were overweight (BMI >24 kg/m^2) and sedentary.* *219 total – 21 F, 198 M. Mean (SD) age 44.9 (2.5) years. Mean (SD) BMI (kg/m^2) 29.54 (3.89) diet group (*n=*55), 28.56 (3.22) exercise group (*n=*54), 28.57 (3.47) diet and exercise group (*n=*67), 28.30 (3.15) control group (*n=*43).*
Intervention	For initial 8 weeks the intensity and duration of supervised endurance workouts increased progressively then maintained at three times per week for 1 h each session at 60–80% maximum heart rate as assessed at baseline using treadmill; 60% of each workout was aerobic, 25% circuit training and 15% fast walking/jogging, attendance measured and exercise log book kept. Advised to stop smoking.

Control	*Dietary counselling with spouse at baseline then individually at 3- and 9-month follow-up sessions. Diet adapted to individual's risk profile with main focus on energy restriction in those overweight, increase in fish and vegetables, decrease in saturated fat, cholesterol, sugar, and salt restriction for those with elevated BP. Weight targets agreed and set. 180 food-frequency questionnaire at baseline and 12 months. Advised to stop smoking.*
Length of follow-up	12 months
Results	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –0.09 (4.20) in the activity group, and –4.00 (5.05) in the diet group. Mean weight change in the intervention group compared with control was 3.10 (95% CI 1.29 to 4.91).
Quality and comments	TC and LDL levels significantly lower in the exercise and the diet and exercise groups (p<0.05). ITT not done. Only blood analyses blinded. Discrepancy between results in published papers. Good concealment of allocation.

Pritchard 1997 (in Shaw CR) RCT	
Aim	To compare the effects of two weight loss interventions, diet or exercise, on changes in bone, fat and lean tissue
Participants	*Healthy men aged 35 to 55 years who were overweight (BMI 26 to 35 kg/m^2). 66 total – all men. Mean age (SD) 44.9 (6.5) years in the activity group (*n*=22), 43.6 (6.0) years in the diet group (n=20). Mean BMI (SD) (kg/m^2) 29.2 (2.8) in the activity group, 29.0 (2.8) in the diet. Data for 12 month completers only (*n*=58 overall).*
Intervention	Participants selected their own unsupervised aerobic exercise regimen of at least 3 sessions of 30 min each week at 65–75% maximum heart rate; initial heart rate over 33 h normal activity which included the selected exercise used to determine personal heart rate target zone; eleven participants walked, two jogged, two alternated jogging and swimming, three attended the gym and three rode exercise bikes, participants exercised 3–7 sessions per week, advised to avoid change in food intake, completion of daily adherence calendar, at 13 months dietary intervention was added. (See Diet review for detail of diet intervention.)
Control	*Advised to follow low-fat intake of 20 to 22% energy per day, to avoid foods rich in fat, discouraged from eating more than one sweet per day and more than two alcoholic drinks/day. Personalised diet plan to meet RDI for use in Australia, given* The Weight Loss Guide *by the Australian Heart Foundation. Exercise restricted to pre-study level. Completion of daily adherence calendar. At 13 months, exercise intervention was added.*
Length of follow-up	18 months
Results	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –2.60 (3.00) in the activity group, and –6.40 (3.30) in the diet group. Mean weight change in the intervention group compared with control was 3.80 (95% CI 1.72 to 5.88).
Quality and comments	ITT analysis done. Blinded assessment not done. Real possibility of disclosure of allocation, although some attempt made at concealment. Author provided unpublished report. Data up to 12 months only used. Discrepancy in data between reports.

Wood 1988 (in Shaw CR) RCT	
Aim	To determine the influence of two methods for losing fat weight on the levels of plasma lipids and lipoproteins in overweight sedentary men – decreasing energy intake without increasing exercise (diet), and increasing energy expenditure without altering energy intake (exercise, primarily running)

Participants	*Men aged 30 to 59 years, overweight (120 to 160% IBW) and no regular exercise for past 3 months.* *155 M. Mean (SD) age 44.2 (8.2) years diet group (*n=*51), 44.1 (7.8) years activity group (*n=*52), 45.2 (7.2) years control (*n=*52). Mean (SD) weight 93.0 (8.8) kg diet group, 94.1 (8.6) activity group, and 95.4 (10.6) control. (Results for 131 assessed participants.)* Noted in HTA as highest mean reported weight (kg).
Intervention	Participants received supervised exercise training session to promote increase in energy expenditure and body fat loss of one-third, consisting of 1 h three times per week including callisthenics, walking, jogging and principally running at 60–80% peak heart rate (according to treadmill test results), advised to increase routine physical activity plus two more sessions per week unsupervised exercise; activity logs kept and advised not to change diet including composition, weight stabilisation last 6 weeks.
Control	*Baseline 7 day diet recall and fat body mass used to provide individual counselling including behavioural strategies (no details), to reduce energy intake to produce gradual weight loss and to lose one-third of body fat (assumed a reduction of 7762 kcal for loss of 1 kg adipose tissue). No change in nutrient composition, requested to remain sedentary, included weight stabilisation for last 6 weeks.*
Length of follow-up	24 months
Results	*At 7 months, mean (SD) weight change in kg was –3.00 (2.80) in the activity group, and –7.60 (3.9) in the diet group. Mean weight change in the intervention group compared with control was 4.60 (95% CI 3.17 to 6.03).* *At 12 months, mean (SD) weight change in kg was –4.00 (3.90) in the activity group, and –7.20 (3.70) in the diet group. Mean weight change in the intervention group compared with control was 3.20 (95% CI 1.62 to 4.78).*
Quality and comments	ITT analysis not done. Blinded assessment only in year 2. Random allocation but no description of concealment. Only 12 month outcomes reported in published papers.

Other outcomes

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.20 (0.56) in the activity group, and –0.23 (0.65) in the diet group. Mean TC change in the intervention group compared with control was 0.03 (95% CI –0.21 to 0.27). At 12 months, mean (SD) LDL change in mmol/l was –0.13 (0.49) in the activity group, and –0.18 (0.72) in the diet group. Mean LDL change in the intervention group compared with control was 0.05 (95% CI –0.19 to 0.29). At 12 months, mean (SD) HDL change in mmol/l was 0.04 (0.14) in the activity group, and 0.05 (0.12) in the diet group. Mean HDL change in the intervention group compared with control was –0.01 (95% CI –0.06 to 0.04). At 12 months, mean (SD) TAG change in mmol/l was –0.24 (0.70) in the activity group, and- 0.23 (1.01) in the diet group. Mean TAG change in the intervention group compared with control was –0.01 (95% CI –0.35 to 0.33). At 12 months, mean (SD) DBP change in mmHg was –2.70 (7.00) in the activity group, and –3.40 (7.21) in the diet group. Mean DBP change in the intervention group compared with control was 0.70 (95% CI –2.07 to 3.47). At 12 months, mean (SD) SBP change in mmHg was –2.20 (7.70) in the activity group, and –6.40 (10.10) in the diet group. Mean SBP change in the intervention group compared with control was 4.20 (95% CI 0.71 to 7.69). At 12 months, mean (SD) FPG change in mmol/l was –0.09 (0.42) in the activity group, and –0.21 (0.50) in the diet group. Mean FPG change in the intervention group compared with control was 0.12 (95% CI –0.06 to 0.30). *The activity group had a significant mean change from baseline in fat intake*

	*(as % of energy) of –1.6% (*p*<0.05). No other changes from baseline were significant. This compared with significant changes from baseline in the diet group for energy intake (–550 kcal), protein (–13.4 g), fat (–32.5 g), %energy as fat (–5.1%), carbohydrate (–42.3 g), sugar (–16.8 g), alcohol (–2.5 g), cholesterol (–121 mg), saturated fatty acids (–13.6 g), monounsaturated fatty acids (–12.3 g) and polyunsaturated fatty acids (–4.9 g).* *At 12 months, $\dot{V}O_{2max}$ had significantly increased by 4.0 ml/kg per min compared with the diet group (1.70 ml/kg per min).*
Quality and comments	Dietary intake assessed through a validated food-frequency questionnaire. Activity was supervised, and home activity was recorded (no details). Also participants interviewed at 12 months about changes in activity habits.

Pritchard 1997 (in Shaw CR) RCT	
Results	*At 12 months, significant differences from baseline were seen in the activity group compared with diet for index of activity (+15.6 vs +3.4%) and energy expenditure (+14.6 vs +5.9%) (*p*<0.05).* *At 12 months, the activity group increased energy intake by 3.1% compared with a decrease of 30.4% in the diet group. The activity group decreased fat intake by 1.0% compared with 32.0% in the diet group. Energy from protein decreased in the activity group and increased in the diet group (–2.3 vs +23.3%). Also there was a significant increase in dietary calcium in the activity group compared with diet (+30.3 vs –13.6%).* *Also at 12 months, bone mass and bone mineral density decreased in both groups (–0.8 vs –1.4 and –1.1 vs –1.5%, respectively). Fat mass decreased in both groups (–11.0 vs –19.4%).*
Quality and comments	Dietary intake estimated from participants' 3-day food diaries. Activity from 3-day diaries and 24-h activity logs monthly.

Wood 1988 (in Shaw CR) RCT	
Results	*At 7 months, there was no significant differences between the activity and diet groups for changes in TC, LDL, TAG, HDL levels.* *At 12 months, mean (SD) TC change in mmol/l was –0.25 (0.64) in the activity group, and –0.36 (0.56) in the diet group. Mean TC change in the intervention group compared with control was 0.11 (95% CI –0.14 to 0.36).* *At 12 months, mean (SD) LDL change in mmol/l was –0.25 (0.61) in the activity group, and –0.31 (0.64) in the diet group. Mean LDL change in the intervention group compared with control was 0.06 (95% CI –0.20 to 0.32).* *At 12 months, mean (SD) HDL change in mmol/l was 0.11 (0.15) in the activity group, and 0.12 (0.16) in the diet group. Mean HDL change in the intervention group compared with control was –0.01 (95% CI –0.08 to 0.06).* *At 12 months, mean (SD) TAG change in mmol/l was –0.16 (0.53) in the activity group, and –0.27 (0.72) in the diet group. Mean TAG change in the intervention group compared with control was 0.11 (95% CI –0.16 to 0.38).* *At 12 months, mean (SD) DBP change in mmHg was –4.10 (8.00) in the activity group, and –5.60 (7.30) in the diet group. Mean DBP change in the intervention group compared with control was 1.50 (95% CI –1.85 to 4.85).* *At 12 months, mean (SD) SBP change in mmHg was –6.60 (8.40) in the activity group, and –5.70 (7.90) in the diet group. Mean SBP change in the intervention group compared with control was –0.90 (95% CI –4.47 to 2.67).* *TC:HDL cholesterol ratios were not significantly different between the groups at any time point.* *At 12 months, the activity group showed significant changes from baseline compared with diet for grams of fat per day (–2.2 vs 2.0) (*p*<0.05). No other changes in outcomes were significant (% body fat, energy per day, saturated fat, mono- and poly-unsaturated fat, alcohol, calcium, potassium, sodium levels).* *At 12 months, $\dot{V}O_{2max}$ and treadmill test duration increased significantly in the activity group compared with diet (4.1 vs 0.0 $\dot{V}O_{2max}$, and 0.3 vs –0.8 treadmill test duration in min).*

Quality and comments	Dietary intake estimated from participants' 7-day food diaries. Supervised exercise.

Reported harms

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Harms	*One death and two cancers (allocation not known).*
Quality and comments	…

Pritchard 1997 (in Shaw CR) RCT	
Harms	Two participants withdrew before completion due to ill health unrelated to the study.
Quality and comments	…

Wood 1988 (in Shaw CR) RCT	
Harms	*One diagnosis of cancer reported in year 2.*
Quality and comments	…

Generalisability

ODES 1995 (in Shaw CR Anderssen 1996) RCT	
Country and setting	Norway. Community-based?
Participants (included/excluded)	*Included if aged 41 to 50 years, sedentary (exercise no more than once per week), BMI >24 kg/m^2, DBP 86 to 99 mmHg, TC 5.2 to 7.74 mmol/l, HDL <1.2 mmol/l, fasting serum TAG >1.4 mmol/l. Excluded if overt diabetes or CVD, other disease or drugs that could interfere with test results, treatment with antihypertensive drugs, acetylsalicylic acid, lipid-lowering diet, personal traits unsuitable for inclusion.*
Recruitment	Participants recruited from continuous screening programme of 40-year-old men and women in Oslo. No further details reported.
Intervention (mode and intensity)	12 months, contacted 158 times (baseline, three times per week and follow-up at 12 months)
Duration of active intervention	*12 months*
Control (mode and intensity)	Dietary intervention lasted 12 months. 4 contacts (baseline, 3, 9, 12 months).
Delivery of intervention/control (who)	N/R other than exercise 'under the guidance of highly qualified instructors'.
Dropout rates	9% in activity group and 5% in diet group at 12 months, (includes 5 excluded)
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Pritchard 1997 (in Shaw CR) RCT	
Country and setting	Australia. Work-based.
Participants (included/excluded)	*Included men aged 35 to 55 years of age, satisfactory cardiovascular fitness test, BMI 26 to 35 kg/m^2, 110 to 130% of IBW, otherwise healthy.* *No details of exclusion criteria given.*

Recruitment	Volunteers recruited from a national business corporation, previously screened as being overweight in a corporate health programme.
Intervention (mode and intensity)	18 months of intervention. Contacted 19 times (baseline then monthly. Also encouraged to attend bimonthly motivational group breakfasts or lunch meetings with guest speakers or videos relevant to diet, exercise and health issues).
Duration of active intervention	*12 months*
Control (mode and intensity)	12 months of control. 6 months of diet and exercise. Contacted at baseline and weight monitored monthly
Delivery of intervention/control (who)	N/R
Dropout rates	*5% in the activity group and 25% in the diet at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Wood 1988 (in Shaw CR) RCT	
Country and setting	USA. University clinic.
Participants (included/excluded)	*Included men aged 30 to 59 years, 120 to 160% IBW, no regular exercise for past 3 months, non-smokers, clinically healthy, resting clinic BP <160/100 mmHg, plasma cholesterol <8.28 mmol/l, plasma TAG <5.65 mmol/l, average less than four alcoholic drinks per day, expected to reside in Stanford area for at least 12 months, normal ECG during grade treadmill test.* *Excluded if orthopaedic limitations, medications known to effect BP or plasma lipids.*
Recruitment	Potential participants invited to be screened via mass media. Interviewed by telephone, and scheduled for orientation session if criteria met and still interested.
Intervention (mode and intensity)	First 12 months, no details of frequency of contact. In year 2, monthly mailings, telephone contact of 5 to 10 min each during months 13, 14, 15, 18, 21, 24 (for contact groups). In year 2, contacted twice at 18 and 24 months (no contact groups).
Duration of active intervention	*9 months*
Control (mode and intensity)	Contacted three times in year 1 – baseline and 7, 12 months.
Delivery of intervention/control (who)	Registered dietitian provided individual counselling. Exercise supervised by 'training staff' No details given.
Dropout rates	2% activity, 4% diet in first 12 months. 13% activity 2 (contact) group, 32% in activity 3 (no contact) group at 24 months. 17% diet 2 (contact) group, 20% in diet 3 (no contact) group at 24 months.
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.4 Physical activity and diet vs behaviour therapy

Weight loss

Messier 2004 RCT	
Aim	To determine whether long-term exercise and dietary weight loss are more effective, either separately or in combination, than usual care in improving physical function, pain, mobility in older overweight/obese adults with osteoarthritis
Participants	People with osteoarthritis, aged ≥60 years who were overweight (BMI ≥28 kg/m^2) Total 316 – 227 F, 89 M. Mean (SD) age years 69 (7.16) years activity (*n*=80), 68 (6.34) years BT (*n*=82). Mean (SD) BMI 34.2 9 (kg/m^2) (5.37) activity, 34.5 (5.43) BT.
Intervention	Three days/week exercise programme consisted of an aerobic phase (15 min), a resistance-training phase (15 min), a second aerobic phase (15 min), and a cool-down phase (15 min). The first 4 months of the 18-month intervention was facility-based. At any time after the first 4 months, participants who wished to exercise at home underwent a 2-month transition phase during which he or she alternated attendance between the facility and the home. Hence, some participants remained in a facility-based programme, others opted for a home-based programme, and some participants chose a combined facility–home-based programme. Provided with an aerobic exercise prescription that included walking within a heart rate range of 50–75% of heart rate reserve. The resistance-training portion of the programme consisted of two sets of 12 repetitions of the following exercises: leg extension, leg curl, heel raise and step-up. Cuff weights and weighted vests were used to provide resistance. A 1.0–1.5-min rest interval separated each exercise. Following two orientation sessions, participants began the exercise programme using the lowest possible resistance. Resistance was increased after the participant performed two sets of 12 repetitions for twp consecutive days. *For participants in the home-based programme, weights were exchanged at the participant's request or after a determination was made during face-to-face or telephone contact to increase the weights. Telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Exercise and attendance logs were used to gather data and monitor progress.* *Diet: to produce and maintain an average weight loss of 5% during the 18-month intervention period. Classified as a 600 kcal/day deficit/LED diet.*

Control	Goal was to produce and maintain an average weight loss of 5% during the 18-month intervention period. Dietary intervention was divided into three phases: intensive (months 1–4), transition (months 5–6) and maintenance (months 7–18). Major emphasis of the intensive phase was to heighten awareness of the importance of and need for changing eating habits in order to lower energy intake. Behaviour change was facilitated using self-regulatory skills. These skills included self-monitoring, goal setting, cognitive restructuring, problem-solving, and environmental management. One introductory individual session was followed by 16 weekly sessions (three group sessions and one individual session each month). Each group session included problem-solving, the review of a specific topic, and tasting of several well-balanced, low-fat, nutritious foods prepared with widely available ingredients. The individual sessions were used to review individual progress, solve problems, answer questions and set goals. The transition phase included sessions every other week for 8 weeks (three group sessions and 1 individual session). The goals for this phase included assisting participants who had not reached their weight loss goals in establishing new goals, and maintaining and preventing relapse in those participants who had reached their weight loss goals. The maintenance phase included monthly meetings and phone contacts, alternated every 2 weeks. Additionally, newsletters that provided pertinent nutritional information and notice of upcoming meetings were mailed at regular intervals. The goals of the maintenance phase included assisting participants who had reached their weight loss goals to maintain this weight loss, and providing counselling for participants who had a difficult time losing weight and adhering to the intervention. Adherence to the intervention was based on attendance at scheduled sessions and completion of the monthly assessment of weight.
Length of follow-up	*18 months*
Results	*At 18 months, mean (SD) weight change in kg was –3.46 (6.89) in the activity group, and –4.61 (7.22) in the BT group. Mean weight change in the intervention group compared with BT was –1.15 (95% CI –1.02 to 3.32).*
Quality and comments	*ITT analysis done. Blinded assessment done. Good concealment of allocation. SDs calculated*

Other outcomes

Messier 2004 RCT	
Results	*No significant differences were seen for self-reported physical function, motility, or pain (although pain did improve in all groups over time) in the activity group compared with BT only.*
Quality and comments	…

Reported harms

Messier 2004 RCT	
Harms	Two deaths occurred, but were unrelated to the interventions. One participant tripped and sustained a laceration to his head. No details of allocation.
Quality and comments	…

Generalisability

Messier 2004 RCT	
Country and setting	USA. Older Americans Independence Centre.
Participants (included/excluded)	Included if aged 60 years or older, calculated BMI ≥28 kg/m^2, knee pain on most days of the month, sedentary activity pattern with <20 min of formal exercise once weekly for the past 6 months, self-reported difficulty in at least one of the following activities ascribed to knee pain: walking one-quarter of a mile (three to four city blocks), climbing stairs, bending, stooping, kneeling (e.g., to pick up clothes), shopping, house cleaning or other self-care activities, getting in and out of bed, standing up from a chair, lifting and carrying groceries, or getting in and out of the bath, radiographic evidence of grade I–III tibiofemoral or patellofemoral OA based on weight-bearing anteroposterior and sunrise view radiographs, and willingness to undergo testing and intervention procedures. Excluded if serious medical condition that prevented safe participation in an exercise programme, including symptomatic heart or vascular disease (angina, peripheral vascular disease, congestive heart failure), severe hypertension, recent stroke, chronic obstructive pulmonary disease, severe insulin-dependent diabetes mellitus, psychiatric disease, renal disease, liver disease, active cancer other than skin cancer, and anaemia, a Mini-Mental State Examination score of <24, inability to finish the 18-month study or unlikely to be compliant, inability to walk without a cane or other assistive device, participation in another research study, reported alcohol consumption of more than 14 drinks per week, ST segment depression of at least 2 mm at an exercise level of 4 METS or less, hypotension, or complex arrhythmias during a graded exercise test, inability to complete the protocol, in the opinion of the clinical staff, because of frailty, illness, or other reasons.
Recruitment	Mass mailings to age-eligible persons within the target area, targeted mailings to employees of the university and medical centre, presentations to various groups of older adults, mass media advertisement, and placement of posters (with pull-off reply cards attached) in strategic locations. Also, strategies were developed to enhance recruitment among racial minorities, including advertisements and interviews on minority-run radio stations, newspaper ads in predominantly African American publications, letters to churches attended mainly by minorities, and inserts in these church bulletins. Initial screening for major eligibility criteria was via telephone.
Intervention (mode and intensity)	*Three days/week exercise for 4 months (facility-based), then either home- or facility-based. For participants in the home-based programme, telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Assessment at baseline, 6, 18 months.*
Duration of active intervention	18 months
Control (mode and intensity)	One introductory individual session was followed by 16 weekly sessions (three group sessions and one individual session each month). The transition phase included sessions every other week for 8 weeks (three group sessions and one individual session). The maintenance phase included monthly meetings and phone contacts, alternated every 2 weeks.
Delivery of intervention/control (who)	Exercise: not reported BT: not reported.

Dropout rates	*20% activity, 23% information at 24 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.5 Physical activity and diet vs control (no treatment)

Weight loss

ODES 1995 (in Shaw CR and HTA) RCT	
Aim	The primary aim of the trial was to compare the isolated and combined effects of the diet and exercise on the variables fibrinogen, fibrinolytic capacity, coagulation factor VII, and platelet volume. Secondary aims were the effects on other coagulation and fibrinolytic components and activities; lipids and lipoproteins; fatty acids; glucose and insulin response to a glucose load; clinical, physiological and anthropometric variables; and quality of life
Participants	*Men and women aged 41 to 50 years who were overweight (BMI >24 kg/m^2) and sedentary.* *219 total – 21 F, 198 M. Mean (SD) age 44.9 (2.5) years. Mean (SD) BMI (kg/m^2) 29.54 (3.89) diet group (*n=*55), 28.56 (3.22) exercise group (*n=*54), 28.57 (3.47) diet and exercise group (*n=*67), 28.30 (3.15) control group (*n=*43).*
Intervention	For initial 8 weeks the intensity and duration of supervised endurance workouts increased progressively then maintained at three times per week for 1 h each session at 60–80% maximum heart rate as assessed at baseline using treadmill; 60% of each workout was aerobic, 25% circuit training and 15% fast walking/jogging, attendance measured and exercise log book kept. Advised to stop smoking. Dietary counselling with spouse at baseline then individually at 3 and 9 month follow-up sessions. Diet adapted to individual's risk profile with main focus on energy restriction in those overweight, increase in fish and vegetables, decrease in saturated fat, cholesterol, sugar, and salt restriction for those with elevated BP. Weight targets agreed and set. 180 food-frequency questionnaire at baseline and 12 months.
Control	*Told not to change lifestyle and that after 12 months would receive dietary advice and supervised physical training. Advised to stop smoking.*
Length of follow-up	12 months
Results	*Only 12 month outcomes reported.* At 12 months, mean (SD) weight change in kg was –5.60 (4.84) in the activity and diet group, and 1.10 (2.62) in the control group. Mean weight change in the intervention group compared with control was –6.70 (95% CI –8.11 to –5.29).
Quality and comments	TC and LDL levels significantly lower in the exercise and the diet and exercise groups (p<0.05). ITT not done. Only blood analyses blinded. Discrepancy between results in published papers. Good concealment of allocation.

Wood 1991 (in HTA) RCT	
Aim	To test the hypothesis that exercise (walking or jogging) will increase HDL-cholesterol levels in moderately overweight, sedentary people who adopt a hypoenergetic National Cholesterol Education Programme (NCEP) diet
Participants	*Sedentary people (exercise less than twice per week) who were moderately overweight (BMI 28 to 34 kg/m^2 for men, 24 to 20 kg/m^2 for women).* *264 total – 132 F, 132 M. Mean (SD) age 39.1 (6.4) years women, 40.3 (6.3) years men. Mean BMI (kg/m^2) (SD) 27.9 (2.2) women, 30.7 (2.2) men.* (Noted as lowest mean BMI in HTA) *87 allocated to diet, 90 to diet and exercise and 87 to control.*

Intervention (including details of diet)	*NCEP step 1 diet consisting of 55% energy as carbohydrate, 30% as fat (saturated fat ≤10%), dietary cholesterol <300 mg/day, energy reduction. Activity was aerobic exercise (brisk walking or jogging) at 60–80% maximum heart rate initially for 25 min three times per week increasing to 45 min three times per week by month 4, monthly activity logs kept.*
Control	Instructed to maintain usual diet and exercise patterns.
Length of follow-up	*12 months*
Results	*Only 12 months outcomes reported.* Women: At 12 months, mean (SD) weight change in kg was –5.10 (5.30) in the activity and diet group, and 1.30 (5.20) in the control group. Mean weight change in the intervention group compared with control was –6.40 (95% CI –8.69 to –4.11). Men: At 12 months, mean (SD) weight change in kg was –8.70 (5.70) in the activity and diet group, and 1.70 (4.80) in the control group. Mean weight change in the intervention group compared with control was –10.40 (95% CI –12.73 to –8.07).
Quality and comments	Significant differences between men in both intervention groups vs control for DBP (p<0.001), TC for women in diet group vs control (p≤0.01), and diet and exercise group vs control (p≤0.05), and LDL levels in women in both intervention groups vs control (p≤0.05). Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment.

Midwest Exercise Trial 2003 RCT	
Aim	To determine the efficacy of a known quantity of exercise to prevent weight gain or to facilitate weight loss in sedentary, overweight and moderately obese adults
Participants	People who were overweight (BMI 25 to 24.9 kg/m^2) Total 131 – 43F, 31M (completers only). Women: Mean (SD) age 24 (5) years activity (n=25), 21 (4) years control (n=18). Mean (SD) BMI (kg/m^2) 28.7 (3.2) activity, 29.3 (2.3) control. Men: Mean (SD) age 22 (5) years activity (n=16), 24 (4) years control (n=15). Mean (SD) BMI 9 (kg/m^2) 29.7 (2.9) activity, 29.7 (2.9) control.
Intervention	*Exercise consisted primarily of walking on motor-driven treadmills; however, alternate activities such as stationary biking and walking on stationary elliptical trainers were allowed for 20% of the total exercise sessions (one of 5 days). Each participant's exercise prescription was calculated from a maximal treadmill test conducted at baseline and was updated by the results of maximal treadmill tests conducted at 4-month intervals.* *Duration of exercise progressed from 20 min at baseline to 45 min at 6 months and the intensity of exercise progressed from 60% of heart rate reserve at baseline to 75% at 6 months. This level of exercise corresponded to 55–70% of maximal oxygen consumption and was maintained for the remainder of the study. The targeted, minimum energy equivalent of exercise was about 400 kcal per session (about 2000 kcal/week), and this was gradually achieved during the first 6 months and then maintained for the remainder of the study.* *Participants consumed an ad libitum diet that was 30–35% energy as fat, 45–55% as carbohydrate, 10–25% as protein.*
Control	Identical testing, except for that related to the 16-month exercise programme. Instructed to maintain usual physical activity and dietary intake patterns.
Length of follow-up	*16 months*

Results	*Women (MET 2003a):* *At 4 months, mean (SD) weight change in kg was 0.40 (6.03) in the activity and diet group, and 1.50 (6.34) in the control group. Mean weight change in the intervention group compared with control was –1.10 (95% CI –4.86 to 2.66).* *At 9 months, mean (SD) weight change in kg was 0.10 (5.94) in the activity and diet group, and 1.90 (6.45) in the control group. Mean weight change in the intervention group compared with control was –1.80 (95% CI –5.58 to 1.98).* *At 12 months, mean (SD) weight change in kg was 0.70 (6.11) in the activity and diet group, and 2.40 (6.59) in the control group. Mean weight change in the intervention group compared with control was –1.70 (95% CI –5.57 to 2.17).* *At 16 months, mean (SD) weight change in kg was 0.60 (6.08) in the activity and diet group, and 2.90 (6.74) in the control group. Mean weight change in the intervention group compared with control was –2.30 (95% CI –6.22 to 1.62).* *Men (MET 2003b):* *At 4 months, mean (SD) weight change in kg was –2.90 (6.74) in the activity and diet group, and 0.10 (5.94) in the control group. Mean weight change in the intervention group compared with control was –3.00 (95% CI –7.47 to 1.47).* *At 9 months, mean (SD) weight change in kg was –5.30 (7.41) in the activity and diet group, and –1.20 (6.25) in the control group. Mean weight change in the intervention group compared with control was –4.10 (95% CI –8.92 to 0.72).* *At 12 months, mean (SD) weight change in kg was –4.60 (7.22) in the activity and diet group, and –0.60 (6.08) in the control group. Mean weight change in the intervention group compared with control was –4.00 (95% CI –8.69 to 0.69).* *At 16 months, mean (SD) weight change in kg was –5.20 (7.39) in the activity and diet group, and –0.50 (6.06) in the control group. Mean weight change in the intervention group compared with control was –4.70 (95% CI –9.45 to 0.05).* *Exercise prevented weight gain in women and produced weight loss in men. Men in the exercise group had significant mean ± SD decreases in weight (5.2±4.7 kg), BMI (calculated as weight in kilograms divided by the square of height in meters) (1.6±1.4), and fat mass (4.9±4.4 kg) compared with controls. Women in the exercise group maintained baseline weight, BMI, and fat mass, and controls showed significant mean ± SD increases in BMI (1.1±2.0), weight (2.9±5.5 kg), and fat mass (2.1±4.8 kg) at 16 months.*
Quality and comments	*No baseline differences between intervention and control groups.* *Significance differences between men and women for height, weight, % body fat, fat mass, fat-free mass and* VO_{2max}. *Assessment not blinded. ITT analysis not done. Random allocation but no description of concealment. SDs calculated.*

Other outcomes

ODES 1995 (in Shaw CR and HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.48 (0.89) in the activity and diet group, and –0.16 (0.59) in the control group. Mean TC change in the intervention group compared with control was –0.32 (95% CI –0.60 to –0.04). At 12 months, mean (SD) LDL change in mmol/l was –0.39 (0.81) in the activity and diet group, and –0.22 (0.59) in the control group. Mean LDL change in the intervention group compared with control was –0.17 (95% CI –0.43 to 0.09).

	At 12 months, mean (SD) HDL change in mmol/l was 0.13 (0.15) in the activity and diet group, and 0.02 (0.10) in the control group. Mean HDL change in the intervention group compared with control was 0.11 (95% CI 0.06 to 0.16). At 12 months, mean (SD) TAG change in mmol/l was –0.58 (0.97) in the activity and diet group, and 0.17 (0.92) in the control group. Mean TAG change in the intervention group compared with control was –0.75 (95% CI –1.11 to –0.39). At 12 months, mean (SD) DBP change in mmHg was –5.20 (7.26) in the activity and diet group, and –0.70 (8.52) in the control group. Mean DBP change in the intervention group compared with control was –4.50 (95% CI –7.60 to -1.40). At 12 months, mean (SD) SBP change in mmHg was –5.90 (8.87) in the activity and diet group, and –0.50 (11.15) in the control group. Mean SBP change in the intervention group compared with control was –5.40 (95% CI –9.37 to –1.43). At 12 months, mean (SD) FPG change in mmol/l was –0.26 (0.64) in the activity and diet group, and 0.07 (0.46) in the control group. Mean FPG change in the intervention group compared with control was –0.33 (95% CI –0.54 to –0.12). *At 12 months, significant changes from baseline were seen in the activity and diet group for energy intake (–382 kcal), protein (–7.7 g), fat (–26.5 g), % energy as fat (–5.3%), sugar (–19.6 g), cholesterol (–94 mg), saturated fatty acids (–12.1 g), monounsaturated fatty acids (–10.2 g) and polyunsaturated fatty acids (–2.9 g).* *At 12 months,* $\dot{V}O_{2max}$ *had increased by 6.7 ml/kg per min, which was significantly different to the control group (*p<*0.05). No figures were reported for the control group.*
Quality and comments	Dietary intake assessed through a validated food-frequency questionnaire. Activity was supervised, and home activity was recorded (no details). Also participants interviewed at 12 months about changes in activity habits.

Wood 1991 (in HTA) RCT	
Results	Women: At 12 months, mean (SD) TC change in mmol/l was –0.28 (0.52) in the activity and diet group, and –0.03 (0.47) in the control group. Mean TC change in the intervention group compared with control was –0.25 (95% CI –0.47 to –0.03). Women: At 12 months, mean (SD) LDL change in mmol/l was –0.29 (0.46) in the activity and diet group, and –0.03 (0.41) in the control group. Mean LDL change in the intervention group compared with control was –0.26 (95% CI –0.45 to –0.07). Women: At 12 months, mean (SD) HDL change in mmol/l was 0.02 (0.18) in the activity and diet group, and –0.05 (0.24) in the control group. Mean HDL change in the intervention group compared with control was 0.07 (95% CI –0.02 to 0.16). Women: At 12 months, mean (SD) TAG change in mmol/l was –0.02 (0.26) in the activity and diet group, and 0.13 (0.37) in the control group. Mean TAG change in the intervention group compared with control was –0.15 (95% CI –0.29 to –0.01). Women: At 12 months, mean (SD) DBP change in mmHg was –2.00 (4.10) in the activity and diet group, and 0.90 (5.30) in the control group. Mean DBP change in the intervention group compared with control was –2.90 (95% CI –4.97 to –0.83). Women: At 12 months, mean (SD) SBP change in mmHg was –3.60 (7.70) in the activity and diet group, and –0.20 (6.60) in the control group. Mean SBP change in the intervention group compared with control was –3.40 (95% CI –6.52 to –0.28). Men: At 12 months, mean (SD) TC change in mmol/l was –0.38 (0.87) in the activity and diet group, and –0.14 (0.64) in the control group. Mean TC change in the intervention group compared with control was –0.24 (95% CI –0.58 to

	0.10). Men: At 12 months, mean (SD) LDL change in mmol/l was –0.27 (0.78) in the activity and diet group, and –0.20 (0.59) in the control group. Mean LDL change in the intervention group compared with control was –0.07 (95% CI –0.38 to 0.24). Men: At 12 months, mean (SD) HDL change in mmol/l was 0.14 (0.18) in the activity and diet group, and –0.05 (0.15) in the control group. Mean HDL change in the intervention group compared with control was 0.19 (95% CI 0.12 to 0.26). Men: At 12 months, mean (SD) TAG change in mmol/l was –0.48 (0.75) in the activity and diet group, and 0.18 (0.67) in the control group. Mean TAG change in the intervention group compared with control was –0.66 (95% CI –0.97 to –0.35). Men: At 12 months, mean (SD) DBP change in mmHg was –4.90 (5.70) in the activity and diet group, and 2.10 (5.00) in the control group. Mean DBP change in the intervention group compared with control was –7.00 (95% CI –9.37 to –4.63). Men: At 12 months, mean (SD) SBP change in mmHg was –5.40 (8.30) in the activity and diet group, and 0.10 (7.70) in the control group. Mean SBP change in the intervention group compared with control was –5.50 (95% CI –9.03 to –1.97). *Women: at 12 months, significant decreases from baseline were seen in the activity and diet group compared with the control groups for total energy intake (–2057 vs 60 kJ/day,* p≤*0.001), total fat intake (–8.8 vs –0.9%,* p≤*0.001), saturated fat (–3.9 vs –0.4,* p≤*0.001) and cholesterol intake (–113 vs –5 mg/day,* p≤*0.001). A significant increase was seen for aerobic capacity (+6.4 vs 0.0 mg/kg per min,* p≤*0.001). Also, the estimated 12 year CHD risk decreased by 3.5 events/1000 persons in the activity and diet group compared with an increase of 1.3 in the control group (*p≤*0.001).* *Men: at 12 months, significant changes in baseline were seen in the* activity and diet *group compared with the control groups for total energy intake (–2368 vs 155 kJ/day,* p≤*0.001), total fat intake (–9.5 vs 0.8%,* p≤*0.001), saturated fat (–4.2 vs –0.2,* p≤*0.001) and cholesterol intake (–185 mg/day vs 7 mg/day,* p≤*0.001). A significant increase was seen for aerobic capacity (+8.6 mg/kg per min vs –0.2 mg/kg per min,* p≤*0.001). Also, the estimated 12 year CHD risk decreased by 21.8 events/1000 persons in the activity and diet group compared with an increase of 0.6 in the control group (*p≤*0.001).*
Quality and comments	*Significant differences between men in both intervention groups vs control for DBP (*p<*0.001), TC for women in diet group vs control (*p≤*0.01), and diet and exercise group vs control (*p≤*0.05), and LDL levels in women in both intervention groups vs control (*p≤*0.05).* Dietary intake estimated from participants' 7-day food diaries, with further probing for more detail by trained interviewers when collecting the data by telephone. Activity assessed by supervising staff.

Midwest Exercise Trial 2003 RCT	
Results	*For both women and men,* VO_{2max} *increased in both intervention and control groups over the 16 months, but were significantly increased in the activity and diet group.* *No significant differences were seen from baseline for energy intake (kcal), carbohydrate or fat intake in any group.* *A significant increase from baseline in protein intake (g) was seen in the intervention group of men (102 g to 106 g at16 months), but this was not seen in any of the other groups.* *FPG was reported at 9 and 16 months, but SDs for the mean change was not. However, only the intervention group of women showed a significant change from control (5.37 vs 5.66 mmol/l at 9 months, 5.06 vs 5.35 mmol/l at 16 months, no p value given).*
Quality and	Possible difference between baseline energy intake for men (3084 kcal

comments	intervention vs 3524 kcal control). Dietary intake was measured during a 2-week period when all meals were taken in the university cafeteria, and food consumption outside was measured using diet recalls. Activity was supervised and recorded by a study investigator.

Reported harms

ODES 1995 (in Shaw CR and HTA) RCT	
Harms	*One death and two cancers (allocation not known).*
Quality and comments	…

Wood 1991 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Midwest Exercise Trial 2003 RCT	
Harms	No major adverse events occurred during the study.
Quality and comments	…

Generalisability

ODES 1995 (in Shaw CR and HTA) RCT	
Country and setting	Norway. Community-based?
Participants (included/excluded)	*Included if aged 41 to 50 years, sedentary (exercise no more than once per week), BMI >24 kg/m^2, DBP 86 to 99 mmHg, TC 5.2 to 7.74 mmol/l, HD L<1.2 mmol/l, fasting serum TAG >1.4 mmol/l. Excluded if overt diabetes or CVD, other disease or drugs that could interfere with test results, treatment with antihypertensive drugs, acetylsalicylic acid, lipid-lowering diet, personal traits unsuitable for inclusion.*
Recruitment	Participants recruited from continuous screening programme of 40-year old men and women in Oslo. No further details reported.
Intervention (mode and intensity)	12 months, contacted 158 times (baseline, three times per week and follow-up at 12 months)
Duration of active intervention	*12 months*
Control (mode and intensity)	*12-month control. Contacted at baseline and 12 months.*
Delivery of intervention/control (who)	N/R other than exercise 'under the guidance of highly qualified instructors'.
Dropout rates	3% in activity and diet group and 0% in control at 12 months, (includes 5 excluded)
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Wood 1991 (in HTA) RCT	
Country and setting	USA. University clinic?

Participants (included/excluded)	*Included if aged between 25 and 49 years, 120 to 150% IBW, BMI (kg/m^2) 28 to 34 for men, BMI 24 to 30 for women, non-smokers, sedentary (exercise less than twice per week, <30 min per time), resting BP <160/95 mmHg, plasma cholesterol <6.72 mmol/l, plasma TAG <5.65 mmol/l, average less than four alcoholic drinks per day, generally good health.* *Excluded if medication known to affect BP or lipid metabolism, pregnancy, lactating or taking oral contraception in past 6 months or planning pregnancy in subsequent 2 years.*
Recruitment	Potential participants were invited to be screened via mass media, followed with telephone interviews.
Intervention (mode and intensity)	12-month intervention. Contacted 25 times (baseline then weekly for first 3 months, then every other week for 3 months, then monthly)
Duration of active intervention	*12 months for diet. Less clear for activity. Activity was increased unto the maximum at 4 months, and monthly logs were then maintained – so assume 4 months for activity?*
Control (mode and intensity)	*Contacted twice (baseline and 12 months)*
Delivery of intervention/control (who)	Dietary recommendations were presented by a registered dietitian. Group sessions assumed to be dietitian? No details of who supervised activity.
Dropout rates	*18% in diet and activity group and 10% in control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Analyses restricted to individuals with complete data only.

Midwest Exercise Trial 2003 RCT	
Country and setting	USA. University clinics – no further details.
Participants (included/excluded)	Included if aged 17–35 years old and had BMI between 25.0 and 34.9 kg/m^2, met or exceeded the 85th percentile for triceps skinfold thickness of the second National Health and Nutrition Examination Survey population. Participants were sedentary at the time of intake and did not exceed 500 kcal/week of physical activity as measured by a physical activity recall questionnaire. Excluded if had a history of chronic disease (i.e., diabetes, heart disease, etc), elevated BP (>140/90 mmHg), elevated lipid concentrations (cholesterol >6.72 mmol/l; TAG >5.65 mmol/l), or elevated fasting glucose concentrations (>7.8 mmol/l) were excluded. Additionally, participants were excluded if they were smokers, if they took medications that would affect physical performance (i.e., ß-blockers) or metabolism (i.e., thyroid medications or steroids), or if they lacked the ability to perform laboratory tests or participate in exercise of moderate intensity.
Recruitment	Participants were recruited from the University of Nebraska-Kearney, The University of Kansas, and their respective surrounding communities. Participants were 'compensated' for participation – no details.
Intervention (mode and intensity)	*Exercise sessions (25 min at baseline to 45 min at 6 months) on 5 days per week for 16 months.* *Assessments at baseline, 4, 9, 12, 16 months. Also additional exercise assessment (about every 2 months and 4 months). Diet assessments at baseline, 9, and 16 months. Also multiple diet recall assessments.*
Duration of active intervention	16 months
Control (mode and intensity)	Assessments at baseline, 4, 9, 12, 16 months. Diet assessments at baseline, 9, and 16 months. Also multiple diet recall assessments.

Delivery of intervention/control (who)	Research assistant supervised exercise sessions.
Dropout rates	*44% dropout overall at 16 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.6 Physical activity and diet vs information

Weight loss

FDPS 2001 (in HTA – diet and physical activity vs control) RCT	
Aim	To determine the feasibility and effects of a programme of changes in lifestyle designed to prevent or delay the onset of type 1 diabetes in participants with IGT.
Participants	People who were overweight (BMI >25 kg/m^2), aged between 40 and 66 years old, and with IGT (plasma glucose 7.8 to 11.0 mmol/l). *522 total – 350 F, 172 M. Mean (SD) age 55 (7) years overall. Mean (SD) BMI 31.3 (4.6), treatment (n=265) , 31.0 (4.5) control (n=257)*
Intervention	Participants informed at start of risk factors for diabetes, 3-day food diary at baseline provided basis for dietary advice in second session, advised to reduce weight to goal of BMI less than 25 kg/m^2 but in practice weight targets were 5–10 kg weight loss; advised to consume >50% energy as carbohydrate, <10% as saturated fat, 20% as mono- and polyunsaturated fat or up to 25% if surplus is from monounsaturated fat; <300 mg/day cholesterol and 1 g protein/kg IBW per day, encouraged to increase fibre intake to 15 g/1000 kcal, encouraged to use low-fat milk products, low-fat meat products, soft margarine and vegetable oil rich in monounsaturated fatty acids (primarily rapeseed oil); energy content re-evaluated if no weight loss at visits, if no weight loss in first 6–12 months and BMI >30 kg/m^2 a VLED is considered (6–12 week duration with group meetings every 1–2 weeks); dietary advice individually tailored and person responsible for preparing meals in family invited to attend sessions (if not the participant), advice tailored to participants educational level. Participants individually guided to increase endurance exercise (programme differed between study centres) also when possible there was a supervised progressive individually tailored circuit type resistance training twice weekly, encouraged to perform 30 min daily moderate exercise, 3-day food diary kept every 3 months, 24-h exercise diary kept every 3 months and 12-month physical activity history completed on annual visit along with 2 km walking test.
Control	*At baseline participants advised to adjust total energy intake to reduce BMI to below 25 kg/m^2, also less than 30% of energy intake from fat, reduce alcohol intake and stop smoking, verbal and written dietary advice, verbal general information regarding health benefits of recreational exercise, additional routine advice at yearly follow-up where 3 day food record assessed and 2 km walking test performed.*
Length of follow-up	*2 to 6 years (mean 3.2 years)*
Results	*Used figures from Lindstrom 2003 as latest publication, so results are different from the HTA figures.* At 12 months, mean (SD) weight change in kg was –4.50 (5.00) in the activity and diet group, and –1.00 (3.70) in the diet group. Mean weight change in the intervention group compared with control was –3.50 (95% CI –4.27 to –2.73) At 24 months, mean (SD) weight change in kg was –3.50 (5.50) in the activity and diet group, and –0.80 (4.40) in the diet group. Mean weight change in the intervention group compared with control was –2.70 (95% CI –3.60 to –1.80). At 36 months, mean (SD) weight change in kg was –3.50 (5.10) in the activity and diet group, and –0.90 (5.40) in the diet group. Mean weight change in the intervention group compared with control was –2.60 (95% CI –3.59 to –1.61).

Quality and comments	Blinded assessment stated as done. ITT analysis not done. Random allocation but no description of concealment. Significant difference between groups regarding SBP (mmHg, SD): 136 (17) control group vs 140 (18) intervention group (*p*=0.03). Twenty-two participants had VLED in year 1 and 25 in year 2 of 3–8 weeks duration and 500–800 kcal/day; before final inclusion criteria decided 4% participants included with one abnormal OGTT only, 6% included based on high plasma glucose (not less than 6.4 mmol/l fasting or random sample after a fast of at least 4 h) together with one high 2 h plasma glucose concentration. Authors contacted, reply received regarding numbers of participants assessed, changes in BP and lipids, energy content of VLED, causes of death and serious adverse events including group allocation.

Other outcomes

FDPS 2001 (in HTA) RCT	
Results	*Used values from Lindstrom 2003 as latest publication, so results are different from the HTA values.* *At 12 months, mean (SD) TC change in mmol/l was –0.10 (0.70) in the activity and diet group, and –0.10 (0.70) in the information group. Mean TC change in the intervention group compared with control was 0.00 (95% CI –0.12 to 0.12).* *At 36 months, mean (SD) TC change in mmol/l was –0.10 (0.90) in the activity and diet group, and 0.10 (0.80) in the information group. Mean TC change in the intervention group compared with control was –0.20 (95% CI –0.36 to –0.04).* *At 12 months, mean (SD) HDL change in mmol/l was 0.05 (0.19) in the activity and diet group, and 0.02 (0.17) in the information group. Mean HDL change in the intervention group compared with control was 0.03 (95% CI 0.00 to 0.06).* *At 36 months, mean (SD) HDL change in mmol/l was 0.14 (0.20) in the activity and diet group, and 0.11 (0.19) in the information group. Mean HDL change in the intervention group compared with control was 0.03 (95% CI –0.01 to 0.07).* *At 12 months, mean (SD) TAG change in mmol/l was –0.02 (0.60) in the activity and diet group, and 0.00 (0.70) in the information group. Mean TAG change in the intervention group compared with control was –0.20 (95% CI –0.31 to –0.09).* *At 36 months, mean (SD) TAG change in mmol/l was –0.10 (0.60) in the activity and diet group, and 0.00 (0.80) in the information group. Mean TAG change in the intervention group compared with control was –0.10 (95% CI –0.23 to 0.03).* *At 12 months, mean (SD) FPG change in mmol/l was –0.20 (0.70) in the activity and diet group, and 0.00 (0.70) in the information group. Mean FPG change in the intervention group compared with control was –0.20 (95% CI –0.32 to –0.08).* *At 36 months, mean (SD) FPG change in mmol/l was0.00 (0.70) in the activity and diet group, and 0.10 (0.70) in the information group. Mean FPG change in the intervention group compared with control was –0.10 (95% CI –0.23 to 0.03). TC:HDL-cholesterol ratios were significantly lower in the activity and diet group compared with information at both 12 and 36 months (*p<*0.005).* *The proportion of sedentary individuals was 14% and 30% at year 1 (*p<*0.0001 for difference between groups) and 17 and 29% at year 3 (*p=*0.0028) in the intervention and control groups, respectively. However, the total amount of reported time spent physically active did not change, but moderate-to-vigorous Leisure Time Physical Activity (LTPA) increased in the intervention group compared with the control group at years 1 and 3.* *The % energy as carbohydrate increased; the % energy of fat, saturated fat, and also monounsaturated fat decreased; the fibre density increased; and cholesterol intake decreased more in the intervention group than the control*

	group during the first year. The absolute amounts of fat decreased, and energy intake decreased in the intervention group more than in the control group. At 3 years the reductions in energy, fat (% energy and g), saturated fat (% energy), and monounsaturated fat (% energy), and the increase in carbohydrates (% energy) and fibre density were still statistically significantly greater in the intervention group.
Quality and comments	Dietary intake was assessed using a 3-day food record at baseline (before the randomisation visit) and before every annual visit. Activity was assessed using the validated Kuopio Ischaemic Heart Disease Risk Factor Study 12-month LTPA questionnaire at baseline and at every annual visit.

Reported harms

FDPS 2001 (in HTA) RCT	
Harms	One death and two cases of breast cancer were reported in the intervention group, and one participant developed cancer of the large intestine in the diet only group. During the first 3 years of the study, 22 people (9%) in the intervention group and 51 (20%) of the diet only group developed diabetes (p=0.0001). The use of VLED preparations did not affect diabetes risk; 8% of the users developed diabetes in 3 years.
Quality and comments	…

Generalisability

FDPS 2001 (in HTA) RCT	
Country and setting	Finland. Five participating centres – no further details.
Participants (included/excluded)	*Included if aged 40–65 years, BMI >25 kg/m^2, IGT (2 h plasma glucose 7.8–11.0 mmol/l), OGTT 75 g with a non-diabetic fasting glucose concentration (plasma glucose <7.8 mmol/l), mean value of two OGTTs (less strict criteria used in ≤1% of total number of participants).* *Excluded if previous diagnosis of diabetes mellitus (other than gestational diabetes mellitus), persons involved regularly in vigorous exercise programme, participants receiving treatment to lower plasma glucose (other than routine dietary and health advice), chronic disease making 6-year survival improbable, other medical characteristics likely to interfere with study participation, unbalanced clinical conditions such as thyroid and liver disease.*
Recruitment	From epidemiological surveys, opportunistic population screening with special emphasis on people in high-risk groups (obese, first degree relatives of people with type 2 diabetes). Also through advertisements in local newspapers.
Intervention (mode and intensity)	2–6 years, contacted at baseline, at 1–2 weeks, at 5–6 weeks then at 3, 4 and 6 months and every 3 months thereafter
Duration of active intervention	Diet: 36 months. Physical activity: not clear
Control (mode and intensity)	*2–6 years, contacted at baseline then at annual intervals*
Delivery of intervention/control (who)	A nutritionist gave individualised and group information. The study physician and the nutritionist informed participants of general risk factors for diabetes. Physical activity was delivered either by an exercise instructor or physiotherapist if part of the study team, or if not, by commercial services.

Dropout rates	*13% in the physical activity and diet group and 21% in the diet group at 36 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Data for completers only.

1.5.7 Physical activity and diet vs diet alone

Weight loss

ODES 1995 (in Shaw CR and HTA) RCT	
Aim	The primary aim of the trial was to compare the isolated and combined effects of the diet and exercise on the variables fibrinogen, fibrinolytic capacity, coagulation factor VII and platelet volume. Secondary aims were the effects on other coagulation and fibrinolytic components and activities; lipids and lipoproteins; fatty acids; glucose and insulin response to a glucose load; clinical, physiological and anthropometric variables; and quality of life
Participants	*Men and women aged 41 to 50 years who were overweight (BMI >24 kg/m^2) and sedentary.* *219 total – 21 F, 198 M. Mean (SD) age 44.9 (2.5) years. Mean (SD) BMI (kg/m^2) 29.54 (3.89) diet group (*n=*55), 28.56 (3.22) exercise group (*n=*54), 28.57 (3.47) diet and exercise group (*n=*67), 28.30 (3.15) control group (*n=*43).*
Intervention	For initial 8 weeks the intensity and duration of supervised endurance workouts increased progressively then maintained at three times per week for 1 h each session at 60–80% maximum heart rate as assessed at baseline using treadmill; 60% of each workout was aerobic, 25% circuit training and 15% fast walking/jogging, attendance measured and exercise log book kept. Advised to stop smoking. Dietary counselling with spouse at baseline then individually at 3- and 9-month follow-up sessions. Diet adapted to individual's risk profile with main focus on energy restriction in those overweight, increase in fish and vegetables, decrease in saturated fat, cholesterol, sugar, and salt restriction for those with elevated BP. Weight targets agreed and set. 180 food-frequency questionnaire at baseline and 12 months.
Control	*Dietary counselling with spouse at baseline then individually at 3- and 9-month follow-up sessions. Diet adapted to individual's risk profile with main focus on energy restriction in those overweight, increase in fish and vegetables, decrease in saturated fat, cholesterol, sugar, and salt restriction for those with elevated BP. Weight targets agreed and set. 180 food-frequency questionnaire at baseline and 12 months. Advised to stop smoking.*
Length of follow-up	12 months
Results	*Only 12-month outcomes reported.* At 12 months, mean (SD) weight change in kg was –5.60 (4.84) in the activity and diet group, and –4.00 (5.05) in the diet group. Mean weight change in the intervention group compared with control was –1.60 (95% CI –3.41 to 0.21).
Quality and comments	TC and LDL levels significantly lower in the exercise and the diet and exercise groups (p<0.05). ITT not done. Only blood analyses blinded. Discrepancy between results in published papers. Good concealment of allocation.

Pavlou 1989 1 (in HTA) RCT	
Aim	To determine the role of exercise in relation to the type of diet, rate of weight loss and defined exercise experience on long-term maintenance

Participants	Healthy men. *160 total (for complete study) – all men. Mean (SD) age 41.5 (7.59) years activity and LED, 42.9 (6.63) years LED (Pavlou 1ab). Mean (SD) age 45.1 (10.0) years activity and food based PSMF, 49.6 (8.4) years food-based PSMF (Pavlou 1cd). Mean (SD) age 41.8 (10.44) years activity and liquid PSMF, 41.8 (7.57) years liquid PSMF (Pavlou 1ef). Mean (SD) age 46.1 (9.33) years activity and VLED, 44.5 (9.6) years VLED (Pavlou 1gh). Mean BMI 32.54 kg/m^2 activity and LED, 32.4 LED (Pavlou 1ab). Mean BMI 32.07 kg/m^2 activity and food based PSMF, 31.5 food-based PSMF (Pavlou 1cd). Mean BMI 30.13 kg/m^2 activity and liquid PSMF, 34.82 liquid PSMF (Pavlou 1ef). Mean BMI 31.89 kg/m^2 activity and VLED, 33.78 VLED (Pavlou 1gh). Data for completers only. No details of allocation to each group.*
Intervention (including details of diet)	All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts. LED (group a): BEDD where 1000 kcal/day selected from usual four food groups in quantities thought to meet basic requirements PSMF (group c): ketogenic diet of meat, fish and fowl used as only dietary source to provide equivalent of 1.2 g high biological value protein per kg of IBW or 1000 kcal/day, no carbohydrate and all fat ingested came from meat, fish and fowl; 2.8 g potassium chloride daily PSMF (group e): DPC-70; assumed PSMF 420 kcal/day diet of powdered protein-carbohydrate mix derived from calcium caseinate, egg albumin and fructose dissolved in water or other non-energy liquid, fat content zero, fortified with vitamins and minerals to meet US Recommended Daily Allowance, mix five packets per day in 30oz (85 g) of non-energy liquid and consume no other nutrients; 2.8 g potassium chloride daily VLED (group g): DPC 800; assumed VLED 800 kcal/day diet provided in powdered form to be consumed similarly to DPC-70, provided a complete mixture of nutrients and similar nutritionally to BEDD except for less energy; Activity: exercise 90 min supervised exercise programme three times/week from baseline to week 8 which consisted of 35–60 min of aerobic activity e.g. walk-jog-run (70–85% maximum heart rate), callisthenics and relaxation techniques
Control	*All participants attended weekly educational sessions up to week 8 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 8, non-energy liquids including coffee were allowed in unrestricted amounts.* *LED (group b): BEDD where 1000 kcal/day selected from usual four food groups in quantities thought to meet basic requirements* *PSMF (group d): ketogenic diet of meat, fish and fowl used as only dietary source to provide equivalent of 1.2 g high biological value protein per kg of IBW or 1000 kcal/day, no carbohydrate and all fat ingested came from meat, fish and fowl; 2.8 g potassium chloride daily* *PSMF (group f): DPC-70; assumed PSMF 420 kcal/day diet of powdered protein-carbohydrate mix derived from calcium caseinate, egg albumin and fructose dissolved in water or other non-energy liquid, fat content zero, fortified with vitamins and minerals to meet US Recommended Daily Allowance, mix five packets per day in 30oz (85 g) of non-energy liquid and consume no other nutrients; 2.8 g potassium chloride daily* *VLED (group h): DPC 800; assumed VLED 800 kcal/day diet provided in powdered form to be consumed similarly to DPC-70, provided a complete mixture of nutrients and similar nutritionally to BEDD except for less energy; Participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks*

Length of follow-up	*86 weeks.*
Results	Only 18-month outcomes reported. Published figures showed results over the initial 12 weeks, but difficult to determine the numbers exactly. At 18 months, mean (SD) weight change in kg was –9.19 (8.52) in the activity and LED group, and –3.57 (6.93) in the LED group. Mean weight change in the intervention group compared with control was –5.62 (95% CI –12.30 to 1.06). At 18 months, mean (SD) weight change in kg was –8.64 (8.36) in the activity and food PSMF group, and –1.13 (6.23) in the food PSMF group. Mean weight change in the intervention group compared with control was –7.51 (95% CI –12.62 to –2.40). At 18 months, mean (SD) weight change in kg was –9.68 (8.65) in the activity and liquid PSMF group, and –0.93 (6.18) in the liquid PSMF group. Mean weight change in the intervention group compared with control was –8.75 (95% CI –15.08 to –2.42). At 18 months, mean (SD) weight change in kg was –12.40 (9.42) in the activity and VLED group, and –3.45 (6.89) in the VLED group. Mean weight change in the intervention group compared with control was –8.95 (95% CI –14.46 to –3.44).
Quality and comments	Blinded assessment not done. Possible ITT analysis. Random allocation but no description of concealment. Weight data derived from graph and SDs calculated.

Pavlou 1989 2 (in HTA) RCT	
Aim	To determine the role of exercise in relation to the type of diet, rate of weight loss and defined exercise experience on long-term maintenance.
Participants	Healthy men (no weight inclusion criteria). *24 total – all men. Mean (SD) age 49.2 (6.48) years activity and LED, 44.8 (7.84) years LED (Pavlou 2ab) Mean (SD) age 46.1 (5.14) years activity and food based PSMF, 48.1 (4.65) years food based PSMF (Pavlou 2cd). Mean BMI 31.75 (kg/m^2) activity and LED, 31.92 LED (Pavlou 2ab). Mean BMI 31.11 (kg/m^2) activity and food based PSMF, 30.4 food-based PSMF (Pavlou 2cd). Data for completers only. No details of numbers allocated.*
Intervention (including details of diet)	All participants attended weekly educational sessions up to week 12 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 12, non-energy liquids including coffee were allowed in unrestricted amounts. LED (group a): BEDD where 1000 kcal/day selected from usual four food groups in quantities thought to meet basic requirements PSMF (group c): PSMF, ketogenic diet of meat, fish and fowl used as only dietary source to provide equivalent of 1.2 g high biological value protein per kg of IBW or 1000 kcal/day, no carbohydrate and all fat ingested came from meat fish and fowl; 2.8 g potassium chloride daily Exercise: 90 min supervised exercise programme three times/week from baseline to week 12 which consisted of 35–60 min of aerobic activity e.g. walk–jog–run (70–85% maximum heart rate), callisthenics and relaxation techniques

Control	*All participants attended weekly educational sessions up to week 12 that included behaviour modification, diet and general nutrition and exercise education; all participants given multivitamins, daily food and activity record to week 12, non-energy liquids including coffee were allowed in unrestricted amounts.* *LED (group b): BEDD where 1000 kcal/day selected from usual four food groups in quantities thought to meet basic requirements.* *PSMF (group d): PSMF, ketogenic diet of meat, fish and fowl used as only dietary source to provide equivalent of 1.2 g high biological value protein per kg of IBW or 1000 kcal/day, no carbohydrate and all fat ingested came from meat fish and fowl; 2.8 g potassium chloride daily* *No exercise: participants to continue normal daily activity and not to participate in any form of additional supervised and/or unsupervised physical activity during initial 8 weeks*
Length of follow-up	168 weeks
Results	*Only 18- and 36-month outcomes reported. Published figures showed results over the initial 12 weeks, but difficult to determine exact numbers from graphs.* At 18 months, mean (SD) weight change in kg was –11.83 (9.26) in the activity and LED group, and –5.75 (7.54) in the LED group. Mean weight change in the intervention group compared with control was –6.08 (95% CI –16.19 to 4.03). At 18 months, mean (SD) weight change in kg was –14.04 (9.89) in the activity and food PSMF group, and –7.29 (7.98) in the food PSMF group. Mean weight change in the intervention group compared with control was –6.75 (95% CI –17.89 to 4.39). At 36 months, mean (SD) weight change in kg was –10.67 (8.93) in the activity and LED group, and –3.25 (6.83) in the LED group. Mean weight change in the intervention group compared with control was –7.42 (95% CI –16.97 to 2.13). At 36 months, mean (SD) weight change in kg was –13.00 (9.59) in the activity and food PSMF group, and –3.83 (7.10) in the food PSMF group. Mean weight change in the intervention group compared with control was –9.17 (95% CI –19.63 to 1.29).
Quality and comments	Blinded assessment not done. Possible ITT analysis. Random allocation but no description of concealment. Weight data derived from graph and SDs calculated.

Wood 1991 (in HTA) RCT	
Aim	To test the hypothesis that exercise (walking or jogging) will increase HDL-cholesterol levels in moderately overweight, sedentary people who adopt a hypoenergetic National Cholesterol Education Programme (NCEP) diet
Participants	*Sedentary people (exercise less than twice per week) who were moderately overweight (BMI 28 to 34 kg/m^2 for men, 24 to 20 kg/m^2 for women).* *264 total – 132 F, 132 M. Mean (SD) age 39.1 (6.4) years women, 40.3 (6.3) years men. Mean BMI (SD)(kg/m^2) 27.9 (2.2) women, 30.7 (2.2) men.* (Noted as lowest mean BMI in HTA.) *Eighty-seven allocated to diet, 90 to diet and exercise, and 87 to control.*
Intervention (including details of diet)	NCEP step 1 diet consisting of 55% energy as carbohydrate, 30% as fat (saturated fat ≤10%), dietary cholesterol <300 mg/day, energy reduction. Activity was aerobic exercise (brisk walking or jogging) at 60–80% maximum heart rate initially for 25 min three times per week increasing to 45 min three times per week by month 4, monthly activity logs kept
Control	*NCEP step 1 diet consisting of 55% energy as carbohydrate, 30% as fat (saturated fat ≤10%), dietary cholesterol <300 mg/day, energy reduction. Assumed to have been instructed to maintain usual diet and exercise patterns.*

Length of follow-up	*12 months*
Results	*Only 12 months outcomes reported.* Women: At 12 months, mean (SD) weight change in kg was –5.10 (5.30) in the activity and diet group, and 1.30 (5.20) in the diet group. Mean weight change in the intervention group compared with control was –1.00 (95% CI –3.51 to 1.51). Men: At 12 months, mean (SD) weight change in kg was –8.70 (5.70) in the activity and diet group, and –5.10 (5.80) in the diet group. Mean weight change in the intervention group compared with control was –3.60 (95% CI –6.14 to –1.06).
Quality and comments	Significant differences between men in both intervention groups vs control for DBP (p<0.001), TC for women in diet group vs control (p≤0.01), and diet and exercise group vs control (p≤0.05), and LDL levels in women in both intervention groups vs control (p≤0.05). Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment.

Other outcomes

ODES 1995 (in Shaw CR and HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.48 (0.89) in the activity and diet group, and –0.23 (0.65) in the diet group. Mean TC change in the intervention group compared with control was –0.25 (95% CI –0.53 to 0.03). At 12 months, mean (SD) LDL change in mmol/l was –0.39 (0.81) in the activity and diet group, and –0.18 (0.72) in the diet group. Mean LDL change in the intervention group compared with control was –0.21 (95% CI –0.49 to 0.07). At 12 months, mean (SD) HDL change in mmol/l was 0.13 (0.15) in the activity and diet group, and 0.05 (0.12) in the diet group. Mean HDL change in the intervention group compared with control was 0.08 (95% CI 0.03 to 0.13). At 12 months, mean (SD) TAG change in mmol/l was –0.58 (0.97) in the activity and diet group, and –0.23 (1.01) in the diet group. Mean TAG change in the intervention group compared with control was –0.35 (95% CI –0.71 to 0.01). At 12 months, mean (SD) DBP change in mmHg was –5.20 (7.26) in the activity and diet group, and –3.40 (7.21) in the diet group. Mean DBP change in the intervention group compared with control was –1.80 (95% CI –4.44 to 0.84). At 12 months, mean (SD) SBP change in mmHg was –5.90 (8.87) in the activity and diet group, and –6.40 (10.10) in the diet group. Mean SBP change in the intervention group compared with control was 0.50 (95% CI –2.99 to 3.99). At 12 months, mean (SD) FPG change in mmol/l was –0.26 (0.64) in the activity and diet group, and –0.21 (0.50) in the diet group. Mean FPG change in the intervention group compared with control was –0.05 (95% CI –0.26 to –0.16). *At 12 months, significant changes from baseline were seen in the activity and diet group for energy intake (–382 kcal), protein (–7.7 g), fat (–26.5 g), % energy as fat (–5.3%), sugar (–19.6 g), cholesterol (–94 mg), saturated fatty acids (–12.1 g), monounsaturated fatty acids (–10.2 g), and polyunsaturated fatty acids (–2.9 g).* *At 12 months, significant changes from baseline were seen in the diet group for energy intake (–550 kcal), protein (–13.4 g), fat (–32.5 g), % energy as fat (–5.1%), carbohydrate (–42.3 g), sugar (–16.8 g), alcohol (–2.5 g), cholesterol (–121 mg), saturated fatty acids (–13.6 g), monounsaturated fatty acids (–12.3 g) and polyunsaturated fatty acids (–4.9 g).* *At 12 months,* VO_{2max} *had increased by 6.7 ml/kg per min in the activity and*

	diet group, which was significantly different to the diet group (+1.7 ml/kg per min, p<*0.05).*
Quality and comments	Dietary intake assessed through a validated food-frequency questionnaire. Activity was supervised, and home activity was recorded (no details). Also participants interviewed at 12 months about changes in activity habits.

Pavlou 1989 1 (in HTA) RCT	
Results	*No other outcomes by different diet groups were reported. BP reported by exercise and diet vs diet only. Added to summary statistics.* *At 6 months, mean (SD) DBP change in mmHg was –11.50 in the activity and diet group, and –2.70 in the diet group (to calculate SDs).* *At 6 months, mean (SD) SBP change in mmHg was –6.30 in the activity and diet group, and –3.90 in the diet group (to calculate SDs).* At 18 months, mean (SD) DBP change in mmHg was –10.40 (8.30) in the activity and diet group, and 1.70 (8.30) in the diet group. Mean DBP change in the intervention group compared with control was –12.10 (95% CI –15.20 to –9.00). At 18 months, mean (SD) SBP change in mmHg was –7.70 (12.70) in the activity and diet group, and 1.20 (12.70) in the diet group. Mean SBP change in the intervention group compared with control was –8.90 (95% CI –13.65 to –4.15).
Quality and comments	…

Pavlou 1989 2 (in HTA) RCT	
Results	*Only* VO_{2max} *at 8 weeks reported by different diet groups.*
Quality and comments	…

Wood 1991 (in HTA) RCT	
Results	Women: At 12 months, mean (SD) TC change in mmol/l was –0.28 (0.52) in the activity and diet group, and –0.39 (0.61) in the diet group. Mean TC change in the intervention group compared with control was 0.11 (95% CI –0.16 to 0.38). Women: At 12 months, mean (SD) LDL change in mmol/l was –0.29 (0.46) in the activity and diet group, and –0.28 (0.63) in the diet group. Mean LDL change in the intervention group compared with control was –0.01 (95% CI –0.27 to 0.25). Women: At 12 months, mean (SD) HDL change in mmol/l was 0.02 (0.18) in the activity and diet group, and –0.15 (0.26) in the diet group. Mean HDL change in the intervention group compared with control was 0.17 (95% CI 0.06 to 0.28). Women: At 12 months, mean (SD) TAG change in mmol/l was –0.02 (0.26) in the activity and diet group, and 0.09 (0.36) in the diet group. Mean TAG change in the intervention group compared with control was –0.11 (95% CI –0.26 to 0.04). Women: At 12 months, mean (SD) DBP change in mmHg was –2.00 (4.10) in the activity and diet group, and –2.20 (5.10) in the diet group. Mean DBP change in the intervention group compared with control was 0.20 (95% CI –1.98 to 2.38). Women: At 12 months, mean (SD) SBP change in mmHg was –3.60 (7.70) in the activity and diet group, and –4.10 (6.00) in the diet group. Mean SBP change in the intervention group compared with control was 0.50 (95% CI –2.64 to 3.64). Men: At 12 months, mean (SD) TC change in mmol/l was –0.38 (0.87) in the activity and diet group, and –0.42 (0.51) in the diet group. Mean TC change in the intervention group compared with control was 0.04 (95% CI –0.28 to 0.36).

	Men: At 12 months, mean (SD) LDL change in mmol/l was –0.27 (0.78) in the activity and diet group, and –0.39 (0.48) in the diet group. Mean LDL change in the intervention group compared with control was 0.12 (95% CI –0.17 to 0.41). Men: At 12 months, mean (SD) HDL change in mmol/l was 0.14 (0.18) in the activity and diet group, and 0.02 (0.17) in the diet group. Mean HDL change in the intervention group compared with control was 0.12 (95% CI 0.04 to 0.20). Men: At 12 months, mean (SD) TAG change in mmol/l was –0.48 (0.75) in the activity and diet group, and –0.12 (0.59) in the diet group. Mean TAG change in the intervention group compared with control was –0.36 (95% CI –0.66to –0.06). Men: At 12 months, mean (SD) DBP change in mmHg was –4.90 (5.70) in the activity and diet group, and –2.40 (6.60) in the diet group. Mean DBP change in the intervention group compared with control was –2.50 (95% CI –5.22 to 0.22). Men: At 12 months, mean (SD) SBP change in mmHg was –5.40 (8.30) in the activity and diet group, and –4.10 (8.10) in the diet group. Mean SBP change in the intervention group compared with control was –1.30 (95% CI –4.92 to 2.32). *Women: at 12 months, a significant increase was seen for aerobic capacity in the activity and diet group compared with diet alone (+6.4 mg/kg/min vs 1.4 mg/kg/min, p≤0.001). Also, the estimated 12yr CHD risk decreased by 3.5 events/1000 persons in the activity and diet group compared with an decrease of 1.0 in the diet group (*p≤*0.05).* *Men: at 12 months, significant changes in baseline were seen in the activity and diet group compared with the diet groups for total fat intake (–9.5 vs –6.0%,* p≤*0.05). A significant increase was seen for aerobic capacity (+8.6 mg/kg/min vs +1.6 mg/kg/min,* p≤*0.001). Also, the estimated 12 year CHD risk decreased by 21.8 events/1000 persons in the activity and diet group compared with an decrease of 12.9 in the diet group (*p≤*0.05).*
Quality and comments	*Significant differences between men in both intervention groups vs control for DBP (*p*<0.001), TC for women in diet group vs control (*p≤*0.01), and diet and exercise group vs control (*p≤*0.05), and LDL levels in women in both intervention groups vs control (*p≤*0.05).* Dietary intake estimated from participants' 7-day food diaries, with further probing for more detail by trained interviewers when collecting the data by telephone. Activity assessed by supervising staff.

Reported harms

ODES 1995 (in Shaw CR and HTA) RCT	
Harms	*One death and two cancers (allocation not known).*
Quality and comments	…

Pavlou 1989 1 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Pavlou 1989 2 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wood 1991 (in HTA) RCT	
Harms	None reported.

Quality and comments	…

Generalisability

ODES 1995 (in Shaw CR and HTA) RCT	
Country and setting	Norway. Community-based?
Participants (included/excluded)	*Included if aged 41 to 50 years, sedentary (exercise no more than once per week), BMI >24 kg/m^2, DBP 86 to 9 9mmHg, TC 5.2 to 7.74 mmol/l, HDL <1.2 mmol/l, fasting serum TAG >1.4 mmol/l. Excluded if overt diabetes or CVD, other disease or drugs that could interfere with test results, treatment with antihypertensive drugs, acetylsalicylic acid, lipid-lowering diet, personal traits unsuitable for inclusion.*
Recruitment	Participants recruited from continuous screening programme of 40-year old men and women in Oslo. No further details reported.
Intervention (mode and intensity)	12 months, contacted 158 times (baseline, three times per week and follow-up at 12 months)
Duration of active intervention	*12 months*
Control (mode and intensity)	Dietary intervention lasted 12 months. 4 contacts (baseline, 3, 9, 12 months).
Delivery of intervention/control (who)	N/R other than exercise 'under the guidance of highly qualified instructors'.
Dropout rates	3% in activity and diet group and 5% in diet group at 12 months, (includes five excluded)
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Pavlou 1989 1 (in HTA) RCT	
Country and setting	USA. Workplace.
Participants (included/excluded)	*Included men, aged 26–52 years, euthyroid, free from any physical, psychological or metabolic impairment. Exclusion criteria not stated.*
Recruitment	Men were recruited from the Boston Police Department and the Metropolitan District Commission. No further details reported.
Intervention (mode and intensity)	8 weeks plus 18 months post-treatment follow-up (weekly from baseline to week 8 then at 8 months and 18 months post-treatment)
Duration of active intervention	8 weeks for diet and activity
Control (mode and intensity)	As above
Delivery of intervention/control (who)	No details.
Dropout rates	31% overall at 18 months post-treatment.
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Pavlou 1989 2 (in HTA) RCT	
Country and setting	USA. Workplace
Participants (included/excluded)	*Included men aged 26–52 years, euthyroid, free from any physical, psychological or metabolic impairment. No details of exclusion.*

Recruitment	Men were recruited from the Boston Police Department and the Metropolitan District Commission. No further details reported.
Intervention (mode and intensity)	12 weeks plus 36 months post-treatment follow-up, contacted 16 times (weekly from baseline to week 12 then at 6, 8 and 18 months post-treatment)
Duration of active intervention	8 weeks for diet and activity
Control (mode and intensity)	As above
Delivery of intervention/control (who)	No details.
Dropout rates	13% overall at 36 months post-treatment
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Wood 1991 (in HTA) RCT	
Country and setting	USA. University clinic?
Participants (included/excluded)	*Included if aged between 25 and 49 years, 120 to 150% IBW, BMI 28 to 34 kg/m^2 for men, BMI 24 to 30 kg/m^2 for women, non-smokers, sedentary (exercise less than twice per week, <30 min per time), resting BP <160/9 5mmHg, plasma cholesterol <6.72 mmol/l, plasma TAG <5.65 mmol/l, average less than four alcoholic drinks per day, generally good health.* *Excluded if medication known to affect BP or lipid metabolism, pregnancy, lactating or taking oral contraception in past 6 months or planning pregnancy in subsequent 2 years.*
Recruitment	Potential participants were invited to be screened via mass media, followed with telephone interviews.
Intervention (mode and intensity)	12-month intervention. Contacted 25 times (baseline then weekly for first 3 months, then every other week for 3 months, then monthly)
Duration of active intervention	*12 months for diet. Less clear for activity. Activity was increased unto the maximum at 4 months, and monthly logs were then maintained – so assume 4 months for activity?*
Control (mode and intensity)	12-month intervention. Contacted 25 times (baseline then weekly for first 3 months, then every other week for 3 months, then monthly)
Delivery of intervention/control (who)	Dietary recommendations were presented by a registered dietitian. Group sessions assumed to be dietitian? No details of who supervised activity.
Dropout rates	*18% in diet and activity group and 10% in diet at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Analyses restricted to individuals with complete data only.

1.5.8 Physical activity and behaviour therapy vs information

Weight loss

Wing 1998 (in HTA) RCT	
Aim	To assess the effect of lifestyle intervention over 2 years on changes in weight, CHD risk factors, and incidence of diabetes in overweight adults with a parental history of diabetes
Participants	Adults aged 40 to 55 years who did not have diabetes, and were overweight (30 to 100% of IBW). *154 total – 122 F, 32 M. Mean (SD) age 46.4 (4.5) years exercise (*n*=37), 45.3 (4.9) control (*n*=40). Mean (SD) BMI (kg/m^2) 36.0 (3.7) exercise, 36.0 (5.4) control.*
Intervention	Exercise behaviour topic each week, 50–60 min walk with therapist at each weekly meeting (second supervised walk available each week for weeks 1–10), gradually increased exercise to estimated energy expenditure of 1500 kcal per week (e.g. 3 miles brisk walking 5 days per week), other activities periodically introduced to the participants such as aerobics and line dancing. Each meeting included a lecture on a topic related to changing exercise behaviour (stimulus control, problem-solving, reducing barriers, exercising in different weather conditions, stretching).
Control	*Participants received LEARN behavioural manual with information on healthy eating, exercise and behavioural strategies; participants encouraged to lose weight and exercise on their own, only participated in the assessments*
Length of follow-up	24 months
Results	*At 6 months, mean weight change (SD) was –2.10 (4.20) kg in the activity and BT group compared with –1.50 (2.70) kg in the information group. Mean weight change in the intervention group compared with information was –0.60 (95% CI –2.31 to 1.11).* *At 12 months, mean weight change (SD) was –0.40 (4.80) kg in the activity and BT group compared with –0.30 (4.50) kg in the information group. Mean weight change in the intervention group compared with information was –0.10 (95% CI –2.52 to 2.32).* *At 24 months, mean weight change (SD) was 1.00 (4.70) kg in the activity and BT group compared with –0.30 (4.50) kg in the information group. Mean weight change in the intervention group compared with information was 1.30 (95% CI –0.99 to 3.59)*
Quality and comments	Author confirmed main study and sub-study results. Blinded assessment done. ITT analysis done. Random allocation but no description of concealment.

Messier 2004 RCT	
Aim	To determine whether long-term exercise and dietary weight loss are more effective, either separately or in combination, than usual care in improving physical function, pain, mobility in older overweight/obese adults with osteoarthritis
Participants	People with osteoarthritis, aged 60 years and older who were overweight (BMI ≥28 kg/m^2). Total 316 – 227 F, 89 M. Mean (SD) age years 69 (6.97) years activity and BT (*n*=76), 69 (0.88) years information (*n*=78). Mean (SD) BMI (kg/m^2) 34.0 (6.10) activity and BT, 34.2 (5.30) information.

Intervention	Exercise programme 3 days/week consisted of an aerobic phase (15 min), a resistance-training phase (15 min), a second aerobic phase (15 min), and a cool-down phase (15 min). The first 4 months of the 18-month intervention was facility-based. At any time after the first 4 months, participants who wished to exercise at home underwent a 2-month transition phase during which he or she alternated attendance between the facility and the home. Hence, some participants remained in a facility-based programme, others opted for a home-based programme, and some participants chose a combined facility-home-based programme. Provided with an aerobic exercise prescription that included walking within a heart rate range of 50–75% of heart rate reserve. The resistance-training portion of the programme consisted of two sets of 12 repetitions of the following exercises: leg extension, leg curl, heel raise, and step-up. Cuff weights and weighted vests were used to provide resistance. A 1.0–1.5-min rest interval separated each exercise. Following two orientation sessions, participants began the exercise programme using the lowest possible resistance. Resistance was increased after the participant performed two sets of 12 repetitions for two consecutive days. For participants in the home-based programme, weights were exchanged at the participant's request or after a determination was made during face-to-face or telephone contact to increase the weights. Telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Exercise and attendance logs were used to gather data and monitor progress. Goal was to produce and maintain an average weight loss of 5% during the 18-month intervention period. Dietary intervention was divided into three phases: intensive (months 1–4), transition (months 5–6), and maintenance (months 7–18). Major emphasis of the intensive phase was to heighten awareness of the importance of and need for changing eating habits in order to lower energy intake. Behaviour change was facilitated using self-regulatory skills. These skills included self-monitoring, goal setting, cognitive restructuring, problem-solving, and environmental management. One introductory individual session was followed by 16 weekly sessions (three group sessions and one individual session each month). Each group session included problem-solving, the review of a specific topic, and tasting of several well-balanced, low-fat, nutritious foods prepared with widely available ingredients. The individual sessions were used to review individual progress, solve problems, answer questions and set goals. *The transition phase included sessions every other week for 8 weeks (three group sessions and one individual session). The goals for this phase included assisting participants who had not reached their weight loss goals in establishing new goals, and maintaining and preventing relapse in those participants who had reached their weight loss goals.* *The maintenance phase included monthly meetings and phone contacts, alternated every 2 weeks. Additionally, newsletters that provided pertinent nutritional information and notice of upcoming meetings were mailed at regular intervals. The goals of the maintenance phase included assisting participants who had reached their weight loss goals to maintain this weight loss, and providing counselling for participants who had a difficult time losing weight and adhering to the intervention. Adherence to the intervention was based on attendance at scheduled sessions and completion of the monthly assessment of weight.*

Control	The group met monthly for 1 h for the first 3 months. A health educator, who scheduled videotaped presentations and physician talks on topics concerning OA, obesity and exercise, organised the healthy lifestyle programme. Patients were advised to follow the American College of Rheumatology and European League Against Rheumatism recommendations for weight loss and exercise as treatments for OA. Question-and-answer sessions followed each presentation. Monthly phone contact was maintained during months 4–6, followed by contact every other month during months 7–18. During phone contact, information on pain, medication use, illnesses and hospitalisation was obtained.
Length of follow-up	*18 months*
Results	*At 18 months, mean (SD) weight change in kg was –5.20 (7.37) in the activity and BT group, and –1.10 (6.23) in the information group. Mean weight change in the intervention group compared with information was –4.10 (95% CI –6.26 to –1.94).*
Quality and comments	*ITT analysis done. Blinded assessment done. Good concealment of allocation. SDs calculated*

Other outcomes

Wing 1998 (in HTA) RCT	
Results	*At 6 months, mean (SD) TC change in mmol/l was 0.12 (0.72) in the activity and BT group, and 0.12 (0.50) in the information group. Mean TC change in the activity and BT group compared with information was 0.00 (95% CI –0.30 to 0.30).* *At 6 months, mean (SD) LDL change in mmol/l was 0.03 (0.52) in the activity and BT group, and 0.08 (0.46) in the information group. Mean LDL change in the activity and BT group compared with information was –0.05 (95% CI –0.29 to 0.19).* *At 6 months, mean (SD) HDL change in mmol/l was 0.02 (0.16) in the activity and BT group, and –0.02 (0.11) in the information group. Mean HDL change in the activity and BT group compared with information was 0.04 (95% CI –0.03 to 0.11).* *At 6 months, mean (SD) TAG change in mmol/l was 0.12 (1.64) in the activity and BT group, and 0.29 (0.32) in the information group. Mean TAG change in the activity and BT group compared with information was –0.17 (95% CI –0.74 to 0.40).* *At 6 months, mean (SD) DBP change in mmHg was –1.70 (12.20) in the activity and BT group, and –2.20 (8.00) in the information group. Mean DBP change in the activity and BT group compared with information was 0.50 (95% CI –4.50 to 5.50).* *At 6 months, mean (SD) SBP change in mmHg was –2.40 (18.90) in the activity and BT group, and –2.00 (10.50) in the information group. Mean SBP change in the activity and BT group compared with information was –0.40 (95% CI –7.80 to 7.00).* *At 6 months, mean (SD) FPG change in mmol/l was 0.00 (0.70) in the activity and BT group, and 0.10 (0.50) in the information group. Mean FPG change in the activity and BT group compared with information was –0.10 (95% CI –0.40 to 0.20).* *At 6 months, mean (SD) change in %HbA_{1c} was 0.10 (0.30) in the activity and BT group, and 0.20 (0.40) in the information group. Mean %HbA_{1c} change in the activity and BT group compared with information was –0.10 (95% CI –0.27 to 0.07).* *At 12 months, mean (SD) TC change in mmol/l was 0.36 (0.82) in the activity and BT group, and 0.39 (0.70) in the information group. Mean TC change in the activity and BT group compared with information was –0.03 (95% CI –0.43*

to 0.37).
At 12 months, mean (SD) LDL change in mmol/l was 0.15 (0.54) in the activity and BT group, and 0.24 (0.66) in the information group. Mean LDL change in the activity and BT group compared with information was –0.09 (95% CI –0.40 to 0.22).
At 12 months, mean (SD) HDL change in mmol/l was 0.16 (0.18) in the activity and BT group, and 0.08 (0.16) in the information group. Mean HDL change in the activity and BT group compared with information was 0.08 (95% CI –0.01 to 0.17).
At 12 months, mean (SD) TAG change in mmol/l was 0.26 (2.19) in the activity and BT group, and 0.40 (1.25) in the information group. Mean TAG change in the activity and BT group compared with information was –0.14 (95% CI –1.07 to 0.79).
At 12 months, mean (SD) DBP change in mmHg was 0.90 (9.70) in the activity and BT group, and 4.90 (8.20) in the information group. Mean DBP change in the activity and BT group compared with information was –4.00 (95% CI –8.67 to 0.67).
At 12 months, mean (SD) SBP change in mmHg was 1.10 (15.80) in the activity and BT group, and 1.10 (9.60) in the information group. Mean SBP change in the activity and BT group compared with information was 0.00 (95% CI –6.82 to 6.82).
At 12 months, mean (SD) FPG change in mmol/l was 0.10 (0.70) in the activity and BT group, and 0.00 (0.60) in the information group. Mean FPG change in the activity and BT group compared with information was 0.10 (95% CI –0.24 to 0.44).
At 24 months, mean (SD) TC change in mmol/l was 0.33 (0.64) in the activity and BT group, and 0.18 (0.53) in the information group. Mean TC change in the activity and BT group compared with information was 0.15 (95% CI –0.14 to 0.44).
At 24 months, mean (SD) LDL change in mmol/l was 0.22 (0.61) in the activity and BT group, and 0.03 (0.46) in the information group. Mean LDL change in the activity and BT group compared with information was 0.19 (95% CI –0.08 to 0.46).
At 24 months, mean (SD) HDL change in mmol/l was 0.05 (0.17) in the activity and BT group, and 0.04 (0.24) in the information group. Mean HDL change in the activity and BT group compared with information was 0.01 (95% CI –0.09 to 0.11).
At 24 months, mean (SD) TAG change in mmol/l was 0.33 (1.46) in the activity and BT group, and 0.52 (1.14) in the information group. Mean TAG change in the activity and BT group compared with information was –0.19 (95% CI –0.84 to 0.46).
At 24 months, mean (SD) DBP change in mmHg was 2.00 (8.00) in the activity and BT group, and 2.00 (8.00) in the information group. Mean DBP change in the activity and BT group compared with information was 0.00 (95% CI –3.98 to 3.98).
At 24 months, mean (SD) SBP change in mmHg was 0.90 (13.90) in the activity and BT group, and –1.50 (12.00) in the information group. Mean SBP change in the activity and BT group compared with information was 2.40 (95% CI –4.06 to 8.86).
At 24 months, mean (SD) FPG change in mmol/l was 0.40 (0.90) in the activity and BT group, and 0.20 (0.40) in the information group. Mean FPG change in the activity and BT group compared with information was 0.20 (95% CI –0.15 to 0.55).
At 24 months, mean (SD) change in %HbA_{1c} was –0.10 (0.50) in the activity and BT group, and –0.10 (0.30) in the information group. Mean %HbA_{1c} change in the activity and BT group compared with information was 0.00 (95% CI –0.21 to 0.21).
At 6, 12, and 24 months, the activity and BT group reported non-significant decreases from baseline in energy intake and percentage of energy from fat (only Block Food-frequency of %fat was significant at 24 months). However,

	greater, often non significant decreases were seen in the information group. VO_{2max} increased in the activity and BT group significantly at 6 months, but decreased at 24 months (not significant). The information group showed no significant changes from baseline. *At 24 months, the relative risk (if weight loss of 4.5 kg compared with no weight loss) of developing diabetes in the activity and BT group was about 0.88 and about 0.88 in the information group. For people with IGT, the relative risks were about 0.91 and 0.88 respectively.*
Quality and comments	Dietary intake assessed using self-completed questionnaires and 3-day food diaries. Activity assessed using self-completed questionnaire (administered as an interview).

Messier 2004 RCT	
Results	*At 18 months, significant improvements were seen for self-reported physical function, stair climb time, and pain in the activity and BT group compared with information (p<0.05).*
Quality and comments	…

Reported harms

Wing 1998 (in HTA) RCT	
Harms	7% in the information group and 14% of the activity and BT group developed diabetes during the 24-month study. The development of diabetes was associated with increased initial IGT.
Quality and comments	…

Messier 2004 RCT	
Harms	Two deaths occurred, but were unrelated to the interventions. One participant tripped and sustained a laceration to his head. No details of allocation.
Quality and comments	…

Generalisability

Wing 1998 (in HTA) RCT	
Country and setting	USA. No further details – university hospital?
Participants (included/excluded)	Included if aged 40–55 years, non-diabetic (confirmed by OGTT), one or two biological parents with type 2 diabetes, 30–100% above IBW. Excluded if diagnosis of diabetes.
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*Two years, contacted approximately 52 times (baseline, weekly for first 6 months then every 2 weeks for next 6 months then two × 6 week course during second year)*
Control (mode and intensity)	Contacted at baseline, 6 months, 1 year and at 2 years.
Duration of active intervention	24 months

Delivery of intervention/control (who)	Group meetings were led by a multidisciplinary team, with primary therapists being a behaviour therapist and an exercise physiologist
Dropout rates	*16% activity and BT and 23% information at 24 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Messier 2004 RCT	
Country and setting	USA. Older Americans Independence Centre.
Participants (included/excluded)	Included if aged 60 years or older, calculated BMI 28 kg/m^2 or more, knee pain on most days of the month, sedentary activity pattern with <20 min of formal exercise once weekly for the past 6 months, self-reported difficulty in at least one of the following activities ascribed to knee pain: walking one-quarter of a mile (three to four city blocks), climbing stairs, bending, stooping, kneeling (e.g., to pick up clothes), shopping, house cleaning or other self-care activities, getting in and out of bed, standing up from a chair, lifting and carrying groceries, or getting in and out of the bath, radiographic evidence of grade I–III tibiofemoral or patellofemoral OA based on weight-bearing anteroposterior and sunrise view radiographs, and willingness to undergo testing and intervention procedures. Excluded if serious medical condition that prevented safe participation in an exercise programme, including symptomatic heart or vascular disease (angina, peripheral vascular disease, congestive heart failure), severe hypertension, recent stroke, chronic obstructive pulmonary disease, severe insulin-dependent diabetes mellitus, psychiatric disease, renal disease, liver disease, active cancer other than skin cancer, and anaemia, a Mini-Mental State Examination score of <24, inability to finish the 18-month study or unlikely to be compliant, inability to walk without a cane or other assistive device, participation in another research study, reported alcohol consumption of more than 14 drinks per week, ST segment depression of at least 2 mm at an exercise level of 4 METS or less, hypotension, or complex arrhythmias during a graded exercise test, inability to complete the protocol, in the opinion of the clinical staff, because of frailty, illness, or other reasons.
Recruitment	Mass mailings to age-eligible persons within the target area, targeted mailings to employees of the university and medical centre, presentations to various groups of older adults, mass media advertisement, and placement of posters (with pull-off reply cards attached) in strategic locations. Also, strategies were developed to enhance recruitment among racial minorities, including ads and interviews on minority-run radio stations, newspaper ads in predominantly African American publications, letters to churches attended mainly by minorities, and inserts in these church bulletins. Initial screening for major eligibility criteria was via telephone.

Intervention (mode and intensity)	*Exercise 3 days/week for 4 months (facility-based), then either home or facility-based. For participants in the home-based programme, telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Assessment at baseline, 6, 18 months. Also introductory individual session was followed by 16 weekly sessions (three group sessions and one individual session each month).* *The transition phase included sessions every other week for 8 weeks (three group sessions and one individual session).* *The maintenance phase included monthly meetings and phone contacts, alternated every 2 weeks. Contacts for the two interventions were done consecutively on the same day and at the same location.*
Duration of active intervention	18 months
Control (mode and intensity)	Group met monthly for 1 h for the first 3 months. Monthly phone contact was maintained during months 4–6, followed by contact every other month during months 7–18.
Delivery of intervention/control (who)	Exercise and BT: not reported Information: health educator, who scheduled videotaped presentations and physician talks on topics concerning OA, obesity, and exercise, organised the healthy lifestyle programme.
Dropout rates	*24% activity and BT, 14% information at 24 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.9 Physical activity, diet and behaviour therapy vs control (no treatment)

Weight loss

Jalkanen 1991 (in HTA) RCT	
Aim	To test the effect of a non-pharmacological weight-reduction programme in primary care on cardiovascular risk factors among people who were overweight and had hypertension.
Participants	People who were aged between 35 and 39 years, who were overweight (BMI 27 to 34 kg/m^2) and who also had hypertension (DBP ≥95mmHg). Total 50 – 25 F?, 25 M? *Mean age not stated. Mean (SD) weight 86 (14) kg intervention (*n=*25), 80 (11) kg control.*
Intervention	1000–1500 kcal/day diet, education on behaviour modification and exercise, choice of food, medical aspects of overweight and CVD risk factors, leaflets on reduction of salt and fat consumption and increase in exercise, three exercise sessions with physiotherapist, bicycle trips organised and free tickets for local swimming pool
Control	*Usual visit with nurse every 3 months, offered active treatment at end of the study period, received no personal counselling or advice*
Length of follow-up	12 months
Results	At 12 months, mean (SD) weight change in kg was –4.00 (7.05) in the combined group, and 0.00 (5.92) in the control group. Mean weight change in the intervention group compared with control was –4.00 (95% CI –7.65 to –0.35)
Quality and comments	Weight appears different between groups at baseline. ITT possibly done. Blinded assessment not done. Random allocation but no description of concealment. Mean change in weight and risk factors at 12 months calculated from actual values, SDs also calculated, data show no change in weight, HDL-cholesterol and TAG at 12 months in control group.

Jeffery 1993 (in HTA) RCT	
Aim	To determine the effect of food provision and financial incentives in comparison with standard behaviour therapy
Participants	People who were overweight (14 to 32 kg overweight), aged 25 to 45 years. *Total 202 – 101 F, 101 M. Mean age 37.5 years standard intervention (*n=*40), 38.5 years standard plus food provision (*n=*40), 38.1 years standard plus financial incentives (*n=*41), 37.6 standard plus food provision plus financial incentives (*n=*41), 35.7 years control (*n=*40). Mean BMI (kg/m^2) 30.9 standard, 30.8 standard plus food, 31.1 standard plus cash, 31.1 standard plus food and cash, 31.1 control.*

Intervention	Group behavioural counselling including weigh-in, presentations of information by interventionist, group discussion and a review of progress; participants assigned to an individualised energy goal of 1000 or 1500 kcal/day on basis of baseline body weight to produce estimated weight loss of 1kg per week; participants selected a weight loss goal of 14, 18 or 23 kg, if goal reached participants had energy goals adjusted upwards to a level estimated to maintain this body weight; primary dietary instruction emphasised importance of remaining below energy goals, restriction of fat and increased consumption of complex carbohydrate also stressed; participants initially instructed to walk or bike amount equivalent to 50 kcal per day for 5 days per week, gradually increased to final goal of 1000 kcal per week; daily food records kept for first 20 weeks and for 1 week each month thereafter which included exercise taken; behavioural techniques included stimulus control, problem-solving strategies, social assertion, short-term goal setting and reinforcement techniques for enhancing motivation, cognitive strategies for replacing negative thinking with more positive statements and constructive self-statements, relapse prevention and social support.
Control	Received no intervention. Individuals could do whatever they wished to lose weight on their own, and were asked to return for evaluations at 6, 12 and 18 months.
Length of follow-up	*30 months*
Results	*Six-month results were shown in graphically only (see Comments), details not reported in the text.* At 12 months, mean (SD) weight change in kg was –5.87 (7.58) in the combined group, and –1.51 (6.34) in the control group. Mean weight change in the intervention group compared with control was –4.36 (95% CI –8.22 to –0.50) At 18 months, mean (SD) weight change in kg was –5.55 (7.49) in the combined group, and –0.62 (6.09) in the control group. Mean weight change in the intervention group compared with control was –4.93 (95% CI –8.71 to –1.15) At 30 months, mean (SD) weight change in kg was –3.05 (6.78) in the combined group, and 0.25 (5.99) in the control group. Mean weight change in the intervention group compared with control was –3.30 (95% CI –6.83 to 0.23)
Quality and comments	*Only standard intervention vs control used in analysis.* Mean weight change at 12, 18 and 30 months derived from graph, SDs calculated. ITT done? Blinded assessment not done. Random allocation but no description of concealment.

Ost 1976 (in HTA) RCT	
Aim	To compare the effectiveness of behaviour therapy in the treatment of obesity with fenfluramine and a waiting list control group.
Participants	People who were overweight (15% or moreover IBW) Total 45 – 38 F, 7 M. Mean age 40.9 years overall. Mean *(SD) weight 87.0 kg combined (*n=*15), 81.5 kg control (*n=*15).*
Intervention	All participants received 45 min baseline lecture on food and nutrition. Focus of first four sessions was behaviour therapy consisting of situational control of over eating such as cue avoidance. Focus of sessions 5–7 was 500 kcal/day deficit diet with recommended food plan (based on food exchanges) nearest to this value chosen (1000, 1200, 1500 and 1800 kcal food plans), energy count diary completed. Focus of session 8 was to increase energy expenditure and introduction of regular physical exercise and a daily exercise record, diet and exercise designed to produce 0.7 kg of weight loss per week.

Control	*All participants received 45 min baseline lecture on food and nutrition. Waiting list control condition, participants told could not receive treatment at moment due to large number of applicants and would receive treatment at a later date.*
Length of follow-up	68 weeks
Results	At 16 weeks, mean (SD) weight change in kg was –9.35 (4.47) in the combined group, and –3.51 (4.04) in the control group. Mean weight change in the intervention group compared with control was –5.84 (95% CI –9.40 to –2.28). At 12 months, mean (SD) weight change in kg was –4.60 (6.20) in the combined group, and –2.40 (5.30) in the control group. Mean weight change in the intervention group compared with control was –2.20 (95% CI –7.02 to 2.62).
Quality and comments	*Only combined and control groups used for comparisons.* *Significant difference at baseline in weight between combined and control groups.* ITT done? Blinded assessment not done. Random allocation but no description of concealment.

TOHP Phase I 1993 (in HTA) RCT	
Aim	To determine the feasibility and efficacy of selected non-pharmacological interventions in reducing or preventing an increase in DBP
Participants	People aged between 30 and 54 years who were overweight (between 115% and 165% of IBW) and who had a high-normal DBP (80 to 89 mmHg). *Total 564 – 179 F, 385 M. Mean (SD) age 43.1 (6.0) years combined (*n*=308), 42.4 (6.2) years control (*n*=256). Mean (SD) weight 90.2 (13.3) kg combined, 89.3 (13.0) kg control.*
Intervention	Weight reduction intervention focused on reducing energy intake, reducing fat, sugar and alcohol intake; shopping, cooking and food selection behaviours; moderate increase in energy expenditure through walking briskly four to five times per week for 45 min each session at 40–55% heart rate reserve; behavioural self-management through goals, reinforcement, social support, graphing weight, problem-solving, relapse prevention, and coping strategies; food and exercise diaries
Control	*No treatment received.*
Length of follow-up	18 months
Results	At 18 months, mean (SD) weight change in kg was –3.83 (6.12) in the combined group, and 0.07 (4.01) in the control group. Mean weight change in the intervention group compared with control was –3.90 (95% CI –4.77 to –3.03) *At 6 months in the combined group, weight change in men was –6.5 kg compared with –3.7 kg in women.* *At 12 months in the combined group, weight change in men was –5.6 kg compared with –2.7 kg in women.* *At 18 months in the combined group, weight change in men was –4.7 kg compared with –1.6 kg in women.* *Although details of the control group were only reported graphically, the text reports that 'the mean weight of the control men did not change and the mean weight of the control women increased 0.2 kg at 18 months'.* *The difference between men and women was statistically significant for all time points for percentage change from baseline (*p*<0.05). However, the treatment effect was modified more strongly by baseline weight than by sex.*
Quality and comments	Sodium reduction and stress management treatment groups excluded from analyses. Higher proportion of men in combined group than in control (*p*=0.016). ITT possibly done. Blinded assessment not done. Good concealment of allocation.

TOHP Phase II 2001 (in HTA) RCT	
Aim	To determine the feasibility and efficacy of selected non-pharmacological interventions in preventing hypertension
Participants	People aged between 30 and 54 years who were overweight (between about 110 and 165% of IBW) and who had a high-normal DBP (83 to 89 mmHg). *Total 1191 – 409 F, 782 M. Mean (SD) age 43.4 (6.1) years combined (*n*=595), 43.2 (6.1) years control (*n*=596). Mean (SD) weight 93.4 (14.1) kg combined, 93.6 (13.5) kg control.*
Intervention	Four phases of programme including pre-intensive phase of 1–4 months wait before start of treatment when participants advised to prevent weight gain and contacted monthly; intensive phase during initial 14 weeks with mean weight loss goal of at least 4.5 kg or to achieve IBW during first 6 months then to maintain weight, reduced energy intake, count fat intake, increase physical activity four to five times per week at 30–45 min per session at 40–55% heart rate reserve, supervised exercise in four of 14 initial weekly sessions; transitional phase during weeks 15–26 of treatment with behavioural skills such as individual problem-solving, relapse prevention, cognitive reframing and coping imagery; extended phase from week 27 onwards consisted of mini modules including topics such as 'supermarket savvy', 'stress and time management', 'walking across America'.
Control	*No treatment received.*
Length of follow-up	36 to 48 months
Results	*At 6 months, mean (SD) weight change in kg was –4.40 (7.16) in the combined group, and 0.10 (5.94) in the control group. Mean weight change in the intervention group compared with control was –4.50 (95% CI –5.28 to –3.72).* At 12 months, mean (SD) weight change in kg was –3.33 (6.86) in the combined group, and 0.53 (6.06) in the control group. Mean weight change in the intervention group compared with control was –3.86 (95% CI –4.63 to –3.09). At 18 months, mean (SD) weight change in kg was –2.00 (5.80) in the combined group, and 0.07 (4.20) in the control group. Mean weight change in the intervention group compared with control was –2.70 (95% CI –3.30 to –2.10) At 24 months, mean (SD) weight change in kg was –1.22 (6.26) in the combined group, and 1.17 (6.25) in the control group. Mean weight change in the intervention group compared with control was –2.39 (95% CI –3.13 to –1.65) At 36 months, mean (SD) weight change in kg was –0.20 (5.90) in the combined group, and 1.80 (5.30) in the control group. Mean weight change in the intervention group compared with control was –2.00 (95% CI –2.66 to –1.34) *Although baseline weight was a significant predictor of weight loss at 6 months, and reduced the significance of the greater weight loss in men compared with women, greater weight loss in men persisted consistently thereafter, independent of baseline weight.*
Quality and comments	Numbers in each group assumed for 12- and 24-month data derived from graph, SDs calculated. ITT possibly done. Blinded assessment done. Good concealment of allocation.

TONE 1998 (in HTA) RCT	
Aim	To determine whether weight loss or reduced sodium intake is effective in the treatment of older people with hypertension.

Participants	Older people aged 60 to 80 years with hypertension (treated SBP <145 mmHg and DBP <85 mmHg) and who were overweight (BMI ≥27.8 kg/m^2 for men and ≥27.3 kg/m^2 for women). *Total 294 – 162 F, 132 M. Mean (SD) age 66 (5) years combined (*n=*147), 66 (4) years control (*n=*147). Mean (SD) BMI (kg/m^2) 31.0 (2.3) combined, 31.3 (2.3) control.*
Intervention	*Anti-hypertensive medications withdrawn 90 days after first group intervention sessions, drug specific tapering regimens where participants seen weekly and 3 additional biweekly visits to confirm SBP <150 mmHg and DBP < 90 mmHg.* The group goal was ≥4.5 kg weight loss in 6 months then weight maintenance; individual goals were 5–10% weight loss (depending on baseline BMI) by energy deficit and increase in physical activity; behaviour therapy based on social action theory for lifestyle change, self-monitoring of energy intake, eating behaviours and pulse rate; management of eating behaviours, relapse prevention, participants received individual feedback from food intake records and physical activity records, 'calorie counting' of foods, practical advice on purchase and preparation of inexpensive foods available in supermarkets, group practice of safe, low-level exercise.
Control	Anti-hypertensive medications withdrawn 90 days after first group intervention sessions, drug specific tapering regimens where participants seen weekly and 3 additional biweekly visits to confirm SBP <150 mmHg and DBP < 90 mmHg. *Advised to maintain usual diet and physical activity, speakers who lead discussion on topics unrelated to BP, CVD or diet.*
Length of follow-up	*29 months (median)*
Results	At 12 months, mean (SD) weight change in kg was –5.36 (4.56) in the combined group, and –0.48 (3.24) in the control group. Mean weight change in the intervention group compared with control was –4.88 (95% CI –5.84 to –3.92). At 18 months, mean (SD) weight change in kg was –4.77 (4.52) in the combined group, and –0.21 (3.44) in the control group. Mean weight change in the intervention group compared with control was –4.56 (95% CI –5.55 to –3.57). At 24 months, mean (SD) weight change in kg was –4.58 (4.55) in the combined group, and –0.09 (3.53) in the control group. Mean weight change in the intervention group compared with control was –4.49 (95% CI –5.62 to –3.36) At 30 months, mean (SD) weight change in kg was –4.99 (4.11) in the combined group, and –0.05 (4.17) in the control group. Mean weight change in the intervention group compared with control was –4.94 (95% CI –6.47 to –3.41).
Quality and comments	*Report of two arms of a four-arm study; author provided mean and standard deviation change in weight at 12, 18, 24 and 30 months post randomisation.* ITT not done. Blinded assessment done. Random allocation but no description of concealment.

Other outcomes

Jalkanen 1991 (in HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.20 (1.08) in the combined group, and 0.20 (1.08) in the diet group. Mean TC change in the intervention group compared with control was –0.40 (95% CI –1.04 to 0.24). At 12 months, mean (SD) HDL change in mmol/l was 0.10 (0.29) in the combined group, and 0.00 (0.29) in the control group. Mean HDL change in the intervention group compared with control was 0.10 (95% CI –0.07 to

	0.27). At 12 months, mean (SD) TAG change in mmol/l was –0.50 (0.96) in the combined group, and 0.00 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.50 (95% CI –1.07 to 0.07). At 12 months, mean (SD) DBP change in mmHg was –11.00 (8.30) in the combined group, and –11.00 (8.30) in the control group. Mean DBP change in the intervention group compared with control was 0.00 (95% CI –4.65 to 4.65). At 12 months, mean (SD) SBP change in mmHg was –8.00 (12.70) in the combined group, and –15.00 (12.70) in the control group. Mean SBP change in the intervention group compared with control was 7.00 (95% CI –0.11 to 14.11). *Significant increases from baseline in excretion of sodium were seen in both groups (+35 mmol/day combined and +29 mmol/day control,* p<*0.05). The combined group showed a significant increase from baseline in excretion of potassium (+16 mmol/day,* p<*0.01).* *No significant changes were seen from baseline in either group for intake of carbohydrates, or total energy. The combined group decreased fat intake (–14 g/day) compared with the control group that increased fat intake (+9 g/day). Similarly for protein intake (–6 vs +7 g/day, respectively).*
Quality and comments	*Data show no change in weight, HDL-cholesterol and TAG at 12 months in control group.* *Food records kept for 2–3 days three times in the study period.*

Jeffery 1993 (in HTA) RCT	
Results	*Other outcomes were not reported by group.*
Quality and comments	7-day food diary required to be completed for each group session.

Ost 1976 (in HTA) RCT	
Results	*No other outcomes were reported.* *Seven of the control group had tried to reduce weight during the study period. Four stated that the baseline recording of food intake and exercise had influenced their eating habits. Also three reported that the initial lecture had influenced them in a positive way.*
Quality and comments	…

TOHP Phase I 1993 (in HTA) RCT	
Results	*At 6 months, mean (SD) DBP change in mmHg was –6.30 (6.92) in the combined group, and –3.70 (6.18) in the control group. Mean DBP change in the intervention group compared with control was –2.60 (95% CI –3.71 to –1.49).* At 12 months, mean (SD) DBP change in mmHg was –5.40 (8.47) in the combined group, and –3.10 (7.70) in the control group. Mean DBP change in the intervention group compared with control was –2.30 (95% CI –3.69 to –0.91). At 18 months, mean (SD) DBP change in mmHg was –6.16 (5.88) in the combined group, and –3.91 (6.12) in the control group. Mean DBP change in the intervention group compared with control was –2.25 (95% CI –3.25 to –1.25). *At 6 months, mean (SD) SBP change in mmHg was –6.50 (8.65) in the combined group, and –2.70 (7.73) in the control group. Mean SBP change in the intervention group compared with control was –3.80 (95% CI –5.19 to –2.41).* At 12 months, mean (SD) SBP change in mmHg was –5.80 (6.78) in the combined group, and –3.80 (6.16) in the control group. Mean SBP change in the intervention group compared with control was –2.00 (95% CI –3.11 to –

	0.89). At 18 months, mean (SD) SBP change in mmHg was –5.35 (7.19) in the combined group, and –2.45 (7.37) in the control group. Mean SBP change in the intervention group compared with control was –2.90 (95% CI –4.11 to –1.69). *Although there were sex differences in the results for BP, these were largely (but not exclusively) due to the differential weight loss for men and women.* The relative risk of developing hypertension in the intervention group was 0.66 (95% CI 0.46 to 0.94%).
Quality and comments	…

TOHP Phase II 2001 (in HTA) RCT	
Results	*At 6 months, mean DBP change in the intervention group compared with control was –2.70 (95% CI –3.50 to –2.00).* At 18 months, mean (SD) DBP change in mmHg was –4.50 (6.10) in the combined group, and –3.20 (5.80) in the control group. Mean DBP change in the intervention group compared with control was –1.30 (95% CI –2.02 to –0.58). At 36 months, mean (SD) DBP change in mmHg was –3.20 (6.50) in the combined group, and –2.40 (7.00) in the control group. Mean DBP change in the intervention group compared with control was –0.80 (95% CI –1.62 to 0.02). *At 6 months, mean SBP change in the intervention group compared with control was –3.70 (95% CI –4.70 to –2.80).* At 18 months, mean (SD) SBP change in mmHg was –3.60 (7.90) in the combined group, and –1.80 (7.00) in the control group. Mean SBP change in the intervention group compared with control was –1.80 (95% CI –2.70 to –0.90). At 36 months, mean (SD) SBP change in mmHg was –0.80 (8.70) in the combined group, and 0.60 (8.50) in the control group. Mean SBP change in the intervention group compared with control was –1.40 (95% CI –2.44 to –0.36). *At 36 months, women had a smaller reduction in DBP per kg lost than men (0.26 vs 0.41 mmHg,* p=*0.047), but the change in SBP did not differ between men and women.* The relative risk of developing hypertension in the intervention group was 0.58 (95% CI 0.36 to 0.94) at 6 months, 0.78 (95% CI 0.62 to 1.00) at 18 months and 0.81 (95% CI 0.70 to 0.95) at 36 months.
Quality and comments	…

TONE 1998 (in HTA) RCT	
Results	*Other results not reported for overweight participants alone.* The hazard ratio for the primary end point (recurrence of hypertension or cardiovascular events) was 0.65 (95% CI 0.50 to 0.85) for those randomised to weight loss alone compared with controls.
Quality and comments	…

Reported harms

Jalkanen 1991 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Jeffery 1993 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Ost 1976 (in HTA) RCT	
Harms	In the combined group, nine people experienced at least one of the following once or twice during the treatment period: hunger (seven instances), nervousness (three instances), irritation (three instances), tiredness (two instances) and feebleness (two instances). Two reported no side effects at all.
Quality and comments	…

TOHP Phase I 1993 (in HTA) RCT	
Harms	*One death was reported in the intervention group compared with none in the control group.*
Quality and comments	…

TOHP Phase II 2001 (in HTA) RCT	
Harms	*Five people randomised to weight loss died (three CVD) and two in the usual care group died.*
Quality and comments	…

TONE 1998 (in HTA) RCT	
Harms	Two participants with MI were reported in the intervention group. Four people with MI, and two people with cerebrovascular accidents were reported in the control group (which included non-overweight participants). One case of breast cancer and one of pancreatic cancer were reported – no details of group allocation.
Quality and comments	…

Generalisability

Jalkanen 1991 (in HTA) RCT	
Country and setting	*Finland. Primary care hypertension clinics.*
Participants (included/excluded)	*Included if aged 35–59 years, DBP 95 mmHg or more, BMI 27–34 kg/m^2, attending hypertension clinic.* *No exclusion criteria stated.*
Recruitment	Nurses at the clinics selected suitable participants from records.
Intervention (mode and intensity)	12 months, contacted 35 times (baseline then 1.5 h session weekly for first 6 months, then every 3 weeks for next 6 months)
Duration of active intervention	*12 months*
Control (mode and intensity)	*Contacted five times (at baseline then every 3 months for measurements only)*
Delivery of intervention/control (who)	Initial interview with a nutritionist. Doctor delivered lectures on cardiovascular risk factors, medical aspects of being overweight etc. Nutritionist delivered lectures on food selection, low fat cooking etc. Physiotherapist delivered lectures on physical activity. Psychologist delivered lectures on behaviour modification.
Dropout rates	*4% in the combined group and 0% in the control group at 12 months.*

Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

Jeffery 1993 (in HTA) RCT	
Country and setting	USA. Urban communities. Universities? No further details.
Participants (included/excluded)	Included if aged 25–45 years, 14–32 kg overweight, non-smokers, less than three alcoholic drinks per day. Excluded if on special diets, food allergies, not able to exercise, current serious diseases, prescription medications including oral contraceptives
Recruitment	Newspaper advertisements. Radio announcements. Mailed invitations.
Intervention (mode and intensity)	*18 months with follow-up at 30 months, contacted 79 times (baseline then weekly group sessions to week 20 then monthly with weekly weigh-ins)*
Duration of active intervention	18 months
Control (mode and intensity)	Contacted five times; baseline, 6 months, 12 months, 18 months and 30 months
Delivery of intervention/control (who)	Group sessions led by a trained interventionists with advanced degrees in nutrition or behavioural sciences.
Dropout rates	*Overall 13% at 12 months, 15% at 18 months, 24% at 20 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for complete cases only.

Ost 1976 (in HTA) RCT	
Country and setting	Sweden. No further details.
Participants (included/excluded)	*Included if 15% or more overweight.* *No exclusion criteria reported.*
Recruitment	Local newspaper advertisements.
Intervention (mode and intensity)	16 weeks with follow-up at 68 weeks, contacted two times (baseline then 30 min twice per week for 4 weeks then weekly for 12 weeks then at 68 weeks)
Duration of active intervention	16 weeks
Control (mode and intensity)	*Assessed at baseline, 16 weeks and 68 weeks*
Delivery of intervention/control (who)	Three undergraduates with a thorough knowledge of the behavioural method to be used were therapists for the combined group.
Dropout rates	*27% combined and 27% control at 68 weeks.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

TOHP Phase I 1993 (in HTA) RCT	
Country and setting	USA. Multicentre – no further details.

Participants (included/excluded)	*Included if aged 30–54 years, high-normal DBP and not taking antihypertensive drugs for last 2 months, BP based on three visits between 10–30 days apart with cumulative averages of 75–97, 77–94, 80–89 mmHg; BMI 26.1–36.1 kg/m^2 for men and 24.3–36.1 kg/m^2 for women.* *Excluded if clinical or laboratory evidence of cardiovascular or other life-threatening or disabling diseases, diabetes mellitus, chronic renal failure, cancer, pregnancy or wishing to become pregnant, psychiatric disorders, unwillingness or inability to comply with intervention or data collection; cholesterol ≥6.7 mmol/l.*
Recruitment	N/R
Intervention (mode and intensity)	18 months, contacted at baseline then 90 min sessions weekly for first 14 weeks, then every 2 weeks then every month to 18 months
Duration of active intervention	18 months
Control (mode and intensity)	*Assessed five times (baseline, 3, 6, 12 and 18 months)*
Delivery of intervention/control (who)	Group meetings were lead by a registered dietitian and a psychologist or exercise physiologist.
Dropout rates	5% in the combined group and 8% in the control group at 18 months.
Treatment of dropouts (return to baseline, or last measurement?)	If missed an appointment for reasons unrelated to BP, BP treated as missing at random and excluded from the analysis. If the final termination appointment was missed for reasons unrelated to BP, the last valid measure of BP was used.

TOHP Phase II 2001 (in HTA) RCT	
Country and setting	USA. Multicentre – no further details.
Participants (included/excluded)	*Included if 110–165% IBW or BMI 26.1–37.4 kg/m^2 (men), 24.4–37.4 kg/m^2 (women); DBP 83–89 (average of all nine measurements), SBP <140 mmHg, aged 30–54 years, completion and return of 24 h and separate 8 h urine collection and 3-day food record.* *Excluded if medically diagnosed hypertension, history of CVD, diabetes mellitus, malignancy in last 5 years (other than non-melanoma skin cancer), other serious life-threatening illness requiring medical treatment, current use, current use of prescription medication that affects BP and non prescription diuretics, serum creatinine ≥1.7 mg/dl in men and ≥1.5 mg/dl in women or casual serum glucose ≥200 mg/dl; more than 21 alcoholic drinks per week, current pregnancy or intention of pregnancy*
Recruitment	Mass mailings, community screening, media advertising, other referral strategies. Centres were able to tailor the recruitment strategies used as required.
Intervention (mode and intensity)	Minimum of 36 months, contacted three times at baseline plus one individual visit then weekly for 14 weeks, every 2 weeks for the next 6 weeks, three to six mini modules each year supplemented by participant initiated contact every 2 weeks
Duration of active intervention	36 months
Control (mode and intensity)	*Assessed seven times (baseline then every 6 months for a minimum of 36 months)*
Delivery of intervention/control (who)	Group meetings were lead by a dietitian or a health educator.
Dropout rates	8% in the combined group and 7% in the control group at 36 months.

Treatment of dropouts (return to baseline, or last measurement?)	N/R. If participants were prescribed antihypertensive medication, the last value was used. If participants received other medication that affected BP or became pregnant, the value at that visit was treated as missing.

TONE 1998 (in HTA) RCT	
Country and setting	USA. Academic health centres.
Participants (included/excluded)	Included if stable health, aged 60–80 years, mean SBP <145 mmHg, mean DBP <85 mmHg, taking one anti-hypertensive medication, taking two anti-hypertensive medications if successfully stepped down prior to randomisation; obese strata involved people with BMI 27.8 kg/m^2 for men and 27.3kg/m^2 for women; independent in their daily living activities, permission of personal physician, ability to alter diet and increase physical activity. Excluded if cancer in the past 5 years, IDDM, severe hypertension, CVD, peripheral vascular disease, psychiatric illness, current or recent (in last 6 months) drug therapy for asthma or chronic obstructive lung disease, corticosteroid therapy for longer than 1 month, 4.5 kg or more involuntary and unexplained weight loss in the last year, serum creatinine >2 mg/dl, serum potassium >5.5 mEq/l, haemoglobin <11 g/dl, plasma glucose >260 mg/dl, volume of baseline 24 h urine specimen <500 ml, less than 14 alcoholic drinks per week, current or planned participation in another intervention study, another member of household member of TONE.
Recruitment	Mass mailings, BP screening, media advertising, enrolment from participants in previous trials. Centres were able to tailor the recruitment strategies used as required.
Intervention (mode and intensity)	*Median 29 months contacted approximately 45 times (baseline then weekly for first 4 months then fortnightly for the next 3 months then monthly)*
Duration of active intervention	29 months (median)
Control (mode and intensity)	Median 29 months contacted approximately ten times (baseline then quarterly)
Delivery of intervention/control (who)	Groups lead by trained interventionists (often dietitians or exercise counsellors).
Dropout rates	*7% intervention and unclear for the control group at 29 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

1.5.10 Physical activity, diet and behaviour therapy vs information

Weight loss

Lindahl 1999 (in HTA) RCT	
Aim	To assess the effects of lifestyle intervention on cardiovascular risk factors in general, and specifically on fibrinolysis
Participants	People who were overweight (BMI >27 kg/m^2) and had IGT (abnormal OGTT). *Total 186 – 117 F, 69 M. Mean (SE) age 54.8 (0.94) years combined (*n*=93 completed), 56.2 (0.85) years information (*n*=93 completed). Mean (SD) BMI 31.0 (0.33) kg/m^2 combined, 30.2 (0.33) kg/m^2 information.*
Intervention	Full board for initial month which included 140 h of scheduled activities including aerobic exercise of low to moderate intensity for 2.5 h daily; diet of 1800 kcal/day for men and 1500 kcal/day for women consisting of 20% intake from fat and high in fibre to produce a slow but persistent weight decline; behavioural modification strategies included stress management and relapse prevention; no alcohol was permitted and participants were strongly encouraged not to smoke; additional learning session for 4 days at 12 months
Control	*Health survey and 30–60 min counselling session which included oral and written advice on lifestyle changes regarding IGT and obesity, repeated at 12 months*
Length of follow-up	*12 months*
Results	At 12 months, mean (SD) weight change in kg was –5.40 (4.44) in the combined group, and –0.50 (2.75) in the information group. Mean weight change in the intervention group compared with control was –4.90 (95% CI –5.96 to –3.84).
Quality and comments	Fasting glucose and TAG significantly lower in intervention group a (*p*=0.0001, *p*=0.04 respectively) and intervention group b had a higher BMI (*p*=0.06). ITT not done. Blinded assessment not reported. Random allocation but no description of concealment.

Messier 2004 RCT	
Aim	To determine whether long-term exercise and dietary weight loss are more effective, either separately or in combination, than usual care in improving physical function, pain, mobility in older overweight/obese adults with osteoarthritis
Participants	People with osteoarthritis, aged ≥60 years who were overweight (BMI ≥28 kg/m^2) Total 316 – 227 F, 89 M. Mean (SD) age years 69 (7.16) years activity (*n*=80), 69 (0.88) years information (*n*=78). Mean (SD) BMI (kg/m^2) 34.2 (5.37) activity, 34.2 (5.30) information.

Intervention	Exercise programme 3 days/week consisted of an aerobic phase (15 min), a resistance-training phase (15 min), a second aerobic phase (15 min), and a cool-down phase (15 min). The first 4 months of the 18-month intervention was facility-based. At any time after the first 4 months, participants who wished to exercise at home underwent a 2-month transition phase during which he or she alternated attendance between the facility and the home. Hence, some participants remained in a facility-based programme, others opted for a home-based programme, and some participants chose a combined facility–home-based programme. Provided with an aerobic exercise prescription that included walking within a heart rate range of 50–75% of heart rate reserve. The resistance-training portion of the programme consisted of two sets of 12 repetitions of the following exercises: leg extension, leg curl, heel raise and step-up. Cuff weights and weighted vests were used to provide resistance. A 1.0–1.5-min rest interval separated each exercise. Following two orientation sessions, participants began the exercise programme using the lowest possible resistance. Resistance was increased after the participant performed two sets of 12 repetitions for two consecutive days. *For participants in the home-based programme, weights were exchanged at the participant's request or after a determination was made during face-to-face or telephone contact to increase the weights. Telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Exercise and attendance logs were used to gather data and monitor progress.* *Diet: to produce and maintain an average weight loss of 5% during the 18-month intervention period. Classified as a 600 kcal/day deficit/LED diet.* *BT: self-monitoring, goal setting, cognitive restructuring, problem-solving, and environmental management*
Control	The group met monthly for 1 h for the first 3 months. A health educator, who scheduled videotaped presentations and physician talks on topics concerning OA, obesity, and exercise, organised the healthy lifestyle programme. Patients were advised to follow the American College of Rheumatologyand European League Against Rheumatism recommendations for weight loss and exercise as treatments for OA. Question-and-answer sessions followed each presentation. Monthly phone contact was maintained during months 4–6, followed by contact every other month during months 7–18. During phone contact, information on pain, medication use, illnesses and hospitalisation was obtained.
Length of follow-up	*18 months*
Results	*At 18 months, mean (SD) weight change in kg was –3.46 (6.89) in the activity group, and –1.10 (6.23) in the information group. Mean weight change in the intervention group compared with information was –2.36 (95% CI –4.41 to –0.31).*
Quality and comments	*ITT analysis done. Blinded assessment done. Good concealment of allocation. SDs calculated*

Narayan 1998 (in HTA) RCT	
Aim	To test adherence to specific lifestyle interventions among Pima Indians of Arizona, and to compare changes in risk factors for diabetes.
Participants	Pima Indians who were obese (BMI ≥27 kg/m^2 men, ≥25 kg/m^2 women) and were normoglycaemic (2 h plasma glucose <7.8 mmol/l). *Total 95 – 72 F, 23 M. Median age 34 combined (*n*=48), 33 information (*n*=47). Median BMI (kg/m^2) 36.5 combined, 33.2 information.*

Intervention	Structured activity and nutritional intervention programme by an American Diabetes Association recommended dietitian, decrease fat intake and alcohol intake and increase fibre. Increase energy expenditure by 700–1000 kcal/week by e.g. walking 10–12 h per month and keeping activity log. Behavioural techniques included role-playing, modelling and problem-solving, food tasting and grocery store tours.
Control	*Self-directed learning with Pima culture appreciation group meetings to discuss current/historical lifestyles, local speakers, participants contributed to newsletters carrying Pima poetry, stories and folklore; basic printed material regarding healthy eating and exercise information, detailed interview of 40–120 min on health and lifestyle.*
Length of follow-up	*52 weeks*
Results	*At 6 months, mean (SD) weight change in kg was 1.00 (6.20) in the combined group, and 0.50 (6.70) in the information group. Mean weight change in the intervention group compared with control was 0.50 (95% CI –2.17 to 3.17).* At 12 months, mean (SD) weight change in kg was 2.50 (6.62) in the combined group, and 0.80 (6.14) in the information group. Mean weight change in the intervention group compared with control was 1.70 (95% CI –0.94 to 4.34).
Quality and comments	Author confirmed numbers assessed in each group at 12 months, medians assumed similar to means and SDs calculated. ITT not done. Blinded assessment not done. Random allocation but no description of concealment. FPG significantly higher in combined group (p=0.03).

Wing 1998 (in HTA) RCT	
Aim	To assess the effect of lifestyle intervention over 2 years on changes in weight, CHD risk factors, and incidence of diabetes in overweight adults with a parental history of diabetes.
Participants	Adults aged 40 to 55 years who did not have diabetes, and were overweight (30 to 100% of IBW). *154 total – 122 F, 32 M. Mean (SD) age 46.3 (3.8) years combined (*n*=40), 45.3 (4.9) control (*n*=40). Mean (SD) BMI (kg/m^2) 35.7 (4.1) combined, 36.0 (5.4) control.*
Intervention	Diet: 800–1000 kcal/day weeks 1–8 then adjusted to 1200–1500 kcal/day by week 16, food diaries reviewed and feedback given, meal plans and shopping lists, behavioural or nutritional topic given at each session (relapse prevention, stimulus control, dealing with eating out, assertion, behaviour chain analysis, problem-solving) Exercise: 50–60 min walk with therapist at each meeting (second supervised walk available each week for weeks 1–10), gradually increased exercise to estimated energy expenditure of 1500 kcal per week (e.g. 3 miles brisk walking 5 days per week), other activities periodically introduced to the participants such as aerobics and line dancing. Also lectures on a topic related to changing exercise behaviour (stimulus control, problem-solving, reducing barriers, exercising in different weather conditions, stretching). (Same number of meetings as diet and exercise alone, so half time spent on diet and half on exercise.)
Control	*Participants received LEARN behavioural manual with information on healthy eating, exercise and behavioural strategies; participants encouraged to lose weight and exercise on their own, only participated in the assessments*
Length of follow-up	24 months

Results	*At 6 months, mean weight change (SD) was –10.30 (7.70) kg in the combined group compared with –1.50 (2.70) kg in the information group. Mean weight change in the intervention group compared with information was –8.80 (95% CI –11.67 to –5.93).* *At 12 months, mean weight change (SD) was –7.40 (9.70) kg in the combined group compared with –0.30 (4.50) kg in the information group. Mean weight change in the intervention group compared with information was –7.10 (95% CI –10.94 to –3.26).* *At 24 months, mean weight change (SD) was –2.50 (8.40) kg in the combined group compared with –0.30 (4.50) kg in the information group. Mean weight change in the intervention group compared with information was –2.20 (95% CI –5.51 to 1.11)*
Quality and comments	Author confirmed main study and sub-study results. Blinded assessment done. ITT analysis done. Random allocation but no description of concealment.

Djuric 2002 RCT	
Aim	To develop effective weight loss methods for women who have had breast cancer.
Participants	Women who had survived breast cancer and who were obese (BMI between 30 and 45 kg/m^2). Total 48 – all female. Age range 36 to 70 years. Mean (SD) BMI (kg/m^2) 35.5 (3.9) overall. No details by group. Allocated: 13 information (control), 10 Weight Watchers, 13 individualised counselling, 11 comprehensive (Weight Watchers plus counselling).
Intervention	*Individual (Djuric 2002a): Goal of weight loss was initial decrease of 10% of baseline weight at 6 months (adjusted if required – IBW vs reasonable body weight).* *Diet: ADA Exchange list diet plan – energy intake decreased by 500–1000 kcal/day. Target fat intake 20–25% of energy, fruits and vegetables five servings per day, protein up to 20% of energy. Increased fibre.* *Activity: 30 to 45 min of moderate activity most days of the week. Pedometers for self-monitoring and goal setting.* *BT: Written information on environmental control, serving size control, exercise, motivation, goal setting, holiday eating, seasonal foods). Behaviour change goals and problem-solving. Taught goal setting, menu planning, self-efficacy, consideration of body image, social support, social eating, removing road blocks, positive thinking, dealing with high risk situations and slips, cue elimination.*
Control	Given NCI 'Action Guide to Healthy Eating' and 'Food Guide Pyramid' pamphlets. Received no other dietary or exercise instructions or help. Allowed to follow a weight-reduction diet on their own if desired.
Length of follow-up	*12 months*
Results	*Only results at 12 months reported for the information group.* *Individual: At 12 months, mean weight change (SD) was –8.00 (5.50) kg in the combined group compared with 0.85 (6.00) kg in the information group. Mean weight change in the intervention group compared with information was –8.85 (95% CI –14.85 to –2.85).* *At 6 months, 33% of the individual group, and 8% of the information group had achieved a 10% weight loss. At 12 months, 22% of the individual group, and 0% of the information group had achieved a 10% weight loss.*
Quality and comments	*No baseline comparison. Only used information and counselling results in this review.* *Blinded assessment not reported. ITT analysis not done. Random allocation but no description of concealment.*

Mayer-Davis 2004RCT	
Aim	To evaluate lifestyle interventions for people with diabetes who live in rural communities.
Participants	People who were overweight (BMI ≥25 kg/m^2) with diabetes, and aged ≥45 years Total 187 – 122 F, 30 M (completers only). Mean (SD) age 59.7 (8.6) years combined intensive (*n*=49), 58.9 (7.8) combined pragmatic (*n*=47), 62.4 (9.5) years information (*n*=56). Mean (SD) BMI (kg/m^2) 37.6 (6.5) combined intensive, 37.5 (6.7) combined pragmatic, 35.2 (7.5) information. Results for completers only.
Intervention	*Combined intensive: given a study goal of 10% weight loss over 12 months. 25% energy from fat, minimum of 150 min of physical activity per week (similar in intensity to brisk walking). BT included self-monitoring, and additional strategies (DPP included problem-solving, managing cues, stimulus control, positive assertion, positive thinking, holiday eating, social support, goal-setting, motivation). Intervention was modified version of the Diabetes Prevention Programme 2002, with focus on diet and activity.* *Combined pragmatic: as above, but condensed to number of hours reimbursed by Medicare for diabetes education for an individual with diabetes.*
Control	Individual session at baseline where given information on diet and physical activity (American Diabetes Association and American Dietetic Association).
Length of follow-up	*12 months*
Results	*At 12 months, mean weight change (SD) was –2.20 (6.54) kg in the combined group compared with –0.30 (6.00) kg in the information group. Mean weight change in the combined group compared with information was –1.90 (95% CI –4.31 to 0.51).* *Results for 3, 6 months and for the combined pragmatic group were presented graphically only. But only significant difference was between the combined intensive and other groups at 6 months (about –2.7 kg, vs –1.0 kg and –0.4 kg,* p<*0.001).* *At 12 months, 49% combined intensive lost 2kg or more compared with about 36% in the combined pragmatic group and 25% information group.*
Quality and comments	*Blinded assessment not reported. ITT analysis not done. Random allocation but no description of concealment. SDs calculated.*

Wolf 2004 RCT	
Aim	To compare the efficacy of lifestyle case management to usual care given in the primary care setting, as measured by clinical, health-related quality of life (HRQOL), and economic outcomes
Participants	People who were overweight (BMI ≥27 kg/m^2) with type 2 diabetes, and aged ≥20 years Total 144 – 87 F, 57 M. Mean (SD) age 53.3 (8.6) years combined (*n*=73), 53.4 (8.0) information (*n*=71). Mean (SD) BMI (kg/m^2) 37.6 (7.7) combined, 37.3 (6.4) information.
Intervention	*Combined: case manager met with participants individually, in groups, and by phone for assessment, goal setting, education, and support.* *Goals were tailored but based on national dietary recommendations for people with type 2 diabetes and obesity. Individual sessions occurred six times throughout the year, totalling 4 h. Participants attended six 1-h small-group sessions. Brief monthly phone contacts provided support. Goals of the intervention were modest weight loss (5% of initial weight) and dietary intake as well as physical activity reflecting national recommendations.*
Control	Usual care participants received educational material and were free to join other weight management or diabetes care programs
Length of follow-up	*12 months*

Results	*At 12 months, mean weight change (SD) was –2.40 (6.59) kg in the combined group compared with 0.60 (6.08) kg in the information group. Mean weight change in the combined group compared with information was –3.00 (95% CI –5.07 to -0.93).* *More participants in the combined group than the information group lost up to 5% (53 vs. 32%) and 5% (20 vs. 14%) of initial weight (p=0.03).*
Quality and comments	*Blinded assessment not reported. ITT analysis done. Random allocation but no description of concealment. SDs calculated.*

Other outcomes

Lindahl 1999 (in HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.21 (0.70) in the combined group, and –0.06 (0.49) in the information group. Mean TC change in the intervention group compared with information was –0.15 (95% CI –0.32 to 0.02). At 12 months, mean (SD) FPG change in mmol/l was –0.50 (0.68) in the combined group, and –0.31 (1.14) in the information group. Mean TAG change in the intervention group compared with information was –0.19 (95% CI –0.46 to 0.08). At 12 months, mean (SD) TAG change in mmol/l was –0.16 (0.59) in the combined group, and –0.09 (0.59) in the information group. Mean TAG change in the intervention group compared with information was –0.07 (95% CI –0.24 to 0.10). At 12 months, mean (SD) DBP change in mmHg was –3.20 (7.41) in the combined group, and –0.80 (7.41) in the information group. Mean DBP change in the intervention group compared with information was –2.40 (95% CI –4.53 to –0.27). At 12 months, mean (SD) SBP change in mmHg was –4.90 (14.81) in the combined group, and 1.30 (10.79) in the information group. Mean SBP change in the intervention group compared with information was –6.20 (95% CI –9.92 to –2.48). *Physical fitness improved in the intervention group, compared with a decrease in the information group (+4.15 vs –1.12 ml/kg per min,* p=*0.0088).*
Quality and comments	…

Messier 2004 RCT	
Results	*At 18 months, significant improvements were seen in the 6 min walk distance compared with the information only group (*p<*0.05). No significant differences were seen for self-reported physical function, stair-climb time or pain (although pain did improve in all groups over time).*
Quality and comments	…

Narayan 1998 (in HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was 0.20 (1.08) in the combined group, and 0.10 (1.08) in the information group. Mean TC change in the intervention group compared with information was 0.10 (95% CI –0.35 to 0.55). At 12 months, mean (SD) FPG change in mmol/l was 0.10 (1.35) in the combined group, and 0.10 (1.35) in the information group. Mean TAG change in the intervention group compared with information was 0.00 (95% CI –0.56 to 0.06). At 12 months, mean (SD) DBP change in mmHg was 1.10 (8.30) in the combined group, and –1.00 (8.30) in the information group. Mean DBP

	change in the intervention group compared with information was 2.10 (95% CI –1.33 to 5.53). At 12 months, mean (SD) SBP change in mmHg was 6.00 (12.70) in the combined group, and 4.10 (12.70) in the information group. Mean SBP change in the intervention group compared with information was 1.90 (95% CI –3.35 to 7.15). *Levels of activity (MET – h per month) increased in both groups, but the difference was not significant between groups.* *No significant differences between groups were seen for nutrient intake.*
Quality and comments	Activity and dietary information was collected using Pima-modified instruments.

Wing 1998 (in HTA) RCT	
Results	*At 6 months, mean (SD) TC change in mmol/l was –0.33 (0.61) in the combined group, and 0.12 (0.50) in the information group. Mean TC change in the combined group compared with information was –0.45 (95% CI –0.73 to –0.17).* *At 6 months, mean (SD) LDL change in mmol/l was –0.13 (0.58) in the combined group, and 0.08 (0.46) in the information group. Mean LDL change in the combined group compared with information was –0.21 (95% CI –0.47 to 0.05).* *At 6 months, mean (SD) HDL change in mmol/l was –0.06 (0.16) in the combined group, and –0.02 (0.11) in the information group. Mean HDL change in the combined group compared with information was –0.04 (95% CI –0.11 to 0.03).* *At 6 months, mean (SD) TAG change in mmol/l was –0.69 (1.45) in the combined group, and 0.29 (0.32) in the information group. Mean TAG change in the combined group compared with information was –0.98 (95% CI –1.50 to–0.46).* *At 6 months, mean (SD) DBP change in mmHg was –6.90 (10.40) in the combined group, and –2.20 (8.00) in the information group. Mean DBP change in the combined group compared with information was –4.70 (95% CI –9.29 to –0.11).* *At 6 months, mean (SD) SBP change in mmHg was –12.30 (9.50) in the combined group, and –2.00 (10.50) in the information group. Mean SBP change in the combined group compared with information was –10.30 (95% CI –15.24 to –5.36).* *At 6 months, mean (SD) FPG change in mmol/l was –0.20 (0.40) in the combined group, and 0.10 (0.50) in the information group. Mean FPG change in the combined group compared with information was –0.30(95% CI –0.52 to –0.08).* *At 6 months, mean (SD) change in %HbA_{1c} was 0.03 (0.20) in the combined group, and 0.20 (0.40) in the information group. Mean %HbA_{1c} change in the combined group compared with information was –0.17 (95% CI –0.33 to –0.01).* *At 12 months, mean (SD) TC change in mmol/l was 0.32 (0.64) in the combined group, and 0.39 (0.70) in the information group. Mean TC change in the combined group compared with information was –0.07 (95% CI –0.41 to 0.27).* *At 12 months, mean (SD) LDL change in mmol/l was 0.14 (0.54) in the combined group, and 0.24 (0.66) in the information group. Mean LDL change in the combined group compared with information was –0.10 (95% CI –0.41to 0.21).* *At 12 months, mean (SD) HDL change in mmol/l was 0.12 (0.20) in the combined group, and 0.08 (0.16) in the information group. Mean HDL change in the combined group compared with information was 0.04 (95% CI –0.05 to 0.13).* *At 12 months, mean (SD) TAG change in mmol/l was 0.33 (1.65) in the combined group, and 0.40 (1.25) in the information group. Mean TAG change*

	in the combined group compared with information was –0.07 (95% CI –0.82 to 0.68). *At 12 months, mean (SD) DBP change in mmHg was –1.00 (10.20) in the combined group, and 4.90 (8.20) in the information group. Mean DBP change in the combined group compared with information was –5.90 (95% CI –10.71 to –1.09).* *At 12 months, mean (SD) SBP change in mmHg was –2.90 (14.20) in the combined group, and 1.10 (9.60) in the information group. Mean SBP change in the combined group compared with information was –4.00 (95% CI –10.17 to 2.17).* *At 12 months, mean (SD) FPG change in mmol/l was 0.00 (0.50) in the combined group, and 0.00 (0.60) in the information group. Mean FPG change in the combined group compared with information was 0.00 (95% CI –0.28 to 0.28).* *At 24 months, mean (SD) TC change in mmol/l was 0.09 (0.67) in the combined group, and 0.18 (0.53) in the information group. Mean TC change in the combined group compared with information was –0.09 (95% CI –0.39 to 0.21).* *At 24 months, mean (SD) LDL change in mmol/l was 0.12 (0.52) in the combined group, and 0.03 (0.46) in the information group. Mean LDL change in the combined group compared with information was 0.09 (95% CI –0.15 to 0.33).* *At 24 months, mean (SD) HDL change in mmol/l was 0.02 (0.21) in the combined group, and 0.04 (0.24) in the information group. Mean HDL change in the combined group compared with information was –0.02 (95% CI –0.13 to 0.09).* *At 24 months, mean (SD) TAG change in mmol/l was –0.28 (1.33) in the combined group, and 0.52 (1.14) in the information group. Mean TAG change in the combined group compared with information was –0.80 (95% CI –1.41 to –0.19).* *At 24 months, mean (SD) DBP change in mmHg was –0.20 (10.50) in the combined group, and 2.00 (8.00) in the information group. Mean DBP change in the combined group compared with information was –2.20 (95% CI –6.80 to 2.40).* *At 24 months, mean (SD) SBP change in mmHg was –4.80 (15.00) in the combined group, and –1.50 (12.00) in the information group. Mean SBP change in the combined group compared with information was –3.30 (95% CI –10.00 to 3.40).* *At 24 months, mean (SD) FPG change in mmol/l was 0.50 (1.30) in the combined group, and 0.20 (0.40) in the information group. Mean FPG change in the combined group compared with information was 0.30(95% CI –0.17 to 0.77).* *At 24 months, mean (SD) change in %HbA_{1c} was 0.04 (1.08) in the combined group, and –0.10 (0.30) in the information group. Mean %HbA_{1c} change in the combined group compared with information was 0.14 (95% CI –0.25 to 0.53).* *At 6, 12 and 24 months, the combined group reported significant decreases from baseline in energy intake and percentage of energy from fat (block food-frequency of % energy from fat was significant at 24 months). Smaller, often non-significant decreases were seen in the information group.* *VO_{2max} increased in the combined group significantly at 6 months, and was also increased at 24 months (not significant from baseline). The information group showed no significant changes from baseline.* *At 24 months, the relative risk (if weight loss of 4.5 kg compared with no weight loss) of developing diabetes in the combined group was about 0.88 and about 0.88 in the information group. For people with IGT, the relative risks were about 0.92 and 0.88 respectively.*
Quality and comments	Dietary intake assessed using self-completed questionnaires and 3-day food diaries. Activity assessed using self-completed questionnaire (administered as an interview).

Djuric 2002 RCT	
Results	*At 12 months, the combined group had a reported daily energy intake of 1386 compared with 2120 in the information group (–447 vs –126, respectively, from baseline). Also, fat intake was 24% in the combined group compared with 40% in the information group (–11 vs +7%, respectively, from baseline).*
Quality and comments	Dietary intake from self-reported 3-day food records (after initial training from the dietitian)

Mayer-Davis 2004 RCT	
Results	*(No SDs were reported so not able to add to meta-analysis.)* *At 6 months, no secondary metabolic outcomes (lipids, BP, HbA_{1c}) were significantly different between the combined intensive and information, or between the combined pragmatic and information. However, HbA_{1c} did improve in all groups, but there was no difference between the groups.*
Quality and comments	…

Wolf 2004 RCT	
Results	*(No SDs were reported so not able to add to meta-analysis.)* *HbA1c differed between groups over the intervention period (p=0.02), but was not significantly different at 12 months. Change in weight did not predict change in HbA1c level.* *The 12-month between-group differences in lipid levels were not statistically significant.* *By 12 months, participants in the combined group were taking 0.8 (0.05–1.1) fewer total medications per day than those in the information group (p= 0.03)* *More individuals in the combined group decreased total medications compared with those in the information group (45 vs. 28%, respectively), and fewer individuals in the combined group increased medications compared with those in the usual care group (19 vs. 35%) (p=0.03) at 6 months. Although the magnitude of the differences remained similar (decrease: 57 vs. 39%; increase: 17 vs. 32%), these differences were no longer significant by 12 months (P = 0.13).* *There was a decrease in unique medications primarily due to a decrease in diabetes medications (p=0.003). By 12 months, the combined group reduced diabetes medications 0.46 medications per day more than those in the usual care group (p=0.001). Insulin and sulfonylurea decreased most among participants in the combined group, whereas thiazolidinedione increased slightly among the information group.* *Baseline SF-36 scores were lower than national norms but consistent with scores reported among obese individuals. Change in SF-36 scores in the combined group was significantly different from the information group in seven of nine domains. The domains with greatest improvement in the case management group were emotional role (15.1, 3.4–26.8) and physical role (10, 1.2–24.7).*
Quality and comments	…

Reported harms

Lindahl 1999 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Messier 2004 RCT	
Harms	Two deaths occurred, but were unrelated to the interventions. One participant tripped and sustained a laceration to his head. No details of allocation.
Quality and comments	…

Narayan 1998 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wing 1998 (in HTA) RCT	
Harms	7% in the information group and 15.6% of the combined group developed diabetes during the 24-month study. The development of diabetes was associated with increased initial IGT.
Quality and comments	…

Djuric 2002 RCT	
Harms	One woman withdrew for medical problems, but no details were reported.
Quality and comments	…

Mayer-Davis 2004 RCT	
Harms	None reported.
Quality and comments	…

Wolf 2004 RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Lindahl 1999 (in HTA) RCT	
Country and setting	Sweden. Wellness centres.
Participants (included/excluded)	*Included if BMI >27 kg/m^2, abnormal oral glucose tolerance test.* *Excluded if already taken part in lifestyle modification programme, too physically ill to participate.*
Recruitment	From community intervention programme, potential participants were invited to take part in a health survey.
Intervention (mode and intensity)	1 month with 4-day follow-up stay at 12 months (full board at a wellness centre for initial month)
Duration of active intervention	1 month plus 4 days
Control (mode and intensity)	*At baseline and at 12 months*
Delivery of intervention/control (who)	N/R
Dropout rates	4% combined, 0% information at 12 months
Treatment of dropouts (return to baseline, or last measurement?)	Completers only.

Messier 2004 RCT	
Country and setting	USA. Older Americans Independence Centre.
Participants (included/excluded)	Included if aged ≥60 years, calculated BMI ≥28 kg/m^2, knee pain on most days of the month, sedentary activity pattern with <20 min of formal exercise once weekly for the past 6 months, self-reported difficulty in at least one of the following activities ascribed to knee pain: walking one-quarter of a mile (three to four city blocks), climbing stairs, bending, stooping, kneeling (e.g., to pick up clothes), shopping, house cleaning or other self-care activities, getting in and out of bed, standing up from a chair, lifting and carrying groceries, or getting in and out of the bath, radiographic evidence of grade I–III tibiofemoral or patellofemoral OA based on weight-bearing anteroposterior and sunrise view radiographs, and willingness to undergo testing and intervention procedures. Excluded if serious medical condition that prevented safe participation in an exercise programme, including symptomatic heart or vascular disease (angina, peripheral vascular disease, congestive heart failure), severe hypertension, recent stroke, chronic obstructive pulmonary disease, severe insulin-dependent diabetes mellitus, psychiatric disease, renal disease, liver disease, active cancer other than skin cancer, and anaemia, a Mini-Mental State Examination score of <24, inability to finish the 18-month study or unlikely to be compliant, inability to walk without a cane or other assistive device, participation in another research study, reported alcohol consumption of more than 14 drinks per week, ST segment depression of at least 2 mm at an exercise level of 4 METS or less, hypotension, or complex arrhythmias during a graded exercise test, inability to complete the protocol, in the opinion of the clinical staff, because of frailty, illness or other reasons.
Recruitment	Mass mailings to age-eligible persons within the target area, targeted mailings to employees of the university and medical centre, presentations to various groups of older adults, mass media advertisement, and placement of posters (with pull-off reply cards attached) in strategic locations. Also, strategies were developed to enhance recruitment among racial minorities, including advertisements and interviews on minority-run radio stations, newspaper ads in predominantly African American publications, letters to churches attended mainly by minorities, and inserts in these church bulletins. Initial screening for major eligibility criteria was via telephone.
Intervention (mode and intensity)	*Exercise 3 days/week for 4 months (facility-based), then either home- or facility-based. For participants in the home-based programme, telephone contacts were made every other week during the first 2 months of home-based exercise, every third week during the following 2 months, and monthly thereafter. Assessment at baseline, 6, 18 months.*
Duration of active intervention	18 months
Control (mode and intensity)	Group met monthly for 1 h for the first 3 months. Monthly phone contact was maintained during months 4–6, followed by contact every other month during months 7–18.
Delivery of intervention/control (who)	Exercise: N/R Information: health educator, who scheduled videotaped presentations and physician talks on topics concerning OA, obesity and exercise, organised the healthy lifestyle programme.
Dropout rates	*20% activity, 14% information at 24 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Narayan 1998 (in HTA) RCT	
Country and setting	USA. No details.
Participants (included/excluded)	*Included if BMI ≥27 kg/m^2 (men) and ≥25 kg/m^2 (women); normoglycaemia (2 h plasma glucose <7.8 mmol/l), aged 25–54 years.* *Excluded if pregnancy or intention to become pregnant, previous diagnosis of diabetes, current self-reported physical activity ≥20 h per week, prescribed low-fat diet, another household member already randomised to the study, evidence of ischaemic heart disease, chronic illness; current steroid, thiazide or beta-blocker treatment; condition is likely to interfere with informed consent.*
Recruitment	Identified as residents of a specific Indian community (part of an epidemiological study) – then invited for screening.
Intervention (mode and intensity)	52 weeks, contacted minimum 53 times (baseline then weekly group meetings and home visits to week 52)
Duration of active intervention	12 months
Control (mode and intensity)	*52 weeks, contacted 13 times (baseline then monthly to week 52)*
Delivery of intervention/control (who)	Pima Pride (information) group was led by a discussion leader, who was a member of the community. No further details.
Dropout rates	*4% combined, 6% information at 52 weeks*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only

Wing 1998 (in HTA) RCT	
Country and setting	USA. No further details – university hospital?
Participants (included/excluded)	Included if aged 40–55 years, non-diabetic (confirmed by OGTT), one or two biological parents with type 2 diabetes, 30–100% above IBW. Excluded if diagnosis of diabetes.
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*Two years, contacted approximately 52 times (baseline, weekly for first 6 months then every 2 weeks for next 6 months then two × 6-week course during second year)*
Control (mode and intensity)	Contacted at baseline, 6 months, 1 year and at 2 years.
Duration of active intervention	24 months
Delivery of intervention/control (who)	Group meetings were led by a multidisciplinary team, with primary therapists for activity being a behaviour therapist and an exercise physiologist, and for diet a behaviour therapist and a registered dietitian
Dropout rates	*20% combined and 23% information at 24 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Djuric 2002 RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	Included if aged 18 to 70 years, women who had stage I or II breast cancer diagnosed in past 4 years and were free of any recurrence as confirmed by a physician, BMI between 30 and 45 kg/m^2. Chemotherapy/radiation therapy to have been completed at least 3 months previously (except tamoxifen).

Recruitment	Direct mail to 'Race for Cure' participants, press releases, and brochures at breast clinics.
Intervention (mode and intensity)	*Weekly for 3 months, biweekly for months 3 to 6, monthly thereafter (altered as needed for the individual). Also free to call dietitian at any time. Apart from quarterly assessments, all contact done by telephone. Monthly group meeting held, but no requirement to attend.*
Duration of active intervention	12 months
Control (mode and intensity)	Met with dietitian at quarterly intervals for assessment.
Delivery of intervention/control (who)	Contact and counselling by a registered dietitian (experienced in weight loss counselling in clinical settings).
Dropout rates	*31% combined and 15% information at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Mayer-Davis 2004 RCT	
Country and setting	USA. Primary healthcare centres in rural counties.
Participants (included/excluded)	Included if aged 45 years or older, clinical diagnosis of diabetes, BMI ≥25 kg/m^2. Excluded if limitation that prevented full participation (e.g., recent or multiple MI/stroke, metastatic cancer, inability to walk, severe psychiatric disease, dialysis for end stage renal disease).
Recruitment	Medical record review from diabetes registers at the heathcare centres. Local publication strategies (such as posters).
Intervention (mode and intensity)	*Intensive: met weekly for first 4 months, every other week for next 2 months, once a month for last 6 months (1 h sessions). Pattern was three group sessions, followed by an individual session. Assessments at 3, 6, 12 months.* *Pragmatic: four × 1-h sessions over 12 months (three group, one individual). Assessments at 3, 6, 12 months.*
Duration of active intervention	12 months
Control (mode and intensity)	Individual session at baseline, and assessments.
Delivery of intervention/control (who)	Two nutritionists delivered all sessions, after training. Weekly conference calls were held between the study nutritionists and the research nutritionist to ensure continual high quality delivery, with emphasis on appropriate responses to group or individual needs.
Dropout rates	*19% overall at 12 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers at 12 months only (random subject effects allowed for missing values from follow-up visits)

Wolf 2004 RCT	
Country and setting	USA. Unclear.
Participants (included/excluded)	Included if diagnosed with type 2 diabetes (International Classification of Diseases, 9th Revision [ICD-9] codes 250.XX, 357.2, 362.0, 362.02, or 366.41 and confirmed by physician), use of diabetes medications, BMI>=27 kg/m2, age 20 years or older, ability to comprehend English, and membership in the Southern Health Services (SHS) health plan. Excluded if limitation that prevented full participation (e.g., recent or multiple MI/stroke, metastatic cancer, inability to walk, severe psychiatric disease, dialysis for end stage renal disease).
Recruitment	Identification of eligible participants from SHS data

Intervention (mode and intensity)	*Individual sessions occurred six times throughout the year, totalling 4 h. Participants attended six 1-h small-group sessions. Brief monthly phone contacts provided support.*
Duration of active intervention	12 months
Control (mode and intensity)	Not clear – assumed as for assessment
Delivery of intervention/control (who)	Delivered by a modestly priced, registered dietitian.
Dropout rates	*26% combined; 14% information at 12 months*
Treatment of dropouts (return to baseline, or last measurement?)	Used all available data…but no further details

1.5.11 Physical activity, diet and behaviour therapy vs diet

Weight loss

Blonk 1994 (in HTA) RCT	
Aim	To assess the long-term efficacy of a comprehensive weight reduction programme compared with that of a conventional programme
Participants	People who were overweight (BMI >27 kg/m^2) and who had type 2 diabetes. Total 60 – 40 F, 20 M. Median (range) age 59 (42–69) years combined (*n*=27 out of 30 allocated), 58.5 (29–70) diet (*n*=26 out of 30 allocated). Median (range) BMI (kg/m^2) 31.3 (27.2–44.3) combined (*n*=27 out of 30 allocated), BMI 32.8 (27.9–45.8) diet (*n*=26 out of 30 allocated).
Intervention	All participants underwent 3-month run-in prior to randomisation, seen three times for measurements and twice by dietitian who assessed 3 day food records, all participants instructed not to change their dietary habits; Post randomisation all participants received dietary education counselling programme involving visits to the dietitian every 2 months, 500 kcal/day deficit (minimum 1000 kcal/day) 50–55% energy as carbohydrate, 15% as protein, 30% as fat (emphasising unsaturated fat), 25 g fibre and <300 mg cholesterol per day; adherence assessed at each visit by dietary record. Participants additionally received behavioural modification strategies including self-monitoring, stimulus control, self-reinforcement, cognitive restructuring and relapse prevention training; Participants also received exercise training of 30 min bicycle ergometer at 60–80% maximum heart rate and then 30 min of various sports activities
Control	*All participants underwent 3 month run-in prior to randomisation, seen three times for measurements and twice by dietitian who assessed 3-day food records, all participants instructed not to change their dietary habits;* *Post randomisation all participants received dietary education counselling programme involving visits to the dietitian every 2 months, 500 kcal/day deficit (minimum 1000 kcal/day) 50–55% energy as carbohydrate, 15% as protein, 30% as fat (emphasising unsaturated fat), 25 g fibre and <300 mg cholesterol per day; adherence assessed at each visit by dietary record.*
Length of follow-up	*24 months*
Results	*At 6 months, mean (SD) weight change in kg was –2.90 (6.74) in the combined group, and –1.20 (6.25) in the diet group. Mean weight change in the intervention group compared with control was –1.70 (95% CI –5.20 to 1.80).* At 12 months, mean (SD) weight change in kg was –2.74 (6.69) in the combined group, and –2.07 (6.50) in the diet group. Mean weight change in the intervention group compared with control was –0.67 (95% CI –4.22 to 2.88). At 18 months, mean (SD) weight change in kg was –3.14 (6.80) in the combined group, and –1.08 (6.22) in the diet group. Mean weight change in the intervention group compared with control was –2.06 (95% CI –5.57 to 1.45). At 24 months, mean (SD) weight change in kg was –3.50 (6.91) in the combined group, and –2.10 (3.36) in the diet group. Mean weight change in the intervention group compared with control was –1.40 (95% CI –5.01 to 2.21).
Quality and comments	ITT done. Blinded assessment not done. Random allocation but no description of concealment. Author confirmed study participants were randomly allocated to treatment groups; median change in weight at 12, 18 and 24 months derived from graphs assumed similar to mean, SDs calculated.

Other outcomes

Blonk 1994 (in HTA) RCT	
Results	*At 12 months, mean (SD) TC change in mmol/l was –0.20 (5.97) in the combined group, and 0.10 (5.94) in the diet group. Mean TC change in the combined group compared with diet was –0.30 (95% CI –3.51 to 2.91).* *At 12 months, mean (SD) change in %HbA_{1c} was –0.39 (2.58) in the combined group, and –0.01 (2.58) in the diet group. Mean %HbA_{1c} change in the combined group compared with diet was –0.38 (95% CI –1.77 to 1.01).* *At 18 months, mean (SD) change in %HbA_{1c} was –0.30 (2.58) in the combined group, and –0.10 (2.58) in the diet group. Mean %HbA_{1c} change in the combined group compared with diet was –0.20 (95% CI –1.59 to 1.19).* *At 24 months, mean (SD) change in %HbA_{1c} was –0.01 (2.58) in the combined group, and 0.40 (2.58) in the diet group. Mean %HbA_{1c} change in the combined group compared with diet was –0.41 (95% CI –1.80 to 0.98).* *At 24 months, the change in energy intake did not appear to differ between the groups (+7 combined vs –75 kcal/day diet, no statistics reported).* *Carbohydrate and fat intake altered in proportion to the total energy intake.*
Quality and comments	Dietary intake from 3-day food records.

Reported harms

Blonk 1994 (in HTA) RCT	
Harms	One participant from the combined group dropped out due to mesothelioma.
Quality and comments	…

Generalisability

Blonk 1994 (in HTA) RCT	
Country and setting	Netherlands. No further details.
Participants (included/excluded)	*Included if type 2 diabetes (WHO), normal haematological, liver, kidney, thyroid function, BMI >27 kg/m^2.* *Excluded if history of angina, heart failure, intermittent claudication, proliferative retinopathy, subcutaneous insulin injections, diuretics, beta-blocking agents, drugs for hyperlipidaemia and any other drugs which may influence carbohydrate metabolism, regular physical exercise training.*
Recruitment	N/R
Intervention (mode and intensity)	*24 months, contacted 56 times (baseline then 2 monthly dietitian visit, behaviour therapy sessions once a week for first 2 months then at 4, 8, 12, 16 and 20 weeks, exercise sessions twice a month during months 3–6 and once a week during months 9–12 and 15–18).*
Duration of active intervention	24 months
Control (mode and intensity)	24 months, contacted 13 times (baseline then every 2 months).
Delivery of intervention/control (who)	Dietitian provided dietary education. Group sessions on BT led by a psychologist experienced in eating disorders. Group exercise training led by two physiotherapists.
Dropout rates	*10% combined, 13% diet at 24 months.*

Treatment of dropouts (return to baseline, or last measurement?)	N/R – results for completers only?

1.5.12 Physical activity, diet and behaviour therapy vs behaviour therapy

Weight loss

Bacon 2002 RCT	
Aim	To evaluate the effects of a 'health-centred' non-diet wellness programme, and to compare this to a traditional 'weight loss-centred' diet programme
Participants	78 total – all women. Mean (SD) BMI 35.7 (3.6) kg/m^2 overall. Mean (SD) age 39.9 (4.5) years overall. Thirty-nine assigned to each arm.
Intervention	*Participants were taught to moderately restrict their fat and energy intake and were encouraged to monitor their diet by maintaining a food diary and to monitor their weight weekly.* *Walking at an intensity suggested by training heart rate range was encouraged.* *Information presented was similar to most behavioural weight loss programmes: focus included eating behaviours and attitudes, nutrition, social support, exercise. Methods used were self-monitoring, stimulus control, reinforcement and cognitive change.*
Control	Programme consisted of five aspects: body acceptance, eating behaviour, activity, nutrition, social support. Initial treatment focussed on enhancing body- and self-acceptance, leading as full a life as possible, regardless of weight or success at weight control. Also disentangling feelings of self-worth from weight. Secondary phase focussed on eating behaviour: standard nutritional advice was given, with emphasis on regulating quality and quantity of food according to internal cues of hunger, appetite, and satiety. Activity component helped participants to identify and transform barriers to becoming active and to find activities that were fun and appealing. Support group was used to help women see the common experiences, and gain support and to learn strategies for asserting themselves and effecting change.
Length of follow-up	*12 months*
Results	*At 12 weeks, mean (SD) weight change in kg was –3.70 (4.70) in the combined group, and 0.70 (2.30) in the BT group. Mean weight change in the intervention group compared with BT was –4.04 (95% CI –6.50 to –2.30).* *At 24 weeks, mean (SD) weight change in kg was –4.60 (6.50) in the combined group, and 0.50 (3.40) in the BT group. Mean weight change in the intervention group compared with BT was –5.10 (95% CI –8.03 to –2.17).* *At 52 weeks, mean (SD) weight change in kg was –5.90 (6.30) in the combined group, and –0.10 (4.80) in the BT group. Mean weight change in the intervention group compared with BT was –5.80 (95% CI –8.91 to –2.69).*
Quality and comments	*Classified the weight loss-centred programme as D, BT and physical activity, and the health-centred (non-diet) programme as BT.* *No difference between groups for any outcome variables at baseline. ITT not done. Blinded assessment not reported. Random allocation but no description of concealment.*

Other outcomes

Bacon 2002 RCT	
Results	*Both groups showed a significant decrease from baseline at 12 months (5.19 to 4.34 vs 5.19 to 4.37 mmol/l), but there was not a significant difference between the groups. Similarly for LDL and TAG levels, and SBP.* *HDL levels decreased significantly in both groups at 12 months (1.23 to 1.12 vs 1.19 to 1.05 mmol/l), and the difference between groups was significant (*p=*0.03).* *DBP did not change significantly in either group over time.* *No measure of sleep or activity levels were significantly changed in either group. However, daily energy expenditure decreased significantly in both groups, and was significantly decreased in the combined group compared with BT alone at 12 months (*p=*0.000).* *Significant improvements were seen in both groups for measures of eating behaviour (including disordered eating). However, cognitive restraint increased in the diet group and decreased in the non-diet group (*p=*0.000).*
Quality and comments	Activity from a 7-day activity recall questionnaire. Eating Inventory and Eating Disorder Inventory measured eating behaviour.

Reported harms

Bacon 2002 RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Bacon 2002 RCT	
Country and setting	USA. University clinics?
Participants (included/excluded)	Included if white, female, aged 30 to 45 years, BMI ≥30 kg/m^2, non-smoker, not pregnant, not intending to get pregnant, not lactating, practising birth control if heterosexually active, premenopausal. Also restraint score >15 (indicating a history of chronic dieting), no recent MI, no active neoplasms, no diagnosis of type 1 diabetes or insulin dependent type 2 diabetes, no history of cerebrovascular or renal disease. Excluded if taking medications known to affect weight or energy expenditure (except anti-depressants or SSRIs).
Recruitment	Recruited using print, electronic, and televised media.
Intervention (mode and intensity)	*Attended 24 weekly sessions, each 90 min long. A 6-month aftercare programme was offered, no new material was included. Four testing sessions took place at baseline, 12, 24, 52 weeks.*
Duration of active intervention	6 months
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Diet programme was taught by an experienced registered dietitian. Non-diet programme was facilitated by a counsellor who has conducted educational and psychotherapeutic workshops and groups using this approach previously.

Dropout rates	*41% diet group, 26% non-diet group at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.13 Physical activity, diet and behaviour therapy vs physical activity

Weight loss

Messier 2004 RCT	
Aim	To determine whether long-term exercise and dietary weight loss are more effective, either separately or in combination, than usual care in improving physical function, pain, mobility in older overweight/obese adults with osteoarthritis
Participants	People with osteoarthritis, aged 60 years and older who were overweight (BMI ≥28 kg/m^2) Total 316 – 227 F, 89 M. Mean (SD) age years 69 (6.97) years activity and BT (*n*=76), 69 (7.16) years activity (*n*=80). Mean (SD) BMI (kg/m^2) 34.0 (6.10) activity and BT, 34.2 (5.37) activity.
Intervention	*See details previously*
Control	See details previously
Length of follow-up	*18 months*
Results	*At 18 months, mean (SD) weight change in kg was –5.20 (7.37) in the activity and BT group, and –3.46 (6.89) in the activity group. Mean weight change in the intervention group compared with activity was –1.74 (95% CI –3.98 to –0.50).*
Quality and comments	*ITT analysis done. Blinded assessment done. Good concealment of allocation. SDs calculated*

Other outcomes

Messier 2004 RCT	
Results	*At 18 months, no significant improvements were seen for self-reported physical function, motility, or pain between groups.*
Quality and comments	…

Reported harms

Messier 2004 RCT	
Harms	Two deaths occurred, but were unrelated to the interventions. One participant tripped and sustained a laceration to his head. No details of allocation.
Quality and comments	…

Generalisability

Messier 2004 RCT	
Country and setting	USA. Older Americans Independence Centre.
Participants (included/excluded)	See details previously
Recruitment	See details previously
Intervention (mode and intensity)	See details previously
Duration of active intervention	18 months
Control (mode and intensity)	See details previously
Delivery of intervention/control (who)	Exercise and BT: not reported Exercise: not reported
Dropout rates	*24% activity and BT, 20% activity at 24 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.14 Physical activity, diet and behaviour therapy vs diet and behaviour therapy

Weight loss

Wing 1998 (in HTA) RCT	
Aim	To assess the effect of lifestyle intervention over 2 years on changes in weight, CHD risk factors, and incidence of diabetes in overweight adults with a parental history of diabetes
Participants	Adults aged 40 to 55 years who did not have diabetes, and were overweight (30 to 100% of IBW). *154 total – 122 F, 32 M. Mean (SD) age 46.3 (3.8) years combined (*n=*40), 45.0 (4.7) diet and BT (*n=*37). Mean (SD) BMI (kg/m^2) 35.7 (4.1) combined, 36.1 (4.1) diet and BT.*
Intervention	Diet: 800–1000 kcal/day weeks 1–8 then adjusted to 1200–1500 kcal/day by week 16, food diaries reviewed and feedback given, meal plans and shopping lists, behavioural or nutritional topic given at each session (relapse prevention, stimulus control, dealing with eating out, assertion, behaviour chain analysis, problem-solving) Exercise: 50–60 min walk with therapist at each meeting (second supervised walk available each week for weeks 1–10), gradually increased exercise to estimated energy expenditure of 1500 kcal per week (e.g. 3 miles brisk walking 5 days per week), other activities periodically introduced to the participants such as aerobics and line dancing. Also lectures on a topic related to changing exercise behaviour (stimulus control, problem-solving, reducing barriers, exercising in different weather conditions, stretching). (Same number of meetings as diet and exercise alone, so half time spent on diet and half on exercise.)
Control	Diet: 800–1000 kcal/day weeks 1–8 then adjusted to 1200–1500 kcal/day by week 16, food diaries reviewed and feedback given, meal plans and shopping lists, behavioural or nutritional topic given at each session (relapse prevention, stimulus control, dealing with eating out, assertion, behaviour chain analysis, problem-solving)
Length of follow-up	24 months

Results	*At 6 months, mean weight change (SD) was –10.30 (7.70) kg in the combined group compared with –9.10 (6.40) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –1.20 (95% CI –4.64 to 2.24).* *At 12 months, mean weight change (SD) was –7.40 (9.70) kg in the combined group compared with –5.50 (6.90) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –1.90 (95% CI –6.09 to 2.29).* *At 24 months, mean weight change (SD) was –2.50 (8.40) kg in the combined group compared with –2.10 (7.60) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –0.40 (95% CI –4.25 to 3.45).*
Quality and comments	Author confirmed main study and sub-study results. Blinded assessment done. ITT analysis done. Random allocation but no description of concealment.

Foreyt 1993 (in HTA) RCT	
Aim	To compare diet, exercise, and exercise plus diet behavioural treatments in free-living, mildly to moderately obese adults
Participants	People who were aged between 25 and 45 years, and who were overweight (at least 14 kg overweight Metropolitan Life Insurance). Total 80 F, 85 M. Mean age not stated. Mean (SD) weight 97.6 (25.5) kg combined (*n*=42), 93.9 (20.8) kg diet and BT (*n*=42).
Intervention	Help Your Heart Eating Plan consisting of 30% energy as fat, 50% as carbohydrate, 20% as protein; energy intake adjusted so weight loss <1 kg per week, food diaries kept, Contracts to reward behaviour change, stress management, stimulus control and goal setting based on Learn behavioural eating programme. Lectures focused on physical and psychological benefits of exercise, taught a walking programme at an indoor track, graduated exercise with self-monitoring based on heart rate, breathing and effort to 'vigorous' but not 'strenuous' level; exercise increased to goal of three to five sessions of 45 min per week
Control	*Help Your Heart Eating Plan consisting of 30% energy as fat, 50% as carbohydrate, 20% as protein; energy intake adjusted so weight loss was <1 kg per week, food diaries kept,* *Contracts to reward behaviour change, stress management, stimulus control and goal setting based on Learn behavioural eating programme.* *Advised to maintain sedentary lifestyle*
Length of follow-up	2 years
Results	At 12 months, mean weight change (SD) was –8.13 (8.24) kg in the combined group compared with –6.32 (7.70) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –1.81 (95% CI –5.99 to 2.37). At 24 months, mean weight change (SD) was –2.20 (6.70) kg in the combined group compared with 0.90 (7.70) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –3.10 (95% CI –7.94 to 1.74).
Quality and comments	Mean change in weight at 1 year calculated from actual values, SDs also calculated at 1 year. No details of baseline comparability. Blinded assessment not done. ITT analysis not done. Random allocation with attempt at concealment, but some chance of disclosure.

Sikand 1988 (in HTA) RCT	
Aim	To examine the effect of exercise in a VLED programme, in combination with behavioural techniques, nutrition education and group therapy.

Participants	Women who were obese (no definition given). *Total 30 – all women. Mean (SD) age 39.8 (9.1) years combined (*n=*15), 37.8 (8.4) diet and BT (*n=*15). Mean (SD) weight 105.6 (23.6) kg combined, 106.6 (15.2) kg diet and BT.*
Intervention	All participants placed on a VLED (energy content not given) consisting solely of milk-based protein powder for initial 4 months, Received nutritional counselling, group support and discussion of behaviour modification strategies; all participants invited to an ongoing pay-for-service programme offered at clinic sponsoring the study after active treatment period. Received structured aerobic exercise programme twice weekly for first 4 months with additional exercise encouraged on other days
Control	*All participants placed on a VLED (energy content not given) consisting solely of milk based protein powder for initial 4 months.* *Received nutritional counselling, group support and discussion of behaviour modification strategies; all participants invited to an ongoing pay-for-service programme offered at clinic sponsoring the study after active treatment period.* *Participants neither encourage nor discouraged from exercising.*
Length of follow-up	*2 years*
Results	*At 4 months, mean weight change (SD) was –21.80 (12.08) kg in the combined group compared with –17.50 (10.87) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –4.30 (95% CI –14.12 to 5.52).* At 24 months, mean weight change (SD) was –9.10 (9.20) kg in the combined group compared with –0.80 (7.40) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –8.30 (95% CI –16.83 to 0.23).
Quality and comments	Blinded assessment not done. ITT analysis done. Random allocation but no description of concealment.

Wadden 1998 (in HTA) RCT	
Aim	To determine whether exercise improved the maintenance of weight loss 1 year later.
Participants	Women who were overweight (more than 20 kg above IBW Metropolitan Life tables). *Total 128 – all women. Mean (SD) age 40.9 (8.6) overall (*n=*118 of 128 assigned). Mean (SD) BMI (kg/m^2) 36.3 (5.3) overall (*n=*118 of 128 assigned).*
Intervention	925 kcal/day/diet (liquid MR) for weeks 0–16 then 1200–1500 kcal/day to week 48. 90 min group cognitive BT weekly for 28 weeks then biweekly for following 20 weeks. Three × 1 h supervised exercise training per week for first 28 weeks (non-consecutive days) then two sessions per week during weeks 29–48 and one home exercise session per week. Aerobic (HTA group a): step aerobics estimated to expend 300–400 kcal/session. Strength (HTA group b): strength exercise using universal gym of Cybex equipment to expend 150–175 kcal per session, consisted of bench press, latissimus pulldown, chest fly, leg press, leg and arm curls and extensions, sit-ups and back extensions. Mixed (HTA group c): 40% aerobic exercise same as group b and 60% strength exercise same as group c, estimated to expend 225–275 kcal/session.

Control	*925 kcal/day/diet for weeks 0–16 then 1200–1500 kcal/day to week 48.* *90 min group cognitive behaviour therapy weekly for 28 weeks then biweekly for following 20 weeks.* *Advised to continue same lifestyle activities and not to increase exercise from baseline.*
Length of follow-up	*100 weeks*
Results	*Aerobic: At 2 months, mean weight change (SD) was –10.10 (3.70) kg in the combined group compared with –11.40 (3.50) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was 1.30 (95% CI –1.74 to 4.34).* *Strength: At 2 months, mean weight change (SD) was –10.00 (3.90) kg in the combined group compared with –11.40 (3.50) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was 1.40 (95% CI –1.76 to 4.56).* *Mixed: At 2 months, mean weight change (SD) was –10.90 (3.40) kg in the combined group compared with –11.40 (3.50) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was 0.50 (95% CI –2.56 to 3.56).* *Aerobic: At 6 months, mean weight change (SD) was –15.80 (6.80) kg in the combined group compared with –17.70 (5.70) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was 1.90 (95% CI –3.23 to 7.03).* *Strength: At 6 months, mean weight change (SD) was –17.80 (8.80) kg in the combined group compared with –17.70 (5.70) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –0.10 (95% CI –5.96 to 5.76).* *Mixed: At 6 months, mean weight change (SD) was –18.60 (7.30) kg in the combined group compared with –17.70 (5.70) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –0.90 (95% CI –6.37 to 4.57).* *Aerobic: At 12 months, mean weight change (SD) was –13.50 (9.10) kg in the combined group compared with –15.30 (5.30) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was 1.80 (95% CI –3.73 to 7.33).* *Strength: At 12 months, mean weight change (SD) was –17.30 (10.30) kg in the combined group compared with –15.30 (5.30) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –2.00 (95% CI –8.17 to 4.17).* *Mixed: At 12 months, mean weight change (SD) was –16.60 (9.80) kg in the combined group compared with –15.30 (5.30) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –1.30 (95% CI –7.39 to 4.79).* Aerobic: At 24 months, mean weight change (SD) was –8.50 (8.20) kg in the combined group compared with –6.90 (6.30) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –1.60 (95% CI –7.44 to 4.24). Strength: At 24 months, mean weight change (SD) was –10.10 (10.00) kg in the combined group compared with –6.90 (6.30) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –3.20 (95% CI –9.77 to 3.37). Mixed: At 24 months, mean weight change (SD) was –8.60 (10.70) kg in the combined group compared with –6.90 (6.30) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –1.70 (95% CI –8.60 to 5.20).
Quality and comments	Blinded assessment not done. ITT analysis not done. Random allocation but no description of concealment. *Different values to HTA as split control group by three.*

Wing 1988 (in HTA) RCT	
Aim	To determine whether adding exercise to a diet programme promotes weight loss or glycaemic control in people with type 2 diabetes
Participants	People aged 30 to 65 years with type 2 diabetes and who were overweight (more than 20% above IBW) *Total 30 – 21 F, 9 M. Mean (SD) age 56.1 (6.4) years combined (*n*=15), 55.1 (7.2) diet and BT (*n*=15). Mean (SD) BMI (kg/m^2) 38.2 (6.6) combined, 37.9 (6.5) diet and BT.*
Intervention	All participants received behavioural weight control programme including weigh-in, glucose measurement and behavioural modification lecture (slowing down rate of eating, reducing eating signals in the home, social pressures, pre-planning and relapse prevention techniques). 1600 kcal/day diet with daily energy goal to produce 1 kg/week weight loss, reduced fat intake and increase complex carbohydrate intake, food diaries; exercise twice per week as a group and once a week on own, 1 h per session. Walked 3 mile route with therapist three times per week and instructed to exercise additionally once per week on their own
Control	*All participants received behavioural weight control programme including weigh-in, glucose measurement and behavioural modification lecture (slowing down rate of eating, reducing eating signals in the home, social pressures, pre-planning and relapse prevention techniques).* *1600 kcal/day diet with daily energy goal to produce 1 kg per week weight loss, reduced fat intake and increase complex carbohydrate intake, food diaries; exercise twice per week as a group and once a week on own, 1 h per session.* *Instructed not to change baseline level of activity, three meetings per week were used to provide demonstrations and films of new low-energy cooking techniques, portion size estimation and role-ply; numerous social group activities to control for social aspect of exercise condition received by combined group*
Length of follow-up	*62 weeks?*
Results	*Outcomes at 10 weeks were reported but no SDs* *At 10 weeks, mean weight change (SD) was –9.30 (8.55) kg in the combined group compared with –5.60 (7.50) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –3.70 (95% CI –9.70 to 2.30).* At 12 months, mean weight change (SD) was –7.90 (8.15) kg in the combined group compared with –3.80 (6.99) kg in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –4.10 (95% CI –9.77 to 1.57). *Note: 12 months is 62 weeks – 10 weeks intensive intervention and 12 month follow-up*
Quality and comments	*Note: Wing 1988b in HTA analysis.* Blinded assessment done. ITT analysis not done. Random allocation but no description of concealment.

Messier 2004 RCT	
Aim	To determine whether long-term exercise and dietary weight loss are more effective, either separately or in combination, than usual care in improving physical function, pain, mobility in older overweight/obese adults with osteoarthritis
Participants	People with osteoarthritis, aged 60 years and older who were overweight (BMI ≥28 kg/m^2) Total 316 – 227 F, 89 M. Mean (SD) age years 69 (6.97) years activity and BT (*n*=76), 69 (7.16) years activity (*n*=80). Mean (SD) BMI (kg/m^2) 34.0 (6.10) activity and BT, 34.2 (5.37) activity.
Intervention	*See details previously*

Control	See details previously
Length of follow-up	*18 months*
Results	*At 18 months, mean (SD) weight change in kg was –5.20 (7.37) in the combined group, and –4.61 (7.22) in the diet and BT group. Mean weight change in the intervention group compared with diet and BT was –0.59 (95% CI –2.87 to 1.69).*
Quality and comments	*ITT analysis done. Blinded assessment done. Good concealment of allocation. SDs calculated*

Other outcomes

Wing 1998 (in HTA) RCT	
Results	*At 6 months, mean (SD) TC change in mmol/l was –0.33 (0.61) in the combined group, and –0.49 (0.71) in the diet and BT group. Mean TC change in the combined group compared with diet and BT was 0.16 (95% CI –0.16 to 0.48).* *At 6 months, mean (SD) LDL change in mmol/l was –0.13 (0.58) in the combined group, and –0.32 (0.60) in the diet and BT group. Mean LDL change in the combined group compared with diet and BT was 0.19 (95% CI –0.09 to 0.47).* *At 6 months, mean (SD) HDL change in mmol/l was –0.06 (0.16) in the combined group, and –0.10 (0.17) in the diet and BT group. Mean HDL change in the combined group compared with diet and BT was 0.04 (95% CI –0.04 to 0.12).* *At 6 months, mean (SD) TAG change in mmol/l was –0.69 (1.45) in the combined group, and –0.30 (1.45) in the diet and BT group. Mean TAG change in the combined group compared with diet and BT was –0.39 (95% CI –1.09 to 0.31).* *At 6 months, mean (SD) DBP change in mmHg was –6.90 (10.40) in the combined group, and –6.20 (6.90) in the diet and BT group. Mean DBP change in the combined group compared with diet and BT was –0.70 (95% CI –5.02 to 3.62).* *At 6 months, mean (SD) SBP change in mmHg was –12.30 (9.50) in the combined group, and –10.20 (9.20) in the diet and BT group. Mean SBP change in the combined group compared with diet and BT was –2.10 (95% CI –6.62 to 2.42).* *At 6 months, mean (SD) FPG change in mmol/l was –0.20 (0.40) in the combined group, and –0.20 (0.40) in the diet and BT group. Mean FPG change in the combined group compared with diet and BT was 0.00(95% CI –0.19 to 0.19).* *At 6 months, mean (SD) change in %HbA_{1c} was 0.03 (0.20) in the combined group, and 0.10 (0.50) in the diet and BT group. Mean %HbA_{1c} change in the combined group compared with diet and BT was –0.07 (95% CI –0.25 to 0.11).* *At 12 months, mean (SD) TC change in mmol/l was 0.32 (0.64) in the combined group, and 0.26 (0.76) in the diet and BT group. Mean TC change in the combined group compared with diet and BT was 0.06 (95% CI –0.29 to 0.41).* *At 12 months, mean (SD) LDL change in mmol/l was 0.14 (0.54) in the combined group, and 0.12 (0.73) in the diet and BT group. Mean LDL change in the combined group compared with diet and BT was 0.02 (95% CI –0.30 to 0.34).* *At 12 months, mean (SD) HDL change in mmol/l was 0.12 (0.20) in the combined group, and 0.10 (0.16) in the diet and BT group. Mean HDL change in the combined group compared with diet and BT was 0.02 (95% CI –0.07 to 0.11).* *At 12 months, mean (SD) TAG change in mmol/l was 0.33 (1.65) in the*

	combined group, and 0.55 (3.77) in the diet and BT group. Mean TAG change in the combined group compared with diet and BT was –0.22 (95% CI –1.64 to 1.20). *At 12 months, mean (SD) DBP change in mmHg was –1.00 (10.20) in the combined group, and 3.40 (8.10) in the diet and BT group. Mean DBP change in the combined group compared with diet and BT was –4.40 (95% CI –9.08 to 0.28).* *At 12 months, mean (SD) SBP change in mmHg was –2.90 (14.20) in the combined group, and 1.30 (8.30) in the diet and BT group. Mean SBP change in the combined group compared with diet and BT was –4.20 (95% CI –10.02 to 1.62).* *At 12 months, mean (SD) FPG change in mmol/l was 0.00 (0.50) in the combined group, and 0.20 (0.80) in the diet and BT group. Mean FPG change in the combined group compared with diet and BT was –0.20 (95% CI –0.53 to 0.13).* *At 24 months, mean (SD) TC change in mmol/l was 0.09 (0.67) in the combined group, and –0.12 (0.61) in the diet and BT group. Mean TC change in the combined group compared with diet and BT was 0.21 (95% CI –0.10 to 0.52).* *At 24 months, mean (SD) LDL change in mmol/l was 0.12 (0.52) in the combined group, and –0.16 (0.63) in the diet and BT group. Mean LDL change in the combined group compared with diet and BT was 0.28 (95% CI 0.00 to 0.56).* *At 24 months, mean (SD) HDL change in mmol/l was 0.02 (0.21) in the combined group, and 0.02 (0.20) in the diet and BT group. Mean HDL change in the combined group compared with diet and BT was 0.00 (95% CI –0.10 to 0.10).* *At 24 months, mean (SD) TAG change in mmol/l was –0.28 (1.33) in the combined group, and 0.19 (2.42) in the diet and BT group. Mean TAG change in the combined group compared with diet and BT was –0.47 (95% CI –1.39 to 0.45).* *At 24 months, mean (SD) DBP change in mmHg was –0.20 (10.50) in the combined group, and 3.00 (7.80) in the diet and BT group. Mean DBP change in the combined group compared with diet and BT was –3.20 (95% CI –7.66 to 1.26).* *At 24 months, mean (SD) SBP change in mmHg was –4.80 (15.00) in the combined group, and –0.80 (9.40) in the diet and BT group. Mean SBP change in the combined group compared with diet and BT was –4.00 (95% CI -10.06 to 2.06).* *At 24 months, mean (SD) FPG change in mmol/l was 0.50 (1.30) in the combined group, and 0.30 (1.00) in the diet and BT group. Mean FPG change in the combined group compared with diet and BT was 0.20 (95% CI –0.36 to 0.76).* *At 24 months, mean (SD) change in %HbA_{1c} was 0.04 (1.08) in the combined group, and –0.10 (0.50) in the diet and BT group. Mean %HbA_{1c} change in the combined group compared with diet and BT was 0.14 (95% CI –0.27 to 0.55).* *At 6, 12, and 24 months, the combined group reported significant decreases from baseline in energy intake and percentage of energy from fat (block food-frequency of % energy as fat was significant at 24 months). At 6, 12 and 24 months, the diet group reported significant decreases from baseline in energy intake and percentage of energy from fat.* *$\dot{V}O_{2max}$ increased in the combined group significantly at 6 months, and was also increased at 24 months (not significant from baseline). The diet and BT group increased significantly at 6 months (+2.35 vs +3.06 ml/kg per min in the combined group), but not at 24 months from baseline.* *At 24 months, the relative risk (if weight loss of 4.5 kg compared with no weight loss) of developing diabetes in the combined group was about 0.88 and about 0.89 in the diet and BT group. For people with IGT, the relative risks were about 0.92 and 0.96 respectively.*
Quality and	Dietary intake assessed using self-completed questionnaires and 3-day food

comments	diaries. Activity assessed using self-completed questionnaire (administered as an interview).

Foreyt 1993 (in HTA) RCT	
Results	*No group differences were found in cardiovascular fitness (VO_{2max}) at 12 months.*
Quality and comments	…

Sikand 1988 (in HTA) RCT	
Results	*No other outcomes reported.*
Quality and comments	…

Wadden 1998 (in HTA) RCT	
Results	*No other outcomes reported.*
Quality and comments	…

Wing 1988 (in HTA) RCT	
Results	*TC at 12 months – not added, as HTA figures cannot be replicated* *At 12 months, mean (SD) HDL change in mmol/l was 0.06 (0.29) in the combined group, and 0.10 (0.29) in the diet and BT group. Mean HDL change in the combined group compared with diet and BT was –0.04 (95% CI –0.26 to 0.18).* *At 12 months, mean (SD) TAG change in mmol/l was –0.64 (0.96) in the combined group, and 0.03 (0.96) in the diet and BT group. Mean TAG change in the combined group compared with diet and BT was –0.67 (95% CI –1.38 to 0.04).* *At 12 months, mean (SD) %HbA_{1c} change was 0.04 (1.08) in the combined group, and –0.10 (0.50) in the diet and BT group. Mean %HbA_{1c} change in the combined group compared with diet and BT was 0.14 (95% CI –0.27 to 0.55).* *At 12 months, there was a significant reduction in medication in the combined group compared with the diet and BT group (83% had reduced medication compared with 38% respectively,* p<*0.05). There was also a significant reduction in the dosage (50% compared with 0% respectively,* p<*0.01).* *Increased energy expenditure was seen in the combined group compared with the diet and BT group. Energy intake did not differ between the groups, although both groups did decrease intake from baseline.*
Quality and comments	Dietary intake from 3-day food records. Activity from self-reported questionnaires.

Messier 2004 RCT	
Results	*At 18 months, no significant improvements were seen for self-reported physical function, motility, or pain between groups.*
Quality and comments	…

Reported harms

Wing 1998 (in HTA) RCT	
Harms	15.6% in the combined group and 30.3% of the diet and BT group developed diabetes during the 24-month study. The development of diabetes was associated with increased initial IGT.
Quality and	…

comments	

Foreyt 1993 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Sikand 1988 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wadden 1998 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Wing 1988 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Messier 2004 RCT	
Harms	Two deaths occurred, but were unrelated to the interventions. One participant tripped and sustained a laceration to his head. No details of allocation.
Quality and comments	…

Generalisability

Wing 1998 (in HTA) RCT	
Country and setting	USA. No further details – university hospital?
Participants (included/excluded)	Included if aged 40–55 years, non-diabetic (confirmed by OGTT), one or two biological parents with type 2 diabetes, 30–100% above IBW. Excluded if diagnosis of diabetes.
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*Two years, contacted approximately 52 times (baseline, weekly for first 6 months then every 2 weeks for next 6 months then two × 6-week course during second year)*
Duration of active intervention	24 months
Control (mode and intensity)	2 years, contacted approximately 52 times (baseline, weekly for first 6 months then every 2 weeks for next 6 months then two × 6-week course during second year).
Delivery of intervention/control (who)	Group meetings were led by a multidisciplinary team, with primary therapists for activity being a behaviour therapist and an exercise physiologist, and for diet a behaviour therapist and a registered dietitian.
Dropout rates	*20% combined and 5% diet and BT at 24 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Foreyt 1993 (in HTA) RCT	
Country and setting	USA. No further details.

Participants (included/excluded)	*Included if aged between 25–45 years, ≥14 kg overweight (Metropolitan Life Insurance tables), not taking regular exercise, $100 deposit (refunded in increments according to number of sessions attended).* *No exclusion criteria stated.*
Recruitment	Media announcements
Intervention (mode and intensity)	12 months plus follow-up visit at 2 years, contacted 24 times (baseline, 12 weekly then 3 biweekly then 8 monthly then at 2 years).
Duration of active intervention	*12 months*
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	1-h long group sessions led by registered dietitians with training and experience in behaviour modification.
Dropout rates	50% combined and 64% diet and BT at 24 months (only invited completers back at 2 years)
Treatment of dropouts (return to baseline, or last measurement?)	*Completers only*

Sikand 1988 (in HTA) RCT	
Country and setting	USA. No details.
Participants (included/excluded)	Included women, aged 21–60 years, obese (no definition). No exclusion criteria reported.
Recruitment	N/R
Intervention (mode and intensity)	*Four months, with telephone follow-up at 2 years, contacted 34 times (baseline, twice weekly for initial 4 months then at 2 years).*
Duration of active intervention	4 months
Control (mode and intensity)	Four months, with telephone follow-up at 2 years, contacted 18 times (baseline, weekly for initial 4 months then at 2 years).
Delivery of intervention/control (who)	Each visit involved a medical consultation and nutritional counselling but no details of who did these was reported.
Dropout rates	*53% combined, 47% diet and BT at 2 years*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only

Wadden 1998 (in HTA) RCT	
Country and setting	USA. University clinics.
Participants (included/excluded)	Included women, >20 kg above IBW (Metropolitan Life Insurance tables). Excluded if medical contraindications, bulimia nervosa, other major psychiatric disturbance, and medication known to affect weight.
Recruitment	N/R
Intervention (mode and intensity)	*Forty-eight weeks with follow-up at 1-year post-treatment (100 weeks), contacted 40 times (baseline then weekly for initial 28 weeks then biweekly for next 20 weeks then at 100 weeks).*
Duration of active intervention	48 weeks
Control (mode and intensity)	As above

Delivery of intervention/control (who)	Group sessions and refeeding protocol supervised by a registered dietitian. Also clinical psychologists involved in group sessions. Exercise sessions were led by graduate students in exercise physiology.
Dropout rates	*40% overall at 100 weeks.*
Treatment of dropouts (return to baseline, or last measurement?)	Dropouts were retained until time of attrition.

Wing 1988 (in HTA) RCT	
Country and setting	USA. No further details.
Participants (included/excluded)	Included if had type 2 diabetes (as defined by National Diabetes Data Group), >20% above IBW, 30–65 years. Excluded if known CHD, on medication that would affect weight loss and or measurement of heart rate, orthopaedic problems which would limit walking.
Recruitment	N/R
Intervention (mode and intensity)	*62? weeks, contacted 53 times (baseline then three times per week for first 10 weeks then weekly for weeks 11–20 then monthly to 72 weeks)*
Duration of active intervention	62 weeks?
Control (mode and intensity)	As above
Delivery of intervention/control (who)	N/R
Dropout rates	*13% combined, 0% diet and BT at 62 weeks?*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only

Messier 2004 RCT	
Country and setting	USA. Older Americans Independence Centre.
Participants (included/excluded)	See details previously
Recruitment	See details previously
Intervention (mode and intensity)	See details previously
Duration of active intervention	18 months
Control (mode and intensity)	See details previously
Delivery of intervention/control (who)	Exercise and BT: not reported Exercise: not reported
Dropout rates	*24% activity and BT, 20% activity at 24 months*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.5.15 Physical activity, diet and behaviour therapy vs physical activity and behaviour therapy

Weight loss

Wing 1998 (in HTA) RCT	
Aim	To assess the effect of lifestyle intervention over 2 years on changes in weight, CHD risk factors, and incidence of diabetes in overweight adults with a parental history of diabetes

Participants	Adults aged 40 to 55 years who did not have diabetes, and were overweight (30 to 100% of IBW). *154 total – 122 F, 32 M. Mean (SD) age 46.3 (3.8) years combined (*n=*40), 46.4 (4.5) activity and BT (*n=*37). Mean (SD) BMI (kg/m^2) 35.7 (4.1) combined, 36.0 (3.7) activity and BT.*
Intervention	Diet: 800–1000 kcal/day weeks 1–8 then adjusted to 1200–1500 kcal/day by week 16, food diaries reviewed and feedback given, meal plans and shopping lists, behavioural or nutritional topic given at each session (relapse prevention, stimulus control, dealing with eating out, assertion, behaviour chain analysis, problem-solving) Exercise: 50–60 min walk with therapist at each meeting (second supervised walk available each week for weeks 1–10), gradually increased exercise to estimated energy expenditure of 1500 kcal per week (e.g. 3 miles brisk walking 5 days per week), other activities periodically introduced to the participants such as aerobics and line dancing. Also lectures on a topic related to changing exercise behaviour (stimulus control, problem-solving, reducing barriers, exercising in different weather conditions, stretching). (Same number of meetings as diet and exercise alone, so half time spent on diet and half on exercise.)
Control	Exercise behaviour topic each week, 50–60 min walk with therapist at each weekly meeting (second supervised walk available each week for weeks 1–10), gradually increased exercise to estimated energy expenditure of 1500 kcal/week (e.g. 3 miles brisk walking 5 days per week), other activities periodically introduced to the participants such as aerobics and line dancing. Each meeting included a lecture on a topic related to changing exercise behaviour (stimulus control, problem-solving, reducing barriers, exercising in different weather conditions, stretching).
Length of follow-up	24 months
Results	*At 6 months, mean weight change (SD) was –10.30 (7.70) kg in the combined group compared with –2.10 (4.20) kg in the activity and BT group. Mean weight change in the intervention group compared with activity and BT was –8.20 (95% CI –11.27 to –5.13).* *At 12 months, mean weight change (SD) was –7.40 (9.70) kg in the combined group compared with –0.40 (4.80) kg in the activity and BT group. Mean weight change in the intervention group compared with activity and BT was –7.00 (95% CI –10.90 to –3.10).* *At 24 months, mean weight change (SD) was –2.50 (8.40) kg in the combined group compared with 1.00 (4.70) kg in the activity and BT group. Mean weight change in the intervention group compared with activity and BT was –3.50 (95% CI –6.85 to –0.15).*
Quality and comments	Author confirmed main study and sub-study results. Blinded assessment done. ITT analysis done. Random allocation but no description of concealment.

Other outcomes

Wing 1998 (in HTA) RCT	
Results	*At 6 months, mean (SD) TC change in mmol/l was –0.33 (0.61) in the combined group, and 0.12 (0.72) in the activity and BT group. Mean TC change in the combined group compared with activity and BT was –0.45 (95% CI –0.78 to –0.12).* *At 6 months, mean (SD) LDL change in mmol/l was –0.13 (0.58) in the combined group, and 0.03 (0.52) in the activity and BT group. Mean LDL change in the combined group compared with activity and BT was –0.16 (95% CI –0.43 to 0.11).*

At 6 months, mean (SD) HDL change in mmol/l was –0.06 (0.16) in the combined group, and 0.02 (0.16) in the activity and BT group. Mean HDL change in the combined group compared with activity and BT was –0.08 (95% CI –0.16 to 0.00).
At 6 months, mean (SD) TAG change in mmol/l was –0.69 (1.45) in the combined group, and 0.12 (1.64) in the activity and BT group. Mean TAG change in the combined group compared with activity and BT was –0.81 (95% CI –1.57 to–0.05).
At 6 months, mean (SD) DBP change in mmHg was –6.90 (10.40) in the combined group, and –1.70 (12.20) in the activity and BT group. Mean DBP change in the combined group compared with activity and BT was –5.20 (95% CI –10.74 to 0.34).
At 6 months, mean (SD) SBP change in mmHg was –12.30 (9.50) in the combined group, and –2.40 (18.90) in the activity and BT group. Mean SBP change in the combined group compared with activity and BT was –9.90 (95% CI –17.16 to –2.64).
At 6 months, mean (SD) FPG change in mmol/l was –0.20 (0.40) in the combined group, and 0.00 (0.70) in the activity and BT group. Mean FPG change in the combined group compared with activity and BT was –0.20 (95% CI –0.48 to 0.08).
At 6 months, mean (SD) change in %HbA_{1c} was 0.03 (0.20) in the combined group, and 0.10 (0.30) in the activity and BT group. Mean %HbA_{1c} change in the combined group compared with activity and BT was –0.07 (95% CI –0.19 to 0.05).
At 12 months, mean (SD) TC change in mmol/l was 0.32 (0.64) in the combined group, and 0.36 (0.82) in the activity and BT group. Mean TC change in the combined group compared with activity and BT was –0.04 (95% CI –0.42 to 0.34).
At 12 months, mean (SD) LDL change in mmol/l was 0.14 (0.54) in the combined group, and 0.15 (0.54) in the activity and BT group. Mean LDL change in the combined group compared with activity and BT was –0.01 (95% CI –0.29 to 0.27).
At 12 months, mean (SD) HDL change in mmol/l was 0.12 (0.20) in the combined group, and 0.16 (0.18) in the activity and BT group. Mean HDL change in the combined group compared with activity and BT was –0.04 (95% CI –0.14 to 0.06).
At 12 months, mean (SD) TAG change in mmol/l was 0.33 (1.65) in the combined group, and 0.26 (2.19) in the activity and BT group. Mean TAG change in the combined group compared with activity and BT was 0.07 (95% CI –0.93 to 1.07).
At 12 months, mean (SD) DBP change in mmHg was –1.00 (10.20) in the combined group, and 0.90 (9.70) in the activity and BT group. Mean DBP change in the combined group compared with activity and BT was –1.90 (95% CI –7.11 to 3.31).
At 12 months, mean (SD) SBP change in mmHg was –2.90 (14.20) in the combined group, and 1.10 (15.80) in the activity and BT group. Mean SBP change in the combined group compared with activity and BT was –4.00 (95% CI –11.75 to 3.75).
At 12 months, mean (SD) FPG change in mmol/l was 0.00 (0.50) in the combined group, and 0.10 (0.70) in the activity and BT group. Mean FPG change in the combined group compared with activity and BT was –0.10 (95% CI –0.42 to 0.22).
At 24 months, mean (SD) TC change in mmol/l was 0.09 (0.67) in the combined group, and 0.33 (0.64) in the activity and BT group. Mean TC change in the combined group compared with activity and BT was –0.24 (95% CI –0.56 to 0.08).
At 24 months, mean (SD) LDL change in mmol/l was 0.12 (0.52) in the combined group, and 0.22 (0.61) in the activity and BT group. Mean LDL change in the combined group compared with activity and BT was –0.10 (95% CI –0.38 to 0.18).

	At 24 months, mean (SD) HDL change in mmol/l was 0.02 (0.21) in the combined group, and 0.05 (0.17) in the activity and BT group. Mean HDL change in the combined group compared with activity and BT was –0.03 (95% CI –0.12to 0.06). *At 24 months, mean (SD) TAG change in mmol/l was –0.28 (1.33) in the combined group, and 0.33 (1.46) in the activity and BT group. Mean TAG change in the combined group compared with activity and BT was –0.61 (95% CI –1.30 to 0.08).* *At 24 months, mean (SD) DBP change in mmHg was –0.20 (10.50) in the combined group, and 2.00 (8.00) in the activity and BT group. Mean DBP change in the combined group compared with activity and BT was –2.20 (95% CI –6.80 to 2.40).* *At 24 months, mean (SD) SBP change in mmHg was –4.80 (15.00) in the combined group, and 0.90 (13.90) in the activity and BT group. Mean SBP change in the combined group compared with activity and BT was –5.70 (95% CI –12.84 to 1.44).* *At 24 months, mean (SD) FPG change in mmol/l was 0.50 (1.30) in the combined group, and 0.40 (0.90) in the activity and BT group. Mean FPG change in the combined group compared with activity and BT was 0.10 (95% CI –0.45 to 0.65).* *At 24 months, mean (SD) change in %HbA_{1c} was 0.04 (1.08) in the combined group, and –0.10 (0.50) in the activity and BT group. Mean %HbA_{1c} change in the combined group compared with activity and BT was 0.14 (95% CI –0.27 to 0.55).* *At 6, 12, and 24 months, the combined group reported significant decreases from baseline in energy intake and percentage of energy from fat (block food-frequency of % energy as fat was significant at 24 months). At 6, 12, and 24 months, the activity and BT group reported non-significant decreases from baseline in energy intake and percentage of energy from fat (only block food-frequency of % energy as fat was significant at 24 months).* *VO_{2max} increased in the combined group significantly at 6 months, and was also increased at 24 months (not significant from baseline). VO_{2max} increased in the activity and BT group significantly at 6 months, but decreased at 24 months (not significant).* *At 24 months, the relative risk (if weight loss of 4.5 kg compared with no weight loss) of developing diabetes in the combined group was about 0.88 and about 0.88 in the activity and BT group. For people with IGT, the relative risks were about 0.92 and 0.91, respectively.*
Quality and comments	Dietary intake assessed using self-completed questionnaires and 3-day food diaries. Activity assessed using self-completed questionnaire (administered as an interview).

Reported harms

Wing 1998 (in HTA) RCT	
Harms	15.6% in the combined group and 14% of the activity and BT group developed diabetes during the 24-month study. The development of diabetes was associated with increased initial IGT.
Quality and comments	…

Generalisability

Wing 1998 (in HTA) RCT	
Country and setting	USA. No further details – university hospital?
Participants (included/excluded)	Included if aged 40–55 years, non-diabetic (confirmed by OGTT), one or two biological parents with type 2 diabetes, 30–100% above IBW. Excluded if diagnosis of diabetes.
Recruitment	Newspaper advertisements.
Intervention (mode and intensity)	*2 years, contacted approximately 52 times (baseline, weekly for first 6 months then every 2 weeks for next 6 months then two × 6-week course during second year)*
Duration of active intervention	24 months
Control (mode and intensity)	Two years, contacted approximately 52 times (baseline, weekly for first 6 months then every 2 weeks for next 6 months then two × 6-week course during second year).
Delivery of intervention/control (who)	Group meetings were led by a multidisciplinary team, with primary therapists for activity being a behaviour therapist and an exercise physiologist, and for diet a behaviour therapist and a registered dietitian.
Dropout rates	*20% combined and 16% activity and BT at 24 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

1.5.16 Intensity of physical activity

Weight loss

Anderson 1999 RCT	
Aim	To examine short- and long-term changes in weight, body composition, and cardiovascular risk profiles produced by diet combined with either programmed aerobic exercise or lifestyle activity in obese women.
Participants	Forty women with a mean (SD) age of 42.9 (8.3) years, weight of 89.2 (11.6) kg, height of 165.0 (7.1) cm and BMI of 32.9 (4.3) kg/m^2. All women reported not participating in a structured exercise programme for the 6 months prior to the start of the intervention.
Intervention	All participants asked to consume a self-selected, low-fat, LED of approximately 1200 kcal/day as per American Heart Association. All participants received a similar cognitive behavioural weight loss programme, a modified version of the LEARN Programme for Weight Control. The participants in the diet plus structured aerobic exercise attended three step aerobic classes. The length and intensity of classes was gradually increased. It was estimated that participants expended approximately 450 to 500 kcal per step aerobic workout. From weeks 14–16 participants were assisted in developing a long-term individualised programme of structured aerobic exercise.
Comparison	Participants in the lifestyle group were advised to increase their levels of moderately intense physical activity by 30 min/day on most days of the week. They discussed strategies for accumulating activity and expending energy throughout the day. They were taught to incorporate short bouts of activity into their daily schedules. Participants were given three-dimensional accelerometers to wear each week to provide ongoing feedback about their levels of physical activity. Units of physical activity were converted to energy expenditure. Participants were provided a graph of daily activity each week at the end of their group meeting.
Length of follow-up	16 week RCT with 1-year follow-up
Results	Thirty-eight (98%) of 40 women completed the 16-week study. Thirty-three (82.5%) of 40 women completed the entire 68-week study – 16 in the lifestyle group and 17 in the aerobic group. Weight losses of the two groups did not differ significantly at any time. Using an LOCF analysis, researchers found that participants across conditions lost a mean (SD) weight of 2.2 (1.2) kg by week 4, 4.6 (1.8) kg by week 8, and 6.5 (3.0) kg at week 12. At week 16, weight loss in the lifestyle group was 7.9 (4.2) kg and in the aerobic group was 8.3 (3.8) kg (within groups, p<0.001; between groups, p=0.08). Participants in the lifestyle group who were assessed at the 1-year follow-up (week 68) had regained a mean (SD) weight of 0.08 (4.6) kg from the end of treatment while the aerobic group had regained weight of 1.6 (5.5) kg (p=0.06). At week 68 participants were asked to report the percentage of weeks that they accumulated ≥30 min of moderate intensity exercise (e.g. brisk walking) on at least 5 days of the week for the 12 months after the intervention. There were no differences between groups in adherence to physical activity. No differences were found between the most active third, the middle third and the least active third in weight regain at the 3 and 6 month follow-up but at the 9 month visit, the least active group had regained significantly (p<0.02) more weight (3.76 [2.4] kg) than the most active group which, by contrast, had lost weight (–3.14 [4.6] kg). At the 12 month follow-up the least active group had regained significantly more of their lost weight than the middle (0.21[5.5] kg), p=0.021, or the most (–1.98 [4.3] kg) active groups (p=0.001). No differences were found between the most active and the middle group at any time during the follow-up period.
Quality and comments	ITT analysis not described. No blinding possible. There was random allocation, but no description of concealment.

Sponsor details	NIH grant, NRS and RSD Awards

Jacobsen 2003 RCT	
Aim	To compare the effects of long-term (72 weeks) continuous (CON) and intermittent (INT) exercise on attrition and adherence without a behavioural weight loss programme.
Participants	Fifty-two moderately obese (mean BMI >32 kg/m^2), previously sedentary women with oxygen consumption at or below the 'Fair Category' according to the American Heart Associations Fitness Classifications
Intervention	Participants were randomised to one of two levels of exercise. The CON group walked for 30 min at 60–75% of heart rate reserve, three times per week within the Human Performance Laboratory at the University of Nebraska
Comparison	INT group walked briskly at 50–65% of heart rate reserve two times per day, 15 min per session, 5 days/week at their home or work site. A minimum of 2 h was recommended to elapse between exercise sessions.
Length of follow-up	72 weeks
Results	For participants who completed the study, body weight did not change for CON from 80.17±5.75 kg at baseline to 79.70±5.40 at 16 months. For INT body weight did not change form baseline 85.85±13.13 kg to 16 months 85.05±12.90 kg.
Quality and comments	An RCT in which blinding was not possible and allocation concealment was not described. High attrition rate (58%).
Sponsor details	American Heart Association

Jakicic 1999 RCT	
Aim	To investigate whether exercise adherence in obese females, participating in a behavioural weight loss programme, is improved by prescribing daily exercise in multiple short bouts compared with continuous exercise and to determine whether multiple short bouts of daily exercise can produce significant improvements in cardiorespiratory fitness.
Participants	48 sedentary, overweight (mean [SD] BMI 32.8 [4.0] kg/m^2) women between the ages of 25–45 years. Sedentary was defined as <20 min/day of exercise on <3 days per week for 6 months.
Intervention	All participants participated in an 18-month behavioural weight loss programme with weekly meetings during months 1–6, biweekly meetings during months 7–12 and monthly meetings during months 13–18. All participants were also instructed to reduce both daily energy and fat intake. Home-based exercise similar to brisk walking prescribed as follows: 49 women instructed to exercise 5 days/week 20 min/day during weeks 1–4, 30 min/day weeks 5–8 and 40 min/day for the duration of the study. Exercise was performed in one long bout (LB).
Comparison	51 women instructed to exercise 5 days/week with duration progressing from 20 min/day to 40 min/day by the ninth week. The exercise was divided into multiple 10 min bouts that were performed at convenient times throughout the day, progressing from 2–4 short exercise bouts (SB) per day by week 9. 48 women whose exercise prescription was identical to the short bout group except that they were also provided with home treadmills (SBEQ).
Length of follow-up	18 months

Results	115 women of 148 randomised participants completed the study. Using an ITT analysis, there was NS difference weight loss at 6 or 18 months between the LB and either the SB group or the SBEQ group. At 18 months mean (SD) weight loss was significantly greater in the SBEQ group compared with the SB group (–7.4 kg [7.8 kg] vs –3.7 [6.6] kg; $p<0.05$). Weight loss was significantly at 18 months among those who reported exercising for ≥200 min/week compared with those exercising <150 min/week or ≥150 min/week ($p<0.05$). There were no significant differences between LB and SB/SBEQ groups for measures of body composition. However, changes in percentage of body fat and fat mass were significantly greater over time in the SBEQ group compared with the SB group ($p<0.01$ and $p<0.01$).
Quality and comments	Participants were randomly assigned to treatment groups. Allocation concealment not described. Blinding of participants not possible. Blinding of evaluators not described. ITT analysis done.
Sponsor details	NIH

Jakicic 2003 RCT	
Aim	To compare the effects of different durations and intensities of exercise on 12 month weight loss and cardiorespiratory fitness.
Participants	201 women with BMI 27–40 (mean BMI in each treatment group 32.2–32.8); age 21–45; sedentary, exercising less than 3 days/week for less than 20 min/day.
Intervention	All participants participated in an 18-month behavioural weight loss programme with weekly meetings during initial 24 weeks of treatment and biweekly meetings for the remainder of the study period. All participants were also instructed to reduce both daily energy (1200–1500 kcal) and fat intake (20–30%) Participants were randomised to one of four exercise groups of varying intensity and duration. vigorous intensity/high duration moderate intensity/high duration moderate intensity/moderate duration vigorous intensity/moderate duration. Walking was the primary form of exercise and treadmills were provided.
Comparison	See above
Length of follow-up	12 months
Results	Weight loss was significant in all groups but there was no significant difference of either exercise duration or intensity on changes in body weight between groups. A similar pattern of change in BMI was observed. In ITT, mean (SD) weight loss following 12 months of treatment was statistically significant ($p<0.001$) in all exercise groups (vigorous intensity/high duration=8.9 [7.3] kg; moderate intensity/high duration=8.2 [7.6] kg; moderate intensity/moderate duration=6.3 [5.6] kg; vigorous intensity/moderate duration=7.0 [6.4] kg), with no significant difference between groups. Mean (SD) cardiorespiratory fitness levels also increased significantly ($p=0.04$) in all groups (vigorous intensity/high duration=22.0 [19.9]%; moderate intensity/high duration=14.9 [18.6]%; moderate intensity/moderate duration=13.5 [16.9]%; vigorous intensity/moderate duration=18.9 [16.9]%), with no difference between groups. Post hoc analysis revealed that percentage weight loss at 12 months was associated with the level of physical activity performed at 6 and 12 months.
Quality and comments	Participants were randomly assigned to treatment groups. Allocation concealment not described. Blinding of participants not possible. Blinding of evaluators not described. ITT analysis done. A control group that did not perform exercise would also have been a valuable comparator. Participants were women only.
Sponsor details	NIH and NHLBI

Jeffery 1998 RCT

Aim	To examine two strategies for enhancing exercise adherence in obese individuals in a weight loss programme.
Participants	29 men and 167 women
Intervention	Four intervention groups: all received the same behaviour therapy as control. Supervised exercise group had a goal of 1000 kcal/week and had supervised walking sessions three times per week. The trainer group had all of the above but also had a personal trainer who walked with participants and made reminder phone calls before each walking session and scheduled make up sessions as necessary. The incentive group received a financial incentive for walking rather than a trainer: $1 per walk for first 25 walks, $1.50 per walk for the next 50 walks, $2 per walk for next 50 walks and $3 per walk for any remaining walks. The fourth group had both personal trainers and financial rewards for walking.
Comparison	SBT group received a behavioural counselling and diets of 100 kcal/day if weight was <91 kg and 1500 kcal if weight was ≥91 kg. Participants were asked to walk or bike the equivalent of 250 kcal/week and to gradually increase to 1000 kcal/week. Behavioural techniques included stimulus control, problem-solving, social assertion, short term goal-setting and enhancing motivation, relapse prevention, and social support.
Length of follow-up	18 months
Results	Analysis of weight loss controlled for gender and baseline weight and centre. The SBT group had significantly greater weight loss from baseline to 18 months than the four intervention groups (p<0.03).

	Mean weight change in kg		
	Baseline to 6 months	**6 to 18 months**	**Baseline to 18 months**
SBT	–8.3	0.9	–7.6
Supervised	–6.0	2.9	–3.8
Trainer	–5.6	3.4	–2.9
Incentive	–6.7	2.1	–4.5
Trainer plus incentive	–7.9	2.2	–5.1

Quality and comments	RCT in which blinding was not possible. Allocation concealment not discussed.
Sponsor details	NHLBI

Jeffery 2003 RCT

Aim	To evaluate whether prescribing higher exercise levels in behavioural weight loss programs would enhance short and long term weight loss outcomes.
Participants	Obese men and women, age 25–50 years, free from serious concurrent medical or psychological problems thought to interfere with treatment. An effort was made to recruit equal numbers of male and female participants. 58% of the sample was female. n=202
Intervention	Participants were randomly assigned to one of two study groups. All participants received identical training in diet and behaviour control skills (stimulus control, problem-solving, goal setting, social support, motivation, relapse prevention). They were given different EE goals. The high physical activity group was prescribed an EE of 2500 kcal/week.
Comparison	The comparison group, or SBT group was prescribed an EE of 1000 kcal/week.
Length of follow-up	18 months
Results	Mean weight loss at 6, 12, and 18 months were 8.1±7.4, 6.1±8.8, 4.1±8.3 kg in the SBT group and 9.0±7.1, 8.5±7.9, 6.7±8.1 kg in the HPA group. Differences in weight loss between treatments were not significant at 6 months (p=0.45) or 12 months (p=0.07). At 18 months results were significant (p=0.04).

Quality and comments	Participants were randomised by unknown method. Allocation concealment was not described. It was not possible to blind participants or researchers to treatment. Loss to follow-up was considered in the analysis
Sponsor details	NHLBI

Other outcomes

Anderson 1999 RCT	
Results	Changes in body fat and fat-free mass (FFM) At the end of 16 weeks, the lifestyle group reduced mean (SD) body fat by 6.2 (4.1) kg while the aerobic group lost 7.4 (3.7) kg (p<0.001). The percentage of body fat was reduced to 45.5 (6.2)% in the lifestyle group and to 41.9 (4.3)% in the aerobic group after 16 weeks of treatment (p<0.001). Mean reductions in FFM were greater than 1.4 (1.3) kg for the lifestyle group compared with 0.5 (1.3) for the aerobic group (p=0.03). Cardiovascular risk factors: Significant reductions in TC, TAG, LDL and HDL were observed in both groups after 16 weeks of treatment (tables illegible). TC remained unchanged at week 16 but was significantly reduced in the lifestyle group at week 68. No differences were found between treatment groups in the change in serum lipid or lipoprotein levels (p range 0.62–0.93). BP: Resting systolic BP decreased significantly (p<0.001) during the 16 weeks of treatment and remained lower than baseline values in the lifestyle group at week 68, but there were no significant differences. Oxygen uptake: There were significant improvements over time in maximum oxygen uptake (p<0.001) with no significant differences between groups. Mood: There were no significant differences between conditions in baseline or week 16 scores on the Beck Depression Inventory.
Quality and comments	This study also reported changes in body fat, FFM, aerobic fitness, BP, lipids and lipoproteins and mood. The results of this study indicated that an active lifestyle may help to maintain weight loss.

Jacobsen 2003 RCT	
Results	Aerobic capacity significantly improved 8% for CON and 6% for INT. Twenty-four hour energy and macronutrient intake did not change for CON or INT across the duration of this study. Attrition was higher for the continuous group than the intermittent group in the first 24 weeks of the programme (p<0.05). By week 32 of the study, the continuous group had 58% attrition. The attrition rate in the INT group steadily increased in the time period from 24 to 60 weeks.
Quality and comments	….

Jakicic 1999 RCT	
Results	All groups showed an increase in cardiorespiratory fitness from baseline to 18 months with no significant differences between groups.
Quality and comments	Length of exercise times were self-reported and therefore potentially subject to recall bias.

Jakicic 2003 RCT	
Results	All groups showed significant within group increased in oxygen consumption following 12 months of treatment but there were no significant effects of either exercise intensity or duration on changes in cardiorespiratory fitness between

	groups across 12 months of treatment. Changes in body weight and BMI were significantly greater at 12 months in participants who reported ≥200 min/week of exercise compared with those who exercised >150 min or were inconsistent (p<0.001). Weight loss in the group with 150 min/week or more of exercise did not differ from other groups.
Quality and comments	…

Jeffery 1998 RCT	
Results	Used singly, the trainer and incentive interventions each approximately doubled the number of walks attended over 18 months and used together, the number of walks attended was increased threefold. Total attendance at supervised walking sessions over 18 months across treatment groups was correlated with overall weight change (p<0.0001). A dose response relationship was also observed. Little long-term benefit was associated with 1000 kcal/week whereas 2.5 times this amount was associated with near perfect weight maintenance.
Quality and comments	…

Jeffery 2003 RCT	
Results	Across all participants significant associations observed. In the SBT group the total change in exercise energy expended was significantly associated with weight change (p<0.05) and the change in energy expended by walking was marginally associated with weight change (p<0.07). In the High Physical Activity group both the total change in exercise energy expended and the change in heavy intensity exercise energy expended were significantly associated with weight change (p<0.01 for both). Both groups reported significant (p<0.001) declines in energy intake and in the percentage of energy from fat between baseline and at each assessment. The treatment groups did not differ from each other. Also small subset of participants (Raynor 2004) showed increased variety (p<0.001) in low fat breads and vegetables and decreased variety (p<0.001) in high-fat foods and fats, oils and sweets over the 18-month study. This was associated with reduced percentage dietary fat and weight loss.
Quality and comments	…

Harms

Anderson 1999 RCT	
Harms	None reported. However, there is a question about the reported lowering of HDL in participants.
Quality and comments	…

Jacobsen 2003 RCT	
Harms	None reported.
Quality and comments	…

Jakicic 1999 RCT	
Harms	None reported.
Quality and comments	…

Jakicic 2003 RCT	
Harms	None reported.
Quality and comments	…

Jeffery 1998 RCT	
Harms	None reported.
Quality and comments	…

Jeffery 2003 RCT	
Harms	The HPA consistently reported more exercise related injuries or illnesses than did the SBT group and the average difference between the two groups at 18 months was significant (*p* value not provided).
Quality and comments	…

Generalisability

Anderson 1999 RCT	
Country and setting	USA; home setting possible for all exercise interventions
Participants (included/excluded)	Twenty-eight women were white; ten were African American and two were Mexican American. All women were obese but otherwise healthy. Women were included if no structured exercise for 6 months. Excluded if they had a diagnosis of bulimia nervosa, binge eating disorder, significant depression or other psychiatric disturbances.
Recruitment	Not described
Randomisation	N/R
Intervention (mode and intensity)	LEARN: 16 weekly 60-min sessions in groups of ten. Activity: three weekly aerobics classes in a dance studio
Duration of active intervention	Sixteen-week programme followed by four quarterly follow-up meetings and a week 68 report.
Comparison (mode and intensity)	LEARN: as above Activity: self-directed, 30 min/day on most days of the week. Kept daily records.
Delivery of intervention/comparison (who)	LEARN: Group session lead by masters- or doctoral-level psychologists. Activity: lead by a certified aerobics instructor
Dropout rates	2% dropout for 16-week study and 17.5% dropout for 68-week study.
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Jacobsen 2003 RCT	
Country and setting	USA; the CON group exercised in the context of laboratory environment – this may have influenced attrition rates
Participants (included/excluded)	Overweight sedentary females only
Recruitment	N/R
Randomisation	N/R
Intervention (mode and intensity)	See above
Duration of active intervention	72 weeks

Comparison (mode and intensity)	See above
Delivery of intervention/comparison (who)	University of Nebraska researchers
Dropout rates	58% attrition rate, which varied as noted above.
Treatment of dropouts (return to baseline, or last measurement?)	ITT not done but an analysis of baseline physical characteristics for participants who finished the study vs those who withdrew showed that those who withdrew were heavier and younger than those who finished the study.

Jakicic 1999 RCT	
Country and setting	USA; home-based exercise
Participants (included/excluded)	Obese, sedentary women ages 25–45; excluded if taking medication that would limit participation or affect body weight or if unable to participate fully or were pregnant.
Recruitment	Newspaper advertisement
Randomisation	N/R
Intervention (mode and intensity)	Behaviour: 18-month behavioural weight loss programme with weekly meetings during months 1–6, biweekly meetings during months 7–12 and monthly meetings during months 13–18. Activity: Instructed to exercise 5 days/week 20 min/day during weeks 1–4, 30 min/day weeks 5–8 and 40 min/day for the duration of the study.
Duration of active intervention	18 months
Comparison (mode and intensity)	Behaviour: as above Activity: instructed to exercise 5 d/week with duration progressing from 20 min/day to 40 min/day by the ninth week (SB). Identical to the short bout group except that they were also provided with home treadmills (SBEQ).
Delivery of intervention/comparison (who)	No details reported
Dropout rates	23%
Treatment of dropouts (return to baseline, or last measurement?)	Dropouts included in analysis – return to baseline and no exercise assumed.

Jakicic 2003 RCT	
Country and setting	USA; home-based exercise
Participants (included/excluded)	Obese, sedentary women aged 25–45 years; excluded if history of MI; taking medication that would affect heart rate response during exercise or affect metabolism or weight loss; being treated for psychological conditions or pregnant.
Recruitment	N/R
Randomisation	N/R
Intervention (mode and intensity)	Behaviour: weekly meetings during initial 24 weeks of treatment and biweekly meetings for the remainder of the study period. Also contacted in months 7 to 12 biweekly by telephone for about 10 min by a member of the research team. Activity: see above for details
Duration of active intervention	12 months
Comparison (mode and intensity)	As above
Delivery of intervention/comparison (who)	N/R

Dropout rates	*6%*
Treatment of dropouts (return to baseline, or last measurement?)	Baseline values carried forward.

Jeffery 1998 RCT	
Country and setting	Two US urban communities- Pittsburgh, Pennsylvania and Minneapolis-St Paul, Minnesota.
Participants (included/excluded)	Primarily female but this factor was controlled for in the analysis
Recruitment	Media advertisement from two urban communities
Randomisation	N/R
Intervention (mode and intensity)	Behaviour: groups of about 20 people met weekly for 24 weeks, then monthly. Activity: supervised walking sessions three times per week. The trainer group had all of the above but also had a personal trainer who walked with participants and made reminder phone calls before each walking session and scheduled make up sessions as necessary. The incentive group received a financial incentive for walking rather than a trainer: $1 per walk for first 25 walks, $1.50 per walk for the next 50 walks, $2 per walk for next 50 walks and $3 per walk for any remaining walks. The fourth group had both personal trainers and financial rewards for walking.
Duration of active intervention	18 months
Comparison (mode and intensity)	As above for behaviour
Delivery of intervention/comparison (who)	Groups led by trained interventionists with advanced degrees in nutrition or behavioural sciences. Also trainer was student or staff assistant.
Dropout rates	87% of those enrolling completed the 6 month evaluations and 78% completed the 18 month evaluations
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Jeffery 2003 RCT	
Country and setting	USA; home-based exercise for SBT group but HPA group had exercise coaches and a small monetary incentive for achieving or exceeding the EE goal of 2500 kcal/week.
Participants (included/excluded)	Obese middle-aged men and women
Recruitment	Public advertisement
Randomisation	N/R
Intervention (mode and intensity)	SBT: weekly meetings for first 6 months, biweekly 6 to 12 months, monthly from 12 to 18 months. Groups of less than 20 people.
Duration of active intervention	18 months
Comparison (mode and intensity)	As above
Delivery of intervention/comparison (who)	Led by trained interventionists (experience in content and behaviour). Exercise coaches met with small groups before/after each exercise session. Also reviewed progress and provided extra support as needed.

Dropout rates	Retention rates at 6, 12 and 18 months were 90%, 82% and 87% in the SBT group and 94%, 79% and 80% in the HPA group. Examination of the baseline characteristics of study completers and dropouts at 18 months indicated no significant differences in body weight, sex, exercise level, energy intake or percentage of energy from fat.
Treatment of dropouts (return to baseline, or last measurement?)	N/R

1.6 Pharmacological interventions

1.6.1 Orlistat

Included in HTA (O'Meara or Avenell)

Weight loss

Broom 2002 (in Avenell HTA Broom 2001a) RCT	
Aim	To assess the efficacy of orlistat therapy for weight loss and cardiovascular risk factor reduction in obese individuals with one or more defined cardiovascular risk factor (IGT, dyslipidaemia, hypertension).
Participants	People who were obese (BMI ≥28 kg/m^2) with one or more defined cardiovascular risk factor (IGT, dyslipidaemia, hypertension). *Total 522 – 409 F, 113 M. Mean (SD) age 46.7 (11.4) years orlistat (*n=*259), 45.3 (11.5) years control (*n=*263). Mean (SD) BMI (kg/m^2) 37.1 (6.4) orlistat, 37.0 (6.2) control.*
Intervention	Two weeks pre-treatment phase consisting of single-blind placebo and 600 kcal/day deficit (minimum 1200 kcal/day), 30% energy intake from fats, food and beverage intake diary. Diet: deficit diet continued post randomisation to month 6 then reduced a further 300 kcal/day to week 52. Drug: 120 mg orlistat three times daily with main meals.
Control	*As above except* *Drug: placebo three times daily with main meals.*
Length of follow-up	12 months
Results	*Weight loss during the run-in period was not reported.* At 12 months, mean weight change (SD) was –5.80 (8.50) kg in the orlistat group compared with –2.30 (6.40) kg in the control group. Mean weight change in the intervention group compared with control was –3.50 (95% CI –4.79 to –2.21). *At 12 months, more participants in the orlistat group achieved a 5% or more weight loss than in the control group (55.6 vs 24.3%,* p<*0.0001).*
Quality and comments	Blinded assessment not reported. *ITT analysis done?* Random allocation but no description of concealment. SDs for change in risk factor outcomes at 12 months calculated. SDs for change in HbA_{1c} and mean and SD change in fasting plasma glucose at 12 months obtained from Roche report. *Weight loss reported does not take into account the weight loss over the 2-week dietary lead in period.*
Sponsor details	*Roche Pharmaceuticals*

Broom 2002 (in Avenell HTA Broom 2001b) RCT	
Aim	To investigate the effect of orlistat on body weight and plasma lipid parameters in people who were obese and had hypercholesterolaemia.
Participants	People who were obese (BMI ≥30 kg/m^2) and had hypercholesterolaemia. *Total 137 – 83 F, 54 M. Mean (SD) age 52.1 (9.2) years orlistat (*n=*66), 51.0 (10.5) years control (*n=*71).*
Intervention	Diet: 600 kcal/day deficit diet from each of five major food groups with 30% energy intake from fat, maximum 300 mg/day cholesterol. Activity: advice on physical activity. Drug: orlistat 120 mg three times daily with main meals for 52 weeks (double-blind to week 24 then open label design weeks 25–52).

Control	As above except: *Drug: placebo three times daily with main meals for first 24 weeks then orlistat 120 mg three times daily in open label design for weeks 25–52*
Length of follow-up	52 weeks
Results	*No run-in period was included in the trial design.* *At 6 months, mean weight change (SD) was –4.40 (7.16) kg in the orlistat group compared with –2.60 (6.65) kg in the control group. Mean weight change in the intervention group compared with control was –1.80 (95% CI –4.12 to 0.52).* *At 12 months, mean weight change (SD) was –4.97 (5.40) kg in the orlistat group compared with –4.28 (5.82) kg in the control group. Mean weight change in the intervention group compared with control was –0.69 (95% CI –2.57 to 1.19).* *At the end of 24 weeks, 44% of the orlistat group compared with 18% of the placebo group has lost at least 5% of initial body weight (*p<*0.001) and 7.6% compared with 4.2% had lost at least 10% (not significant).*
Quality and comments	Blinded assessment not reported. *ITT analysis done?* Random allocation but no description of concealment. SDs calculated and denominators assumed correct. *SDs calculated for 6-month weight loss using HTA formula. Also, different values to HTA for 12 months as used values from Broom (2002b).*
Sponsor details	Roche Products Limited

Davidson 1999 (in Avenell and O'Meara HTA) RCT	
Aim	To test the hypothesis that orlistat combined with dietary intervention is more effective than placebo plus diet for weight loss and maintenance over 2 years.
Participants	People who were obese (BMI between 30 and 43 kg/m^2). *Total 880 – 741 F, 139 M. Mean (SEM) 43.3 (0.6) years orlistat (*n*=657), 44.0 (0.7) years control (*n*=223). Mean (SEM) BMI (kg/m^2) 36.5 (0.9) orlistat, 36.2 (0.1) control.*
Intervention	500–800 kcal/day deficit with 30% energy intake from fat in 4 weeks single-blind placebo pre-treatment phase. Diet: 500–800 kcal/day deficit with 30% energy intake from fats continued for 2 years, if participant still losing weight in last 3 months of year 1 then energy intake increased 200–300 kcal/day; food diaries kept by participant and used periodically for counselling with dietitian; once daily multivitamin containing all fat-soluble vitamins (CENTRUM) given in year 1 only if serum vitamin values decreased to below reference range on two consecutive visits Activity: participant encouraged to increase activity by walking briskly 20–30 min per week throughout 2 years. BT: four behaviour modification sessions on weight loss in year 1 then four weight-maintenance seminars in year 2. Drug: 120 mg orlistat three times daily for year 1. Re-randomised at week 52 to placebo three times daily orlistat 120 mg three times daily orlistat 60 mg three times daily.
Control	As above except *Drug: placebo three times daily for year 1 and year 2.*
Length of follow-up	2 years

Results	*Both treatment arms lost about 2.3 kg during the run-in period.* At 12 months, mean weight change (SD) was –8.76 (9.48) kg in the orlistat group compared with –5.81 (10.01) kg in the control group. Mean weight change in the intervention group compared with control was –2.95 (95% CI –4.45 to –1.45). *At 12 months, 65.7% of the orlistat group compared with 43.6% of the placebo group lost more than 5% of initial body weight (*p<*0.01). 38.9% of the orlistat group compared with 24.8% of the placebo group lost 10% or more of initial body weight (*p=*0.004).* *At 24 months, mean weight change (SD) was –5.56 (7.49) kg in the orlistat group compared with –0.18 (6.38) kg in the control group. Mean weight change in the intervention group compared with control was –5.38 (95% CI –6.97 to –3.79).* At 24 months compared with 12 months, mean weight change (SD) was 3.20 (5.57) kg in the orlistat group compared with 5.63 (4.93) kg in the control group. Mean weight change in the intervention group compared with control was –2.43 (95% CI –3.64 to –1.22). *At 24 months, 34.1% of the orlistat group compared with 17.5% of the placebo group lost more than 10% of initial body weight (*p=*0.02).* *Of those treated with orlistat for 24 months, weight gain was significantly less (mean 3.2kg) compared with those who received placebo (mean 5.63 kg) (*p<*0.001).*
Quality and comments	Blinded assessment not reported. *ITT analysis done?* Random allocation but no description of concealment. 2-year results only stated for participants receiving placebo/placebo and orlistat. *Used HTA weight maintenance figures and denominators to calculate loss at 24 months with HTA formula SDs.*
Sponsor details	Hoffman-La Roche Inc

NB: have included the 5% and 10% weight loss, but this is >5%, 10% NOT ≥5%, 10% as in other studies.

Finer 2000 (in Avenell and O'Meara HTA) RCT	
Aim	To assess the efficacy and tolerability of orlistat, in combination with dietary advice, in producing and maintaining weight loss over a 12-month period.
Participants	People who were obese (BMI between 30 and 43 kg/m^2). *Total 218 – 193 F, 25 M. Mean (SD) age 41.5 (10.5) years orlistat (*n=*110), 41.4 (10.0) years control (*n=*108). Mean (SD) BMI (kg/m^2) 36.8 (3.6) orlistat, 36.8 (3.7) control.*
Intervention	Pre-treatment phase of 4-week single blind run-in, then: Diet: 600 kcal/day deficit diet (minimum 1200 kcal/day) 30% fat, alcohol 150 g/week, aimed to produce initial weight loss 0.25–0.5 kg/week, reduced further 300 kcal/day at week 24 until week 52 (or reduced to 1000 kcal/day if already at 1200 kcal/day). Drug: 120 mg orlistat three times daily.
Control	As above except *Drug: placebo three times daily.*
Length of follow-up	12 months
Results	*Weight loss during the run-in period was about 3 kg.* At 12 months, mean weight change (SD) was –3.29 (6.85) kg in the orlistat group compared with –1.31 (6.29) kg in the control group. Mean weight change in the intervention group compared with control was –1.98 (95% CI –3.73 to –0.23). *At 12 months, 35% of the orlistat group compared with 21% of the placebo group lost more than 5% of initial body weight (*p=*0.02). 16% of the orlistat group compared with 6% of the placebo group lost more than 10% of initial body weight (*p=*0.02).*
Quality and comments	Blinded assessment done. *ITT analysis done?* Good concealment of allocation. SDs for change in weight calculated.

Sponsor details	Hoffman-La Roche

NB: have included the 5% and 10% weight loss, but this is >5%, 10% NOT ≥5%, 10% as in other studies.

Hauptman 2000 (in Avenell and O'Meara HTA) RCT	
Aim	To evaluate the efficacy of orlistat in producing and maintaining long-term weight loss, and in improving obesity-related risk factors in individuals who are obese and who received limited dietary and behavioural counselling.
Participants	People who were obese (BMI of 30 to 44 kg/m^2). *Total 635 – 497 F, 138 M. Mean (SD) age 42.6 (11.68) years orlistat 60 mg (*n=*213), 43.2 (10.14) years orlistat 120 mg (*n=*210), 41.6 (10.19) years control (*n=*212). Mean (SD) BMI 35.8 (4.38) orlistat 60 mg, 36.0 (2.90) orlistat 120 mg, 36.1 (4.37) control at 4 weeks prior to randomisation.*
Intervention	Four weeks single blind placebo pre-treatment phase of 1200 kcal/day diet for participants who weighed <90 kg initially or 1500 kcal/day for participants who weighed ≥90 initially; 30% energy as fat, 50% as carbohydrate, 20% as protein, maximum 300 mg/day cholesterol, maximum ten alcoholic drinks per week; dietary guidance on intake from study physician at start of pre-treatment only. Diet: diet continued for first 52 weeks then increased by 300 kcal/day for participants still losing weight at end week 52 or no dietary adjustment for those weight stable until week 104. BT: participants viewed videos on behaviour modification techniques for weight control 4 times in first 52 weeks, weight management and diet pamphlets for weight maintenance given 4 times during weeks 53–104 based on 'Live for Life' programme. Activity: all participants encouraged to increase physical activity by brisk walking 20–30 min three to five times per week; dietary records kept ten times during study. Drug – orlistat 60 mg: 60 mg orlistat three times daily with main meals. Drug – orlistat 120 mg: 120 mg orlistat three times daily with main meals.
Control	*As above except* *Drug: placebo three times daily with main meals.*
Length of follow-up	24 months
Results	*Mean change in body weight during the run-in period was –2.73 kg for placebo, –2.49 kg orlistat 60 mg, and –2.54 kg orlistat 120 mg.* *Orlistat 60 mg: at 6 months, mean weight change (SD) was –4.43 (7.17) kg in the orlistat group compared with –1.97 (6.47) kg in the control group. Mean weight change in the intervention group compared with control was –2.46 (95% CI –3.76 to –1.16).* *Orlistat 60 mg: At 12 months, mean weight change (SD) was –4.59 (7.21) kg in the orlistat group compared with –1.41 (6.31) kg in the control group. Mean weight change in the intervention group compared with control was –3.18 (95% CI –4.47 to –1.89).* *Orlistat 60 mg: At 18 months, mean weight change (SD) was –3.29 (6.85) kg in the orlistat group compared with –0.20 (5.97) kg in the control group. Mean weight change in the intervention group compared with control was –3.56 (95% CI –4.79 to –2.33).* *Orlistat 60 mg: At 24 months, mean weight change (SD) was –2.48 (6.62) kg in the orlistat group compared with 1.08 (6.22) kg in the control group. Mean weight change in the intervention group compared with control was –3.05 (95% CI –4.26 to –1.84).* *Orlistat 60 mg: At 18 months compared with 12 months, mean weight change (SD) was 1.30 (6.28) kg in the orlistat group compared with 1.21 (6.26) kg in the control group. Mean weight change in the intervention group compared with control was 0.09 (95% CI –1.10 to 1.28).* *Orlistat 60 mg: At 24 months compared with 12 months, mean weight change (SD) was 2.62 (6.66) kg in the orlistat group compared with 2.49 (6.62) kg in the*

	control group. Mean weight change in the intervention group compared with control was 0.13 (95% CI –1.13 to 1.39). Orlistat 120 mg: At 6 months, mean weight change (SD) was –5.46 (7.46) kg in the orlistat group compared with –1.97 (6.47) kg in the control group. Mean weight change in the intervention group compared with control was –3.49 (95% CI –4.82 to –2.16). Orlistat 120 mg: At 12 months, mean weight change (SD) was –5.40 (7.44) kg in the orlistat group compared with –1.41 (6.31) kg in the control group. Mean weight change in the intervention group compared with control was –3.99 (95% CI –5.31 to –2.67). Orlistat 120 mg: At 18 months, mean weight change (SD) was –3.68 (6.96) kg in the orlistat group compared with –0.20 (5.97) kg in the control group. Mean weight change in the intervention group compared with control was –3.66 (95% CI –4.90 to –2.42). Orlistat 120 mg: At 24 months, mean weight change (SD) was –2.48 (6.62) kg in the orlistat group compared with 1.08 (6.22) kg in the control group. Mean weight change in the intervention group compared with control was –3.56 (95% CI –4.79 to –2.33). Orlistat 120 mg: At 18 months compared with 12 months, mean weight change (SD) was 1.72 (6.40) kg in the orlistat group compared with 1.21 (6.26) kg in the control group. Mean weight change in the intervention group compared with control was 0.51 (95% CI –0.70 to 1.72). Orlistat 120 mg: At 24 months compared with 12 months, mean weight change (SD) was 2.92 (6.74) kg in the orlistat group compared with 2.49 (6.62) kg in the control group. Mean weight change in the intervention group compared with control was 0.43 (95% CI –0.84 to 1.70). *At 12 months, 50.5% of the orlistat 120 mg group compared with 30.7% of the placebo group lost 5% or more of initial body weight (*p<*0.01).* *At 12 months, 48.8% of the orlistat 60 mg group compared with 30.7% of the placebo group lost 5% or more of initial body weight (*p<*0.01).* *At 12 months, 28.6% of the orlistat 120 mg group compared with 11.3% of the placebo group lost 10% or more of initial body weight (*p<*0.01).* *At 12 months, 24.4% of the orlistat 60 mg group compared with 11.3% of the placebo group lost 10% or more of initial body weight (*p<*0.01).* *At 24 months, 34.3% of the orlistat 120 mg group compared with 24.1% of the placebo group lost 5% or more of initial body weight (*p=*0.02).* *At 24 months, 33.8% of the orlistat 60 mg group compared with 24.1% of the placebo group lost 5% or more of initial body weight (*p=*0.03).* *At 24 months, 18.6% of the orlistat 120 mg group compared with 6.6% of the placebo group lost 10% or more of initial body weight (*p=*0.001).* *At 24 months, 14.6% of the orlistat 60 mg group compared with 6.6% of the placebo group lost 10% or more of initial body weight (*p=*0.08).* *Participants in all groups regained some weight during the 24 months, weight regain in year 2 was greater in the placebo group. Weight regain (as a percentage of weight lost in year 1) was 60% in the placebo group compared with 37% and 38% in the orlistat 60 mg and 120 mg groups, respectively.*
Quality and comments	Blinded assessment not reported. *ITT analysis done?* Good concealment of allocation. Change in weight including SDs calculated (change from –4 weeks to week 52 minus change from –4 weeks to week 0), change in risk factors calculated from actual values, SDs also calculated.
Sponsor details	None mentioned, first author at Hoffman-La Roche Inc.

Hill 1999 (in Avenell and O'Meara HTA) RCT	
Aim	To test the hypothesis that orlistat, combined with appropriate dietary and behavioural counselling, effectively diminishes the weight regain that generally occurs after a period of conventional hypo-energetic dieting. Also to evaluate the long-term effects of orlistat on obesity-related CVD risk factors.

Participants	People who were overweight or obese (BMI between 28 and 43 kg/m^2). *Total 720 – 605 F, 115 M. Mean (SEM) age 46.8 (0.8) years orlistat 30 mg (*n=*186), 46.1 (0.7) years orlistat 60 mg (*n=*171), 45.9 (0.7) years orlistat 120 mg (*n=*179), 46.4 (0.7) control (*n=*184). Mean (SEM) BMI (kg/m^2) 32.6 (0.2) orlistat 30 mg, 32.9 (0.2) orlistat 60 mg, 32.8 (0.2) orlistat 120 mg, 32.8 (0.2) control.*
Intervention	Six-month pre-treatment phase consisting of 1000 kcal/day deficit, 30% energy as fat, 50% as carbohydrate, 20% as protein, to produce weight loss 0.5–1 kg/week; dietary counselling, four sessions of behavioural modification programme (University of Minnesota's Wise Weighs) and encouraged to increase activity to brisk walking 20–30 min five times per week, standard multivitamin–multimineral tablets once daily (CENTRUM) from start of pre-treatment to end of study. Diet: from randomisation, participants prescribed maintenance diet where individual energy requirements reassessed according to body weight at week 22 of pre-treatment phase; increase in energy intake prescribed to match anticipated metabolic requirements over 1 year, if participants gained weight they were encouraged to maintain this higher weight. BT: dietary and behavioural counselling given to all, dietary records Drug – orlistat 30 mg: 30 mg orlistat three times daily Drug – orlistat 60 mg: 60 mg orlistat three times daily Drug – orlistat 120 mg: 120 mg orlistat three times daily
Control	As above except: *Drug: placebo three times daily.*
Length of follow-up	12 months
Results	*Mean weight loss over the run-in period (6 months) was –10.33 kg for placebo, –10.06 kg orlistat 30 mg, –10.00 kg orlistat 60 mg and –9.86 kg orlistat 120 mg.* Orlistat 30 mg: At 12 months, mean weight change (SD) was 4.91 (7.30) kg in the orlistat group compared with 4.40 (7.16) kg in the control group. Mean weight change in the intervention group compared with control was 0.51 (95% CI –1.32 to 2.34). Orlistat 60 mg: At 12 months, mean weight change (SD) was 3.84 (7.00) kg in the orlistat group compared with 4.40 (7.16) kg in the control group. Mean weight change in the intervention group compared with control was –0.56 (95% CI –2.36 to 1.24). Orlistat 120 mg: At 12 months, mean weight change (SD) was 2.62 (6.66) kg in the orlistat group compared with 4.40 (7.16) kg in the control group. Mean weight change in the intervention group compared with control was –1.78 (95% CI –3.55 to 0.01). *Treatment with orlistat 120 mg three times per day resulted in significantly less weight regain than placebo. People treated with orlistat 120 mg regained about half as much weight as those in the placebo group.*

	Weight regain at 12 months (as % of weight loss in 6-month lead in)			
Group	*≤25%*	*25 to 50%*	*50 to 75%*	*>75%*
Placebo	*29.9*	*22.8*	*15.2*	*32.1*
Orlistat 30 mg	*32.3*	*20.4*	*18.3*	*29.0*
Orlistat 60 mg	*30.4*	*25.7*	*25.1*	*18.7**
Orlistat 120 mg	*47.5***	*22.9*	*17.3*	*12.3**

**Significantly different from placebo and orlistat 30 mg,* p<*0.05*
***Significantly different from all other groups,* p<*0.05*

Quality and comments	Blinded assessment not reported. *ITT analysis done?* Random allocation but no description of concealment. All outcomes calculated from initial values to week 52 minus initial values to end of 6 month lead-in (denominators differ), SDs for weight change calculated. Body weight significantly different in orlistat 60 mg three times daily from all other groups (p<0.05) accounted for by higher proportion of men to women in the orlistat 60 mg group.
Sponsor details	Hoffman-La Roche

NB: have included the 5% weight loss, but this is >5%, NOT ≥5%, as in other studies.

Hollander 1998 (in Avenell and O'Meara HTA) RCT	
Aim	To investigate the long-term weight loss efficacy of orlistat in obese people with type 2 diabetes, maintained on oral sulfonylureas, and to determine whether this treatment improves glycaemic control and lipid status more than dietary treatment alone.
Participants	People who were obese (BMI 28 to 40 kg/m^2) and who had type 2 diabetes maintained on oral sulfonylureas. Total 321 – 157 F, 164 M. Mean (SD) age 55.4 (8.8) years orlistat (*n*=162), 54.7 (9.7) year control (*n*=159). Mean (SD) BMI 34.5 (3.2) kg/m^2 orlistat, 34.0 (3.4) kg/m^2 control.
Intervention	Five weeks pre-treatment phase single blind with mildly hypoenergetic diet. Diet: then 500 kcal/day deficit from baseline to week 52, additional diet counselling and a standardised commercially available vitamin supplement given if two consecutive vitamin measures fell below reference range. Drug: 120 mg orlistat three times daily taken with meals.
Control	As above except: *Drug: placebo three times daily taken with meals.*
Length of follow-up	12 months
Results	*Weight loss during the run-in period was –2.24kg in the placebo group, and –2.07kg in the orlistat group.* At 12 months, mean weight change (SD) was –3.84 (5.00) kg in the orlistat group compared with –1.43 (5.10) kg in the control group. Mean weight change in the intervention group compared with control was –2.41 (95% CI –3.54 to –1.28). *At 12 months, 48.8% of the orlistat group compared with 22.6% of the placebo group lost 5% or more of initial body weight (*p*<0.001).* *At 12 months, 17.9% of the orlistat group compared with 8.8% of the placebo group lost 10% or more of initial body weight (*p*=0.017).*
Quality and comments	Blinded assessment done. Possible ITT analysis. Good concealment of allocation. All mean and standard deviation change in weight and risk factor outcomes obtained from Roche report.
Sponsor details	Hoffman-La Roche

Lindgarde 2000 (in Avenell HTA) RCT	
Aim	To assess the effect of orlistat on body weight and cardiovascular risk profile in people who are obese.
Participants	People who were obese (BMI 28 to 38 kg/m^2) with at least one obesity associated cardiovascular risk factor. *Total 376 – 239 F, 137 M. Mean (SD) age 53.7 (9.4) years orlistat (*n*=190), 53.2 (9.9) years control (*n*=186). Mean (SD) BMI 33.2 (3.0) kg/m^2 orlistat, 33.2 (3.1) kg/m^2 control. Results from 2 weeks prior to randomisation.*
Intervention	Two weeks single blind placebo plus mildly hypoenergetic diet consisting of 600 kcal/day deficit (minimum 1200 kcal/day) 30% energy from fat. Diet: diet continued up to month 6 when energy content reduced additional 300 kcal/day; participants also received dietary counselling as part of self-help weight control educational package including leaflets and videotape given at start of run-in phase. Activity: participants encouraged to increase physical activity by taking 30 min walk each day. Drug: 120 mg orlistat three times daily.
Control	*As above except:* *Drug: placebo three times daily.*
Length of follow-up	12 months

Results	*During the 2-week run-in period, people lost about 1.4 kg.* At 12 months, mean weight change (SD) was –4.20 (7.03) kg in the orlistat group compared with –2.90 (6.74) kg in the control group. Mean weight change in the intervention group compared with control was –1.30 (95% CI –2.69 to 0.09). *At 12 months, 54.2% of the orlistat group compared with 40.9% of the placebo group lost 5% or more of initial body weight (*p<*0.001).* *At 12 months, 19.2% of the orlistat group compared with 14.6% of the placebo group lost 10% or more of initial body weight (not significant).*
Quality and comments	Blinded assessment not reported. Random allocation but no description of concealment. Possibly ITT, all randomised participants included in ITT analysis, but participants withdrawn by investigators if compliance <60%. Change including SDs, in weight and risk factor outcomes at 12 months calculated (change from –2 weeks to week 52 minus change from –2 weeks to week 0). SDs for change in weight also calculated.
Sponsor details	Roche AB

Rossner 2000 (in Avenell and O'Meara HTA) RCT	
Aim	To determine the effect of orlistat on long-term weight loss, to determine the extent to which orlistat minimises weight regain in the second year of treatment, and to assess the effects of orlistat on obesity-related risk factors
Participants	People who were overweight or obese (BMI 28 to 43 kg/m^2). *Total 718 – 591 F, 127 M. Mean (SD) age 44.7 (10.7) years orlistat 60 mg (*n=*242), 43.6 (11.4) years orlistat 120 mg (*n=*244), 44.3 (10.8) years control (*n=*243). Mean (SD) BMI 35.2 (3.9) kg/m^2 orlistat 60 mg, 34.7 (3.7) kg/m^2 orlistat 120 mg, 35.5 (4.1) kg/m^2 control.*
Intervention	Four weeks pre-treatment phase consisting of single blind placebo and 600 kcal/day deficit, 30% energy intake from fat, Other: all participants ceased taking vitamin supplements prior to study and if vitamin or beta-carotene levels fell below clinical reference range on two consecutive measurements then participants were given supplements; Diet: at randomisation deficit diet continued and during second year diet was adjusted as follows; for participants who had lost ≥3 kg between weeks 40 and 52, daily energy intake was prescribed at a level equivalent to estimated energy intake minus 10% kcal/day; those participants who lost <3 kg no dietary adjustment made Drug – orlistat 60 mg: 60 mg orlistat three times daily with breakfast lunch and dinner Drug – orlistat 120 mg: 120 mg orlistat three times daily with breakfast, lunch and dinner
Control	*As above except:* *Drug: placebo three times daily with breakfast lunch and dinner.*
Length of follow-up	24 months

Results	*Weight loss during the run-in period was not reported, but assumed mean to be about 2 kg.* *Orlistat 60 mg: At 12 months, mean weight change (SD) was –6.50 (7.75) kg in the orlistat group compared with –4.40 (7.16) kg in the control group. Mean weight change in the intervention group compared with control was –2.10 (95% CI –3.43 to –0.77).* *Orlistat 60 mg: At 24 months, mean weight change (SD) was –4.60 (7.22) kg in the orlistat group compared with –2.30 (6.57) kg in the control group. Mean weight change in the intervention group compared with control was –2.30 (95% CI –3.53 to –1.07).* *Orlistat 60 mg: At 24 months compared with 12 months, mean weight change (SD) was 1.90 (6.45) kg in the orlistat group compared with 2.10 (6.51) kg in the control group. Mean weight change in the intervention group compared with control was –0.20 (95% CI –1.35 to 0.95).* Orlistat 120 mg: At 12 months, mean weight change (SD) was –8.13 (8.22) kg in the orlistat group compared with –5.23 (7.40) kg in the control group. Mean weight change in the intervention group compared with control was –2.90 (95% CI –4.30 to –1.50). Orlistat 120 mg: At 24 months, mean weight change (SD) was –5.98 (7.61) kg in the orlistat group compared with –3.06 (6.78) kg in the control group. Mean weight change in the intervention group compared with control was –2.92 (95% CI –4.21 to –1.63). Orlistat 120 mg: At 24 months compared with 12 months, mean weight change (SD) was 2.15 (6.52) kg in the orlistat group compared with 2.17 (6.53) kg in the control group. Mean weight change in the intervention group compared with control was –0.02 (95% CI –1.19 to 1.15). *Significantly more people treated with orlistat 120 mg lost more than 5% of initial body weight after 1 and 2 years of treatment than placebo (*p<*0.001). 31.2% (*p=*0.002) and 38.3% (*p<0*.001) of those in the orlistat 60 mg and 120 mg groups lost more than 10% of their initial body weight after 1 year compared with 18.8% of placebo-treated participants. A weight loss of more than 10% was maintained in the second year by 18.6%, 29.0% (*p<*0.05), and 28.2% (*p<*0.05) of people receiving placebo, orlistat 60 mg, and orlistat 120 mg, respectively.*
Quality and comments	Blinded assessment not reported. Random allocation but no description of concealment. *ITT done?* Roche provided denominators, change in risk factors calculated, SDs calculated, weight change from randomisation to 12 months and 24 months derived from graph. Baseline data for safety population only. *Used HTA formula for SDs. Values for 5/10% read off Figure 3.*
Sponsor details	Hoffman-La Roche

Sjöström 1998 (in Avenell and O'Meara HTA) RCT	
Aim	To assess the efficacy and tolerability of orlistat in promoting weight loss and preventing weight regain in people who are obese over a 2-year period.
Participants	People who were overweight or obese (BMI 28 to 47 kg/m^2) *Total 683 – 567 F, 116 M. Mean (range) age 45.2 (20 to 76) years orlistat (*n=*343), 44.3 (18 to 77) control (*n=*340). Mean BMI 36.1 kg/m^2 orlistat, 36.2 kg/m^2control.*

Intervention	Four weeks pre-treatment consisting of single blind placebo three times daily with meals and 600 kcal/day deficit with 30% energy intake from fat. Diet: first 24 weeks all participants continued 600 kcal/day deficit (minimum 1200 kcal/day) then until week 52 reduced additional 300 kcal/day (minimum 1000 kcal/day); diet designed to cause weight loss of 0.25–0.5 kg/week and consisted of 30% energy intake as fat, 50% as carbohydrate, 20% as protein, 300 mg/day cholesterol, three main meals and optional snack daily, 150 mg/week alcohol; year 2 all participants advised on weight maintenance diet and not to return to hypoenergetic diet; additional dietary counselling or vitamin supplements given when necessary if two consecutive measures were below normal range. Drug: orlistat 120 mg three times daily baseline to week 104
Control	*As above except:* *Drug: placebo three times daily baseline to week 104*
Length of follow-up	*24 months*
Results	Assumed mean weight loss in 4 week run-in was 2.2 kg. At 12 months, mean weight change (SD) was –8.10 (8.21) kg in the orlistat group compared with –3.90 (7.02) kg in the control group. Mean weight change in the intervention group compared with control was –4.20 (95% CI –5.35 to –3.05). *At the end of year 1, 9.3% of the orlistat group vs 2.1% of the placebo group had lost >20% of initial body weight; 29.5 vs 15.6% had lost 10.1–20.0% of bodyweight; 29.7 vs 31.5% had lost 5.1–10.0% of bodyweight; and 23.6 vs 32.7% had lost 0.1–5.0% of bodyweight. 7.9 vs 18.2% had unchanged or increased bodyweight.* *In former placebo-group participants, orlistat reduced bodyweight (LSM difference in weight loss orlistat–placebo 3.6 kg [SE=0.6];* p=*0.001). In former orlistat-group participants, the weight regain was smaller with orlistat than with placebo (LSM difference in weight loss orlistat–placebo 2.4 kg;* p<*0.001). After 2 years of continuous orlistat treatment, 57.1% of the patients maintained a weight loss greater than 5%; the corresponding percentage for 2 years' placebo treatment was 37.4%.*
Quality and comments	Blinded assessment not reported. Good concealment of allocation. *ITT done?* Mean change in weight and risk factor data calculated from actual values. SDs calculated, assumed mean weight loss in 4 week run-in=2.2 kg. Actual weight loss not reported at 24 months for placebo-placebo group, orlistat-orlistat group. No SDs for other outcomes.
Sponsor details	Hoffman-La Roche

NB: have included the 5% and 10% weight loss, but this is >5%, 10% NOT ≥5%, 10% as in other studies.

Other outcomes

Broom 2002 (in Avenell HTA Broom 2001a) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.12 (1.08) in the orlistat group, and 0.16 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.28 (95% CI –0.47 to –0.09). At 12 months, mean (SD) LDL change in mmol/l was –0.30 (0.74) in the orlistat group, and –0.02 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.28 (95% CI –0.41 to –0.15). At 12 months, mean (SD) TAG change in mmol/l was 0.44 (0.96) in the orlistat group, and 0.17 (0.96) in the control group. Mean TAG change in the intervention group compared with control was 0.27 (95% CI 0.75 to 0.43). At 12 months, mean (SD) %HbA_{1c} change was 0.08 (0.43) in the orlistat group, and 0.19 (0.58) in the control group. Mean TAG change in the intervention group compared with control was –0.11 (95% CI –0.20 to –0.02). At 12 months, mean (SD) DBP change in mmHg was –5.50 (8.30) in the orlistat

	group, and –3.10 (8.30) in the control group. Mean DBP change in the intervention group compared with control was –2.40 (95% CI –3.82 to –0.98). At 12 months, mean (SD) SBP change in mmHg was –6.00 (12.70) in the orlistat group, and –2.30 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –3.70 (95% CI –5.88 to –1.52). At 12 months, mean (SD) FPG change in mmol/l was –0.19 (1.26) in the orlistat group, and 0.06 (1.02) in the control group. Mean FPG change in the intervention group compared with control was –0.25 (95% CI –0.45 to –0.05). *No analysis of outcomes independent of weight loss was reported.*
Quality and comments	…

Broom 2002 (in Avenell HTA Broom 2001b) RCT	
Results	*At 6 months, mean (SD) TC change in mmol/l was –0.83 (0.12) in the orlistat group, and –0.27 (0.10) in the control group. Mean TC change in the intervention group compared with control was –0.56 (95% CI –0.60 to –0.52).* *At 6 months, mean (SD) LDL change in mmol/l was –0.71 (0.12) in the orlistat group, and –0.31 (0.12) in the control group. Mean LDL change in the intervention group compared with control was –0.40 (95% CI –0.44 to –0.36).* *At 6 months, mean (SD) HDL change in mmol/l was –0.19 (0.10) in the orlistat group, and –0.11 (0.03) in the control group. Mean LDL change in the intervention group compared with control was –0.08 (95% CI –0.11 to –0.05).* *At 6 months, mean (SD) TAG change in mmol/l was –0.15 (0.25) in the orlistat group, and –0.42 (0.26) in the control group. Mean FPG change in the intervention group compared with control was 0.27 (95% CI 0.18 to 0.36).* *At 12 months, mean (SD) TC change in mmol/l was –0.96 (1.04) in the orlistat group, and –0.67 (1.04) in the control group. Mean TC change in the intervention group compared with control was –0.29 (95% CI –0.64 to 0.06).* *At 12 months, mean (SD) LDL change in mmol/l was –0.91 (1.00) in the orlistat group, and –0.40 (1.05) in the control group. Mean LDL change in the intervention group compared with control was –0.51 (95% CI –0.85 to –0.17).* *At 12 months, mean (SD) HDL change in mmol/l was –0.29 (0.45) in the orlistat group, and –0.23 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.06 (95% CI –0.19 to 0.07).* *At 12 months, mean (SD) FPG change in mmol/l was –0.40 (1.35) in the orlistat group, and –0.10 (1.35) in the control group. Mean FPG change in the intervention group compared with control was –0.30 (95% CI –0.75 to 0.15).* *At 12 months, although the weight loss in both groups was similar, people who had been taking orlistat throughout had significantly improved TC and LDL levels. This was interpreted by the authors as suggesting that orlistat had a lipid-lowering effect independent of weight loss.*
Quality and comments	Not able to calculate FPG at 6 months as no SDs?

Davidson 1999 (in Avenell and O'Meara HTA) RCT	
Results	At 12 months, mean (SD) DBP change in mmHg was –1.00 (8.30) in the orlistat group, and 1.30 (8.30) in the control group. Mean DBP change in the intervention group compared with control was –2.30 (95% CI –3.56 to –1.04). At 12 months, mean (SD) SBP change in mmHg was –0.80 (12.70) in the orlistat group, and 1.00 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –1.80 (95% CI –3.73 to 0.13). At 24 months, mean (SD) TC change in mmol/l was 0.11 (1.08) in the orlistat group, and 0.21 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.10 (95% CI –0.40 to 0.20). At 24 months, mean (SD) LDL change in mmol/l was 0.05 (0.74) in the orlistat group, and 0.04 (0.74) in the control group. Mean LDL change in the intervention group compared with control was 0.01 (95% CI –0.20 to 0.22). At 24 months, mean (SD) HDL change in mmol/l was 0.11 (0.29) in the orlistat group, and 0.15 (0.29) in the control group. Mean HDL change in the intervention

	group compared with control was –0.04 (95% CI –0.12 to 0.04). At 24 months, mean (SD) TAG change in mmol/l was –0.07 (0.96) in the orlistat group, and 0.15 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.22 (95% CI –0.49 to 0.05). At 24 months, mean (SD) FPG change in mmol/l was 0.06 (0.31) in the orlistat group, and 0.26 (0.38) in the control group. Mean FPG change in the intervention group compared with control was –0.20 (95% CI –0.30 to –0.10). *Improvements in TC and LDL levels were independent of the greater weight loss achieved in the orlistat group. Whereas, improvements in insulin levels were associated with weight loss.* *Levels of fat-soluble vitamins and beta-carotene generally remained within the reference range in all treatment groups throughout the study. Vitamins D (*p=*0.001)* and E (p=*0.003)* levels decreased significantly in the orlistat-treated group vs placebo at the end of year 1, but mean serum levels remained within the reference range. When corrected for LDL-cholesterol, vitamin E levels were unchanged in the orlistat-treated participants. Supplementation was required in 14.1% of participants treated with orlistat 120 mg for 2 years vs with 6.5% of placebo recipients. All participants receiving supplementation attained normal serum vitamin levels by the end of the study and no participants were withdrawn due to low values.*
Quality and comments	…

Finer 2000 (in Avenell and O'Meara HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.05 (0.76) in the orlistat group, and 0.30 (0.68) in the control group. Mean TC change in the intervention group compared with control was –0.35 (95% CI –0.54 to –0.16). At 12 months, mean (SD) LDL change in mmol/l was –0.11 (0.63) in the orlistat group, and 0.21 (0.53) in the control group. Mean LDL change in the intervention group compared with control was –0.32 (95% CI –0.47 to –0.17). At 12 months, mean (SD) HDL change in mmol/l was 0.15 (0.23) in the orlistat group, and 0.16 (0.21) in the control group. Mean HDL change in the intervention group compared with control was –0.01 (95% CI –0.07 to 0.05). *More people treated with orlistat were given vitamin supplementation (1.8% vitamin A, 8.0% vitamin D, 3.6% vitamin E compared with 0.9% for each vitamin in the control group). Beta-carotene supplements were given to 0.9% of people in the orlistat group.* *Significant differences were seen in the changes of levels of vitamin E and beta-carotene between the orlistat and placebo groups (–2.08 µmol/l,* p<*0.001, and –0.11 µmol/l,* p<*0.001), but not for vitamins A or D. No significant change occurred in the mean vitamin E:cholesterol ratio at 12 months.* *No analysis of outcomes independent of weight loss was reported.*
Quality and comments	…

Hauptman 2000 (in Avenell and O'Meara HTA) RCT	
Results	*Orlistat 60 mg: At 12 months, significant changes (*p<*0.05) from baseline compared with placebo were seen at 12 months in TC (–0.06 vs 0.30), LDL-cholesterol (–0.07 vs 0.25) and HDL-cholesterol (0.05 vs 0.11).* *Orlistat 60 mg: At 24 months, significant changes (*p<*0.05) from baseline compared with placebo were seen at 12 months in TC (0.05 vs 0.44), and LDL cholesterol (–0.01 vs 0.36).* Orlistat 120 mg: At 12 months, mean (SD) TC change in mmol/l was –0.04 (1.08) in the orlistat group, and 0.30 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.34 (95% CI –0.55 to –0.13). Orlistat 120 mg: At 12 months, mean (SD) LDL change in mmol/l was –0.12 (0.74) in the orlistat group, and 0.25 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.37 (95% CI –0.51 to –0.23). Orlistat 120 mg: At 12 months, mean (SD) HDL change in mmol/l was 0.06 (0.29)

in the orlistat group, and 0.11 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.05 (95% CI –0.11 to 0.01).
Orlistat 120 mg: At 12 months, mean (SD) TAG change in mmol/l was 0.06 (0.96) in the orlistat group, and –0.10 (0.96) in the control group. Mean TAG change in the intervention group compared with control was 0.16 (95% CI –0.02 to 0.34).
Orlistat 120 mg: At 12 months, mean (SD) FPG change in mmol/l was 0.03 (1.35) in the orlistat group, and 0.11 (1.35) in the control group. Mean FPG change in the intervention group compared with control was –0.08 (95% CI –0.34 to 0.18).
Orlistat 120 mg: At 12 months, mean (SD) DBP change in mmHg was –1.00 (8.30) in the orlistat group, and 2.00 (8.30) in the control group. Mean DBP change in the intervention group compared with control was –3.00 (95% CI –4.58 to –1.42).
Orlistat 120 mg: At 12 months, mean (SD) SBP change in mmHg was 2.00 (12.70) in the orlistat group, and 3.00 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –1.00 (95% CI –3.42 to 1.42).
Orlistat 120 mg: At 24 months, mean (SD) TC change in mmol/l was 0.25 (1.08) in the orlistat group, and 0.44 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.19 (95% CI –0.40 to 0.02).
Orlistat 120 mg: At 24 months, mean (SD) LDL change in mmol/l was 0.06 (0.74) in the orlistat group, and 0.36 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.30 (95% CI –0.44 to –0.16).
Orlistat 120 mg: At 24 months, mean (SD) HDL change in mmol/l was 0.07 (0.29) in the orlistat group, and 0.09 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.02 (95% CI –0.08 to 0.04).
Orlistat 120 mg: At 24 months, mean (SD) TAG change in mmol/l was 0.21 (0.96) in the orlistat group, and –0.05 (0.96) in the control group. Mean TAG change in the intervention group compared with control was 0.26 (95% CI 0.08 to 0.44).
Orlistat 120 mg: At 24 months, mean (SD) FPG change in mmol/l was 0.16 (1.35) in the orlistat group, and 0.24 (1.35) in the control group. Mean FPG change in the intervention group compared with control was –0.08 (95% CI –0.34 to 0.18).
Orlistat 120 mg: At 24 months, mean (SD) DBP change in mmHg was 1.00 (8.30) in the orlistat group, and 4.00 (8.30) in the control group. Mean DBP change in the intervention group compared with control was –3.00 (95% CI –4.58 to –1.42).
Orlistat 120 mg: At 24 months, mean (SD) SBP change in mmHg was 4.00 (12.70) in the orlistat group, and 5.00 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –1.00 (95% CI –3.42 to 1.42).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) TC change in mmol/l was 0.29 (1.08) in the orlistat group, and 0.14 (1.08) in the control group. Mean TC change in the intervention group compared with control was 0.15 (95% CI –0.06 to 0.36).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) LDL change in mmol/l was 0.18 (0.74) in the orlistat group, and 0.11 (0.74) in the control group. Mean LDL change in the intervention group compared with control was 0.07 (95% CI –0.07 to 0.21).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) HDL change in mmol/l was 0.01 (0.29) in the orlistat group, and –0.02 (0.29) in the control group. Mean HDL change in the intervention group compared with control was 0.03 (95% CI –0.03 to 0.09).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) TAG change in mmol/l was 0.15 (0.96) in the orlistat group, and 0.05 (0.96) in the control group. Mean TAG change in the intervention group compared with control was 0.10 (95% CI –0.08 to 0.28).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) FPG change in mmol/l was 0.13 (1.35) in the orlistat group, and 0.13 (1.35) in the control group. Mean FPG change in the intervention group compared with control was 0.00 (95% CI –0.26 to 0.26).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) DBP change in mmHg was 2.00 (8.30) in the orlistat group, and 2.00 (8.30) in the control group. Mean DBP change in the intervention group compared with control was 0.00 (95% CI –1.58 to 1.58).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) SBP change

	in mmHg was 2.00 (12.70) in the orlistat group, and 2.00 (12.70) in the control group. Mean SBP change in the intervention group compared with control was 0.00 (95% CI –2.42 to 2.42). *Mean plasma levels of vitamins A, D and E, and beta-carotene remained within the reference range in all treatment groups throughout the 2-year study. Vitamin A and vitamin E levels increased during the study in all treatment groups, while vitamin D and beta-carotene levels decreased in all treatment groups. Two consecutive low vitamin E and beta-carotene values occurred more frequently in people treated with orlistat compared with those given placebo, while the frequency of two consecutive low vitamin A and D values was not significantly different among treatment groups. Supplementation with beta-carotene was required and received by 2.4, 4.3 and 6.3% of those in the placebo, 60 mg orlistat, and 120 mg orlistat groups, respectively. Overall, <1.9% of all the participants required and received vitamin A or E supplementation. Almost all those who needed vitamin supplementation achieved normal levels by the end of the study.* *No analysis of outcomes independent of weight loss were reported.*
Quality and comments	…

Hill 1999 (in Avenell and O'Meara HTA) RCT	
Results	Orlistat 120 mg: At 12 months, mean (SD) TC change in mmol/l was 0.08 (1.08) in the orlistat group, and 0.17 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.09 (95% CI –0.40 to 0.22). Orlistat 120 mg: At 12 months, mean (SD) LDL change in mmol/l was –0.05 (0.74) in the orlistat group, and 0.12 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.17 (95% CI –0.38 to 0.04). Orlistat 120 mg: At 12 months, mean (SD) HDL change in mmol/l was –0.04 (0.29) in the orlistat group, and 0.00 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.04 (95% CI –0.12 to 0.04). Orlistat 120 mg: At 12 months, mean (SD) TAG change in mmol/l was 0.02 (0.96) in the orlistat group, and 0.14 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.12 (95% CI –0.39 to 0.15). *Orlistat 30 mg: at 12 months, compared with placebo, significant differences were seen for levels of TC (LSM% change –3.75,* p=*0.007), and LDL-cholesterol (LSM% change –6.54,* p=*0.001). (Changes from pre-6 month lead in period).* *Orlistat 60 mg: at 12 months, compared with placebo, significant differences were seen for levels of TC (LSM% change –3.37,* p=*0.001), LDL-cholesterol (LSM% change –5.74,* p=*0.006), and HDL cholesterol (LSM% change –5.34,* p=*0.006). (Changes from pre-6 month lead in period).* *The significant changes in TC and LDL levels in the orlistat 120 mg group persisted even after adjustment for the greater weight loss.* *People received standard vitamin supplements throughout the 1-y treatment phase of the trial; accordingly, mean concentrations of vitamins A, D and E and of beta-carotene remained within the reference ranges, although vitamin E and ß-carotene were significantly lower in the orlistat treatment groups than in the placebo group at the end of the study (*p<*0.001). Few participants (<4%) met the criteria for additional vitamin supplementation during the study and those who did receive supplementation had normal values at the end of the study.*
Quality and comments	…

Hollander 1998 (in Avenell and O'Meara HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.05 (0.60) in the orlistat group, and 0.41 (0.70) in the control group. Mean TC change in the intervention group compared with control was –0.46 (95% CI –0.61 to –0.31). At 12 months, mean (SD) LDL change in mmol/l was –0.12 (0.74) in the orlistat group, and 0.22 (0.70) in the control group. Mean LDL change in the intervention group compared with control was –0.34 (95% CI –0.48 to –0.20). At 12 months, mean (SD) HDL change in mmol/l was 0.06 (0.20) in the orlistat

	group, and 0.06 (0.20) in the control group. Mean HDL change in the intervention group compared with control was 0.00 (95% CI –0.04 to 0.04). At 12 months, mean (SD) TAG change in mmol/l was 0.02 (0.80) in the orlistat group, and 0.28 (1.00) in the control group. Mean TAG change in the intervention group compared with control was –0.26 (95% CI –0.46 to –0.06). At 12 months, mean (SD) HbA1c% change was –0.15 (1.00) in the orlistat group, and 0.32 (1.10) in the control group. Mean TAG change in the intervention group compared with control was –0.47 (95% CI –0.71 to –0.23). At 12 months, mean (SD) DBP change in mmHg was –1.01 (8.00) in the orlistat group, and 0.23 (8.90) in the control group. Mean DBP change in the intervention group compared with control was –1.24 (95% CI –3.14 to 0.66). At 12 months, mean (SD) SBP change in mmHg was 0.21 (12.80) in the orlistat group, and 4.15 (14.20) in the control group. Mean SBP change in the intervention group compared with control was –3.94 (95% CI –6.97 to –0.91). At 12 months, mean (SD) FPG change in mmol/l was 0.04 (1.60) in the orlistat group, and 0.70 (1.80) in the control group. Mean FPG change in the intervention group compared with control was –0.66 (95% CI –1.04 to –0.28). *TC and LDL levels were independent of weight loss. Improvements in %HbA_{1c}, however, were related closely to degree of weight loss.* *Non-clinically relevant changes in a number of laboratory parameters occurred at a similar incidence in both treatment groups. There was no evidence for the development of gallstones or renal stones after orlistat treatment. Mean plasma levels of vitamins A, D and E, and beta-carotene remained within the reference range throughout the study. After 52 weeks of treatment, mean vitamin E and beta-carotene levels were significantly lower in the orlistat group compared with the placebo group (*p*<0.001). However, there was no significant change in the vitamin E:LDL ratio in either group. As a consequence of having two or more consecutive low vitamin levels, vitamin D supplementation was instituted in 7% of placebo-treated participants and 17% of orlistat-treated participants; vitamin E supplementation was given to 1% of both treatment groups; and 9% of the orlistat group received beta-carotene supplementation. All people receiving supplementation attained normal levels with treatment, and none were withdrawn because of low vitamin values. In addition, mean PT values, used as a surrogate marker of vitamin K, were not different between the orlistat and placebo groups and did not fall below the reference range.*
Quality and comments	Values in published paper different to HTA values – used HTA values.

Lindgarde 2000 (in Avenell HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was 0.03 (1.08) in the orlistat group, and 0.26 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.23 (95% CI –0.45 to –0.01). At 12 months, mean (SD) LDL change in mmol/l was –0.22 (0.74) in the orlistat group, and 0.07 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.29 (95% CI –0.44 to –0.14). At 12 months, mean (SD) HDL change in mmol/l was 0.03 (0.29) in the orlistat group, and 0.08 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.05 (95% CI –0.11 to 0.01). At 12 months, mean (SD) TAG change in mmol/l was 0.18 (0.96) in the orlistat group, and 0.04 (0.96) in the control group. Mean TAG change in the intervention group compared with control was 0.14 (95% CI –0.05 to 0.33). At 12 months, mean (SD) %HbA_{1c}change was –0.25 (0.78) in the orlistat group, and –0.05 (0.51) in the control group. Mean TAG change in the intervention group compared with control was –0.20 (95% CI –0.33 to –0.07). At 12 months, mean (SD) DBP change in mmHg was –0.90 (8.30) in the orlistat group, and -1.30 (8.30) in the control group. Mean DBP change in the intervention group compared with control was 0.40 (95% CI –1.28 to 2.08). At 12 months, mean (SD) SBP change in mmHg was –0.50 (12.70) in the orlistat group, and –0.90 (12.70) in the control group. Mean SBP change in the

	intervention group compared with control was 0.40 (95% CI –2.17 to 2.97). At 12 months, mean (SD) FPG change in mmol/l was –0.46 (1.35) in the orlistat group, and 0.08 (1.35) in the control group. Mean FPG change in the intervention group compared with control was –0.54 (95% CI –0.81 to –0.27). *Treatment with orlistat was associated with significantly greater improvements in TC, LDL, FPG and HbA_{1c} levels, and these were generally greater for people who had achieved ≥5% or ≥10% weight loss.* *Similar improvements in CHD risk factors were also seen with orlistat in the subgroup of patients with type 2 diabetes. After 54 weeks, mean fasting glucose was reduced by 1.63 mmol/l (13.6%) in the orlistat group, compared with a reduction of 0.28 mmol/l (1.1%) with placebo (*p<*0.01). Orlistat was also associated with a significantly greater improvement in HbA_{1c} (±0.65 [7.5%] vs ±0.14% [1.4%] with placebo;* p<*0.05). The improvement in glycaemic control achieved by people in the orlistat group resulted in a higher proportion of orlistat-treated patients being able to stop or reduce their dosage of anti-diabetic medication (23.3 vs 18.2% of placebo-treated group). Improvements in TC and LDL-cholesterol were also greater with orlistat compared with placebo in patients with type 2 diabetes, although these did not reach statistical significance (± 4.3 vs ±1.0% and 10.4 vs ±3.9%, respectively).*
Quality and comments	…

Rossner 2000 (in Avenell and O'Meara HTA) RCT	
Results	*Orlistat 60 mg: No significant differences were seen (least squares mean difference) between placebo and orlistat 60 mg at 12 months or at 24 months.* Orlistat 120 mg: At 12 months, mean (SD) TC change in mmol/l was –0.35 (1.08) in the orlistat group, and –0.05 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.30 (95% CI –0.49 to –0.11). Orlistat 120 mg: At 12 months, mean (SD) LDL change in mmol/l was –0.33 (0.74) in the orlistat group, and –0.06 (0.70) in the control group. Mean LDL change in the intervention group compared with control was –0.27 (95% CI –0.40 to –0.14). Orlistat 120 mg: At 12 months, mean (SD) HDL change in mmol/l was 0.08 (0.29) in the orlistat group, and 0.15 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.07 (95% CI –0.12 to –0.02). Orlistat 120 mg: At 12 months, mean (SD) TAG change in mmol/l was –0.09 (0.96) in the orlistat group, and –0.08 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.01 (95% CI –0.18 to 0.16). Orlistat 120 mg: At 12 months, mean (SD) DBP change in mmHg was –0.90 (8.30) in the orlistat group, and –1.30 (8.30) in the control group. Mean DBP change in the intervention group compared with control was 0.40 (95% CI –1.09 to 1.89). Orlistat 120 mg: At 12 months, mean (SD) SBP change in mmHg was –2.70 (12.70) in the orlistat group, and –1.90 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –0.80 (95% CI –3.08 to 1.48). Orlistat 120 mg: At 12 months, mean (SD) FPG change in mmol/l was 0.01 (1.35) in the orlistat group, and 0.10 (1.35) in the control group. Mean FPG change in the intervention group compared with control was –0.09 (95% CI –0.33 to 0.15). Orlistat 120 mg: At 24 months, mean (SD) TC change in mmol/l was 0.03 (1.08) in the orlistat group, and 0.31 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.28 (95% CI –0.47 to –0.09). Orlistat 120 mg: At 24 months, mean (SD) LDL change in mmol/l was 0.04 (0.74) in the orlistat group, and 0.28 (0.70) in the control group. Mean LDL change in the intervention group compared with control was –0.24 (95% CI –0.37 to –0.11). Orlistat 120 mg: At 24 months, mean (SD) HDL change in mmol/l was 0.12 (0.29) in the orlistat group, and 0.16 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.04 (95% CI –0.09 to 0.01). Orlistat 120 mg: At 24 months, mean (SD) TAG change in mmol/l was –0.10 (0.96) in the orlistat group, and –0.05 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.05 (95% CI –0.22 to 0.12).

Orlistat 120 mg: At 24 months, mean (SD) DBP change in mmHg was –0.40 (8.30) in the orlistat group, and 0.00 (8.30) in the control group. Mean DBP change in the intervention group compared with control was 0.40 (95% CI –1.09 to 1.89).
Orlistat 120 mg: At 24 months, mean (SD) SBP change in mmHg was –0.60 (12.70) in the orlistat group, and 1.20 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –1.80 (95% CI –4.08 to 0.48).
Orlistat 120 mg: At 24 months, mean (SD) FPG change in mmol/l was 0.04 (1.35) in the orlistat group, and –0.02 (1.35) in the control group. Mean FPG change in the intervention group compared with control was 0.06 (95% CI –0.18 to 0.30).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) TC change in mmol/l was 0.38 (1.08) in the orlistat group, and 0.36 (1.08) in the control group. Mean TC change in the intervention group compared with control was 0.02 (95% CI –0.17 to 0.21).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) LDL change in mmol/l was 0.37 (0.74) in the orlistat group, and 0.34 (0.74) in the control group. Mean LDL change in the intervention group compared with control was 0.03 (95% CI –0.10 to 0.16).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) HDL change in mmol/l was 0.04 (0.29) in the orlistat group, and 0.01 (0.29) in the control group. Mean HDL change in the intervention group compared with control was 0.03 (95% CI –0.02 to 0.08).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) TAG change in mmol/l was –0.01 (0.96) in the orlistat group, and 0.03 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.04 (95% CI –0.21 to 0.13).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) DBP change in mmHg was 1.30 (8.30) in the orlistat group, and 1.30 (8.30) in the control group. Mean DBP change in the intervention group compared with control was 0.00 (95% CI –1.49 to 1.49).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) SBP change in mmHg was 2.10 (12.70) in the orlistat group, and 3.10 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –1.00 (95% CI –3.28 to 1.28).
Orlistat 120 mg: At 24 months compared with 12 months, mean (SD) FPG change in mmol/l was 0.03 (1.35) in the orlistat group, and –0.12 (1.35) in the control group. Mean FPG change in the intervention group compared with control was 0.15 (95% CI –0.09 to 0.39).
*Participants treated with orlistat reported significantly greater satisfaction with their weight loss medication than did placebo participants after 1 and 2 years (*p<*0.001 in the orlistat 120 mg group;* p<*0.05 in the orlistat 60 mg group). Participants taking orlistat 120 mg also expressed greater satisfaction both with losing weight and their weight loss programme (*p=*0.011 and* p=*0.002, respectively, after 2 years). Overall satisfaction with treatment, as expressed by the treatment index, was significantly greater among participants taking orlistat than placebo recipients after 2 years (*p<*0.001 and* p<*0.05 in the orlistat 120 mg and 60 mg groups, respectively).*
*Orlistat-treated participants also reported less overweight distress than participants receiving placebo and this became statistically significant in the orlistat 120 mg group after 2 years (*p<*0.05). There were no significant differences between treatment groups in depression scores after either 1 or 2 years.*
No clinically significant changes were observed in any laboratory parameters. The changes that were noted were sporadic, resolved spontaneously, and occurred with similar frequencies in all treatment groups. Mean plasma levels of vitamins A, D (measured as 25-cholecalciferol), E, and K (determined indirectly from prothrombin time) and beta-carotene remained within reference ranges in all three groups over the 2 years of treatment. No participants were withdrawn because of low vitamin values. For most participants dietary advice and/or vitamin supplementation were sufficient to restore vitamin levels to pre-treatment values and during the study. Twenty-seven people required vitamin supplementation

	because of low vitamin values (placebo, n=*1; orlistat 60 mg,* n=*14; orlistat 120 mg,* n=*12). The majority (73%) of these incidences occurred in Year 1. Differences in mean plasma values for vitamins D and E and beta-carotene between orlistat-treated participants and participants taking placebo were, however, statistically significant (*p<*0.001). The vitamin E:LDL-cholesterol ratio increased during the study, indicating that there was no loss of vitamin E protection against LDL-induced atherogenesis during treatment with orlistat.* *No analysis of association with weight loss was reported.*
Quality and comments	…

Sjöström 1998 (in Avenell and O'Meara HTA) RCT	
Results	At 12 months, mean (SD) TC change in mmol/l was –0.08 (1.08) in the orlistat group, and 0.23 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.31 (95% CI –0.47 to –0.15). At 12 months, mean (SD) LDL change in mmol/l was –0.09 (0.74) in the orlistat group, and 0.13 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.22 (95% CI –0.33 to –0.11). At 12 months, mean (SD) HDL change in mmol/l was 0.10 (0.29) in the orlistat group, and 0.10 (0.29) in the control group. Mean HDL change in the intervention group compared with control was 0.00 (95% CI –0.04 to 0.04). At 12 months, mean (SD) TAG change in mmol/l was –0.07 (0.96) in the orlistat group, and 0.06 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.13 (95% CI –0.27 to 0.01). At 12 months, mean (SD) DBP change in mmHg was –2.10 (8.30) in the orlistat group, and 0.20 (8.30) in the control group. Mean DBP change in the intervention group compared with control was –2.30 (95% CI –3.54 to -1.06). At 12 months, mean (SD) SBP change in mmHg was –2.00 (12.70) in the orlistat group, and 1.00 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –3.00 (95% CI –4.90 to –1.10). At 12 months, mean (SD) FPG change in mmol/l was –0.21 (1.35) in the orlistat group, and –0.06 (1.35) in the control group. Mean FPG change in the intervention group compared with control was –0.15 (95% CI –0.35 to 0.05). *At 24 months, significant differences were seen between the orlistat-orlistat and the placebo-placebo groups for levels of TC, LDL-cholesterol, TAG and FPG, but not for HDL-cholesterol and SBP or DBP.* *TC and LDL levels fell in the orlistat group further than would have been expected from weight loss alone.* *During months 12 to 24, people who remained on orlistat compared with those randomised to placebo regained, on average, half as much weight (LSM 2.4 kg,* p<*0.001).* *There were no clinically or statistically significant changes in the mean values of any laboratory measurements during the study, and the frequency of laboratory abnormalities was evenly distributed between the treatment groups. After an initial small decrease, mean concentrations of vitamins A, D and E, and beta-carotene stabilised and remained within normal clinical ranges throughout the study in both groups. During year one, 41 participants in the orlistat group and 18 in the placebo group had two or more consecutive low vitamin concentrations recorded, but only 16 and four participants, respectively, received vitamin supplementation. During year two, vitamin supplementation was received by four participants in the orlistat/orlistat group, by one placebo/placebo participant, by three participants in the placebo/orlistat group, and by one participant in the orlistat/placebo group. Pharmacokinetic analysis of blood samples showed measurable, but minute, concentrations (0·208–2·078 µg/l) of unchanged orlistat in the plasma of only a few participants at 24 weeks (13/281 [4.6%] orlistat-treated participants), 52 weeks (17/236 [7.2%]), and 104 weeks (2/75 [2.7%]). These findings indicate low systemic absorption of orlistat after 2 years of treatment, with no evidence of accumulation.*
Quality and	No SDs for other outcomes at 24 months. Only results for placebo–placebo and

comments	orlistat–orlistat group at 24 months.

Reported harms

Broom 2002 (in Avenell HTA Broom 2001a) RCT	
Results	*Overall incidence of adverse events was similar in both groups, with the exception of certain GI events, known to be associated with the drug mechanism. 63% in the orlistat group and 47% in the control group reported GI events. Most of these were of mild to moderate intensity and of short duration, occurring and resolving soon after the initiation of orlistat treatment. Thirteen people in the orlistat group and six people in the control group withdrew because of GI events.* *Thirteen people in the orlistat group and 17 in the control group experienced serious adverse events (no details), none of which were considered by the investigators to have a probable causal relationship with the stud medication.* One death from cancer was reported in the orlistat group (not related to the treatment).
Quality and comments	…

Broom 2002 (in Avenell HTA Broom 2001b) RCT	
Results	*95.5% of people in the orlistat group and 85.9% of the control group reported at least one adverse event However, most were normally mild, self-limiting, and with the exception of certain GI system events were not considered by the investigators to be related to the study medication.* *More people in the orlistat group experienced GI adverse events (86.6 vs 42.3%). The majority of events were transient and mild to moderate in intensity. Seven people withdrew from the orlistat group and three people from the control group because of GI events.* *Four serious events (elective cytoscopy and hydrodistension, stroke, sleep disorder, benign breast cyst) occurred in the orlistat group, compared with ten in the control group (radiculitis, cellulitis, limb pain, hiatus hernia, gastric ulcer, oesophageal reflux, anaemia, pregnancy, cholecystectomy).* *In the open label phase, adverse events were reported in 92.9% of those who remained on orlistat, and 96.3% of those who switched to orlistat. Again, GI events were the most commonly reported (54.8% of those who remained, and 75.9% of those who switched). Ten people withdrew during this phase because of the GI events.* *Six adverse events occurred in those people who remained on orlistat (neuropathic toe ulcer, cellulitis, Bell's palsy, bleeding and injury due to road traffic accident, suicide attempt), and one adverse event in those who switched (abdominal pain).*
Quality and comments	…

Davidson 1999 (in Avenell and O'Meara HTA) RCT	
Results	*Overall incidence of adverse events was similar in placebo and orlistat groups. However, there were more adverse GI events associated with orlistat. At least one GI event was experienced by 79% of people in the orlistat group compared with 59% of participants in the placebo group. The majority of those treated with orlistat experienced one or two of these GI events, which typically occurred early during treatment, were mild to moderate in intensity, and generally resolved spontaneously. Seven types of GI events occurred with at least a 5% incidence rate and in twice as many people in the orlistat group: flatus with discharge (40.1%), oily spotting (32.7%), faecal urgency (29.7%), fatty/oily stool (19.8%), oily evacuation (14.3%), faecal incontinence (11.8%), and increased defecation (11.1%).*

	Seven people in the orlistat group and two in the placebo group withdrew because of GI events. The adverse event rate was lower in year 2 than in year 1 and did not differ between groups. *One (0.51%) of the 197 placebo-treated women and three (0.54%) of the 548 women treated with orlistat 120 mg were diagnosed as having breast cancer during the 2-year period following randomisation. One of the orlistat-treated participants had a 1-cm tumour identified 32 days after randomisation. Two participants, one taking orlistat and one taking placebo, had mammograms prior to starting the study that revealed pre-existing breast malignancies.*
Quality and comments	…

Finer 2000 (in Avenell and O'Meara HTA) RCT	
Results	*Except for GI events, adverse events were similar in both groups, mild to moderate in intensity and mainly temporal. GI events occurred more frequently in the orlistat group (82.1 vs 56.4% had at least one GI event). 59% had a specific GI event compared with 15.4% of the control group. Most occurred early in the study and were generally transient (≤4 days). Most people in both groups had only one or two episodes of GI symptoms, but others did experience more. Nine orlistat- and seven placebo-treated people withdrew because of adverse events.* *Gallstone formation was not increased by weight loss associated with orlistat use. 7% and 11% of orlistat- and placebo-treated people developed gallbladder abnormalities. 3% of orlistat- and 2% of placebo-treated participants developed renal abnormalities.*
Quality and comments	…

Hauptman 2000 (in Avenell and O'Meara HTA) RCT	
Results	*In general, adverse events in all groups were transient, mild, or moderate in intensity and resolved without intervention. With the exception of GI events, the incidence and type of adverse events were similar in all treatment groups. Adverse events accounted for the withdrawal of 7.1% (*n=*15), 6.6% (*n=*14), and 11.0% (*n=*23) of those in the placebo and 60-mg and 120-mg orlistat groups, respectively, over 104 weeks of double-blind treatment; this was not significantly different among groups. As expected from the mechanism, the incidence of GI events was higher in the orlistat groups. Over 2 years, 59%, 72% and 79% of people in the placebo, 60-mg orlistat, and 120-mg orlistat groups, respectively, reported GI events (*p=*0.003 for placebo vs 60 mg of orlistat and* p=*0.001 for placebo vs 120 mg of orlistat). Specific GI events possibly or probably related to orlistat treatment occurred significantly more frequently in both orlistat groups compared with placebo (*p=*0.001). Most GI events were mild to moderate in intensity, were limited to only one or two episodes per person, and occurred early during treatment. Few GI events were reported during the second year of the study. Ten people (4.7%) in the 60-mg orlistat group and 12 (5.7%) in the 120-mg orlistat group withdrew from the study prematurely because of GI events, compared with 3 (1.4%) in the placebo group.*
Quality and comments	…

Hill 1999 (in Avenell and O'Meara HTA) RCT	
Results	*During the 1-year treatment period, the percentage of people who reported at least one adverse event was 7–8% greater in the orlistat-treated groups than in the placebo group. This difference was primarily due to an increased incidence of GI events in the orlistat-treated participants, with similar adverse events for all other body systems across treatment groups. The percentage of participants reporting GI events was 68.1% in the placebo group, 82.3% in the 30-mg orlistat group, 91.8% in the 60-mg orlistat group and 95.0% in the 120-mg orlistat group. In general, adverse events were mild to moderate in intensity and resolved without*

	intervention. *Some GI events occurred in a greater percentage of those in the orlistat-treated groups. However, most people experienced only one or two episodes and most GI events were mild to moderate in intensity, occurred early during treatment, and resolved spontaneously. Withdrawals from the study related to GI events were 0.5% in the placebo group, 5.4% in the 30-mg orlistat group, 7.0% in the 60-mg orlistat group and 11.7% in the 120-mg orlistat group.*
Quality and comments	…

Hollander 1998 (in Avenell and O'Meara HTA) RCT	
Results	*Adverse events occurred at a similar overall incidence in both treatment groups. However, there were more GI events associated with orlistat. There were 79% of people in the orlistat group vs 59% in the placebo group who experienced at least one GI event. The majority of those on orlistat experienced one or two of these events. GI events occurred early during treatment, were mild to moderate in intensity, were generally transient, and resolved spontaneously. The number of people who withdrew because of GI events was seven in the orlistat group vs two in the placebo group.*
Quality and comments	…

Lindgarde 2000 (in Avenell HTA) RCT	
Results	*The overall incidence of adverse events was similar in the placebo and orlistat groups, with the exception of certain GI events known to be associated with the inhibitory effect of orlistat on dietary fat absorption. 80% of people in the orlistat group and 39% in the placebo group reported GI events. Most of these were of mild to moderate intensity and of short duration, and most occurred soon after the initiation of orlistat treatment. Five participants in the orlistat group and one in the placebo group withdrew from the study because of GI events. A total of 19 participants in the orlistat group and five in the placebo group experienced serious adverse events, none of which were considered by the investigators to have a probable causal relationship with the study medication. One death occurred in the orlistat group; the participant had type 2 diabetes and severe arteriosclerosis, and died as a result of a brain stem infarction.*
Quality and comments	…

Rossner 2000 (in Avenell and O'Meara HTA) RCT	
Results	*With the predictable exception of more frequent GI events following orlistat treatment, the adverse event profiles were similar in all three treatment groups throughout the study and were generally mild to moderate and resolved spontaneously. The majority of these events occurred early during treatment, were mild to moderate in intensity, resolved spontaneously, and were limited to only one or two episodes per participant. There were 49 severe GI events reported during the 2 years of the study: placebo,* n=*8; orlistat 60 mg,* n=*16; and orlistat 120 mg,* n=*25. The majority of severe GI events (*n=*38) occurred during the first year of the study.* *During the 2 years of this study, two serious adverse events were considered to be at least possibly related to orlistat treatment: one a case of cholelithiasis and one a case of diverticulitis. However, neither resulted in discontinuation of study medication. Six (2.5%) participants in the placebo group, 23 (9.6%) in the orlistat 60 mg group and 19 (7.9%) in the orlistat 120 mg group withdrew from the study prematurely due to adverse events. GI events were the most common side effect associated with premature withdrawal in all three groups with 2 (0.8%), 12 (5%) and 9 (3.7%) participants from the placebo, orlistat 60 mg and orlistat120 mg groups, respectively, discontinuing the study in 2 years.* *Five participants were diagnosed with breast cancer during the 2-year study. One*

	participant in the orlistat 60 mg group was diagnosed 36 days after randomised treatment. Four other cases occurred in postmenopausal women (one in the placebo group and three in the orlistat 120 mg group).
Quality and comments	…

Sjöström 1998 (in Avenell and O'Meara HTA) RCT	
Results	The overall frequency of adverse events was slightly higher in the orlistat group than in the placebo group during year 1 (94 vs 82%); and similar in the four treatment groups during year 2. With the exception of some GI events, the adverse events were judged by the investigators to be unrelated or remotely related to treatment. Most of the GI events happened early in orlistat treatment and were of short duration (≤4 days). Participants treated with orlistat experienced far fewer GI events during year 2 than in year 1. *Serious adverse events were reported by 24 participants in the placebo group and 25 in the orlistat group during year 1, with only one adverse event in each group being judged by the investigators to be related to treatment. Similarly, two serious adverse events that were judged possibly related to treatment happened during year 2. One case of GI neoplasm occurred in a participant treated with placebo for 2 years. No other malignant disorders were observed in the course of this study. The total number of premature withdrawals was higher in the placebo group than in the orlistat group during year 1 (83 vs 61) and virtually the same in both groups during year 2 (45 vs 46). Adverse GI events, however, were a more common reason for premature withdrawals in the orlistat group than in the placebo group.*
Quality and comments	…

Generalisability

Broom 2002 (in Avenell HTA Broom 2001a) RCT	
Country and setting	UK. General practices and hospital clinics.
Participants (included/excluded)	*Included men and non-pregnant women, aged 18–80 years, BMI ≥28 kg/m^2, at least one of the following: IGT (serum glucose ≥8.0 mmol/l, 2 h after a standard OGTT); hypercholesterolaemia (total serum cholesterol ≥5.2 mmol/l or LDL-cholesterol ≥4.2 mmol/l at screening); hypertension (sitting DBP 90–105 mmHg); compliance ≥60% throughout the study. Excluded if lactating, women of child bearing potential not using adequate contraception, MI, coronary artery bypass graft, percutaneous coronary angioplasty in prior 3 months; GI surgery for weight reduction, active GI disorders, such as peptic ulcer disease or malabsorption syndromes; pancreatic disease, history of post surgical adhesions, excessive alcohol intake or substance abuse; participants who required any drug which might alter body weight or plasma lipids such as appetite suppressants, lipid-lowering resins, retinoids and fish oil supplements; administration of systemic steroids (other than hormone replacement therapy) not permitted; concomitant pharmacotherapy for type 2 diabetes, hypertension or hypercholesterolaemia not permitted.*
Recruitment	Initial screening visit, but no details of how recruited.
Randomisation	Done using a minimisation algorithm: primary defined cardiovascular risk factor, study centre, BMI, weight loss during run-in.
Intervention (mode and intensity)	12 months, contacted 13 times (baseline then at monthly intervals).
Duration of active intervention	52 weeks
Control (mode and intensity)	As above

Delivery of intervention/control (who)	N/R, but '80% of participants were treated at GP centres where staff would *not* be as experienced at dietary counselling/weight management as staff at specialist obesity centres'.
Dropout rates	30% orlistat, 40% control at 12 months
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Broom 2002 (in Avenell HTA Broom 2001b) RCT	
Country and setting	UK. Outpatient clinics specialising in obesity and/or dyslipidaemia.
Participants (included/excluded)	*Included if aged ≥18 years, women of childbearing potential if using adequate protection, BMI ≥30 kg/m^2, total plasma cholesterol ≥6.5 mmol/l, or plasma LDL-cholesterol ≥4.2 mmol/l.* *Excluded if myocardial infarction or major surgery in last 3 months; GI or pancreatic disease, type 1 diabetes, uncontrolled hypertension, history of carcinoma, GI surgery for weight loss, post-surgical adhesions, bulimia or laxative abuse, drug or alcohol abuse, treatment with drugs altering appetite or lipid concentrations, fish oil supplements, retinoids, systemic steroids (other than sex hormone replacements) or anticoagulants.*
Recruitment	Recruited from specialist outpatient clinics. No further details.
Randomisation	No details other than participants were randomised.
Intervention (mode and intensity)	*52 weeks contacted 11 times (baseline, every 4 weeks up to week 24 then at weeks 30, 36, 44 and 52)*
Duration of active intervention	Twenty-four weeks double-blind, then 28 week open-label trial where people could choose to remain/switch to orlistat as desired.
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Dietary advice was provided initially and reinforced at the open-label stage by a state-registered dietitian.
Dropout rates	*33% orlistat, 15.5% control at 52 weeks (from paper, not HTA report)*
Treatment of dropouts (return to baseline, or last measurement?)	Missing values replaced using the LOCF method.

Davidson 1999 (in Avenell and O'Meara HTA) RCT	
Country and setting	USA. Clinical research centres – no further details.
Participants (included/excluded)	*Included if aged >18 years, BMI 30–43 kg/m^2, adequate contraception in women of childbearing potential, all vitamin and mineral preparations were discontinued 8 weeks prior to start of study, 75% or more treatment compliance by capsule count during 4 week run-in period, 70% or more treatment adherence in year 1 in order to continue to year 2.* *Excluded if weight loss >4 kg in previous 3 months, frequently changed smoking habits or had stopped smoking in last 6 months, history of or presence of substance abuse, excessive alcohol intake, significant cardiac, renal, hepatic, GI, psychiatric or endocrine disorder; drug-treated type 2 diabetes mellitus, concomitant use of medications altering appetite or lipid levels.*
Recruitment	*Recruited through the clinical research centres.*
Randomisation	Weight change in the 4-week lead-in period was used to stratify for randomisation (a measure of weight loss potential).
Intervention (mode and intensity)	24 months, contacted 23 times (baseline, every 2 weeks to week 16 then every 4 weeks to week 52 then every 8 weeks to week 104)
Duration of active intervention	*24 months*
Control (mode and intensity)	*As above*

Delivery of intervention/control (who)	Dietitians provided instruction on dietary intake recording as part of the behaviour modification programme, and then used the diaries for counselling. No further details for BT or activity components.
Dropout rates	31% orlistat, 41% control at 12 months. 31% orlistat120-placebo, 29% orlistat120–orlistat120, 33% orlistat120–orlistat60, 57% placebo–placebo at 24 months.
Treatment of dropouts (return to baseline, or last measurement?)	The last value carried-forward technique was used for years 1 and 2 analyses. The last value carried-forward analysis method uses all follow-up data, including that obtained from participants who withdrew prematurely, with the last recorded data point used in statistical analysis. All reported data are the actual observed values rather than derived data from carrying forward the last recorded values.

Finer 2000 (in Avenell and O'Meara HTA) RCT	
Country and setting	UK. Centres – no further details.
Participants (included/excluded)	*Included if aged ≥18 years, BMI 30–43 kg/m², women of childbearing potential if using adequate contraceptive precautions, >75% compliance (returned tablets) during run-in phase* *Excluded if weight loss >4 kg in 3 months prior to screening, history of severe systemic disease including diabetes, uncontrolled hypertension, previous GI disease, surgery for weight reduction, history of post-surgical adhesions, history of or presence of cancer, psychiatric or neurological disorder requiring chronic medications or liable to prejudice participant compliance, alcohol or substance abuse, bulimia or laxative abuse, pregnancy, lactation, post-menopausal women, amenorrhoeic <1 year, drugs capable of influencing body weight, resins for lipid lowering, anti-coagulants, digoxin or lipid-soluble vitamin supplements within previous month.*
Recruitment	*Recruited at five centres in the UK by local advertisement or by referral from general practitioners.*
Randomisation	Weight change in the 4-week lead-in period was used to stratify for randomisation (a measure of weight loss potential).
Intervention (mode and intensity)	12 months, contacted 17 times (baseline, before and after 4 week run-in, every 2 weeks until week 12 then every month until month 12)
Duration of active intervention	*12 months*
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	No details reported
Dropout rates	36% orlistat, 42% control at 12 months
Treatment of dropouts (return to baseline, or last measurement?)	LOCF.

Hauptman 2000 (in Avenell and O'Meara HTA) RCT	
Country and setting	USA. Primary care centres.

Participants (included/excluded)	*Included if aged >18 years, BMI 30–44 kg/m^2, completed 4-week pre-treatment phase with 75% or more compliance (by capsule count). Excluded if pregnant, lactating, women of childbearing potential not taking adequate contraception; weight loss >4 kg last 3 months, history of significant cardiac, renal, hepatic, GI disorders; uncontrolled hypertension or other clinically significant condition; GI surgery for weight reduction; bulimia or laxative and/or substance abuse, abnormal laboratory measures (values 10% or greater than reference value for the normal range and sufficient to require medical follow-up by study physician); change in smoking habits in previous 6 months, use of any drug which might influence body weight or food intake in 8 weeks prior to screening.*
Recruitment	N/R
Randomisation	No details, but participants had to be compliant during the run-in to be entered into the double-blind phase.
Intervention (mode and intensity)	104 weeks, contacted 21 times (baseline, every 2 weeks for first month then every 4 weeks until week 52 then every 8 weeks until week 104).
Duration of active intervention	24 months
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	Participants received dietary guidance from the study physician only at the start of the placebo lead-in phase. Participating physicians did not receive any specific training in nutrition or weight management techniques beyond the same instructional materials given to the participants. Registered dietitians or behavioural psychologists were *not* involved in nutritional or behavioural counselling at any stage of the study. No group meetings or counselling sessions were held.
Dropout rates	28% orlistat 60 mg, 28% orlistat 120 mg, 42% control at 24 months.
Treatment of dropouts (return to baseline, or last measurement?)	The LOCF technique was employed for 1- and 2-year analyses. However, all reported data are the actual observed values rather than derived data from carrying forward the last recorded values.

Hill 1999 (in Avenell and O'Meara HTA) RCT	
Country and setting	USA. Clinical research centres.
Participants (included/excluded)	*Included if aged ≥18 years, BMI 28–43 kg/m^2, lost ≥8% of initial body weight during 6 month run-in phase* *Excluded if ever had significant medical disorders, uncontrolled hypertension, recurrent nephrolithiasis, symptomatic cholelithiasis, active GI disorders, type 2 diabetes, pancreatic disease, cancer, pregnancy, lactating women, history or presence of substance abuse, eating disorders, excessive alcohol intake, significantly abnormal laboratory test results, previous GI surgery for weight reduction, history of post-surgical adhesions, any medications known to influence body weight, appetite or lipid concentrations taken in 8 weeks prior to screening.*
Recruitment	N/R
Randomisation	Only people who lost ≥8% of initial weight during the 6-month run-in period were randomised. Randomisation was stratified by weight loss (≤10% or not).
Intervention (mode and intensity)	12 months, contacted 11 times (baseline, every 2 weeks during month 1 then every month to month 5 then every 2 months to month 12)
Duration of active intervention	12 months (after 6 months pre-treatment)
Control (mode and intensity)	*As above*

Delivery of intervention/control (who)	N/R
Dropout rates	*25% orlistat 30 mg, 23% orlistat 60 mg, 30% orlistat 120 mg, 27% placebo at 12 months*
Treatment of dropouts (return to baseline, or last measurement?)	Last observation data carried forward. However, all reported data were actual observed rather than derived values, whereas the technique of carrying forward the last observation was applied only for analyses of statistical significance.

Hollander 1998 (in Avenell and O'Meara HTA) RCT	
Country and setting	USA. No details of setting other than 'centres', assumed to be university diabetic clinics?
Participants (included/excluded)	*Included if aged >18 years, BMI 28–40 kg/m^2, type 2 diabetes, clinically stable on glyburide or glypizide for 6 months or more; HbA_{1c} 6.5–10% at screening, fasting plasma glucose 5.6–12.2 mmol/l at end of fourth week of pre-treatment, blood levels of fat soluble vitamins above lower limit of normal reference range, completion and compliance by tablet count of 70% or more during pre-treatment* *Excluded if pregnant, lactating, women of child bearing potential not taking adequate contraceptive measures, clinically relevant conditions e.g. psychiatric disorders, substance abuse, cholecystitis, pancreatic disease, uncontrolled hypertension; significant complications associated with diabetes, weight loss of >4 kg during last 3 months, history of recurrent nephrolithiasis or symptomatic cholelithiasis; GI surgery for weight reduction, history of bulimia or laxative abuse or if they had taken any drug that might influence body weight or plasma lipids in 8 weeks prior to start of study.*
Recruitment	No details reported.
Randomisation	Participants from the run-in period were randomised if they were compliant, HbA_{1c} levels were between 6.5 and 10% at screening, FPG of 5.6–12.2 mmol/l at end of lead in period, blood levels of fat soluble vitamins above the lower limit of the normal reference range. Randomisation was stratified by both weight loss and FPG (four groups).
Intervention (mode and intensity)	12 months, contacted 14–27 times (baseline, weeks 1 and 2 then every 2–4 weeks).
Duration of active intervention	*12 months*
Control (mode and intensity)	As above
Delivery of intervention/control (who)	N/R
Dropout rates	*15% orlistat, 28% placebo at 12 months*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Lindgarde 2000 (in Avenell HTA) RCT	
Country and setting	Sweden. Primary care centres.

Participants (included/excluded)	*Included if aged 18–75 years, BMI 28–38 kg/m^2, not pregnant, fasting serum glucose ≥6.7 mmol/l, or confirmed type 2 diabetes treated with sulfonylurea or metformin but not insulin; total serum cholesterol ≥6.5 mmol/l or more and/or LDL-cholesterol ≥4.2 mmol/l on at least two occasions or prescribed lipid lowering medications; DBP ≥90 mmHg on at least two occasions or confirmed hypertensive treated with antihypertensive medication* *Excluded if insulin treated, women of childbearing potential who were lactating or using inadequate contraception; myocardial infarction within 3 months prior to screening, GI surgery for weight reduction, active GI disorders, such as peptic ulcer disease or malabsorption syndromes (with the exception of controlled lactose intolerance), pancreatic disease, history of post-surgical adhesions, excessive alcohol or substance abuse, participants requiring any drug which might alter body weight or plasma lipids, such as appetite suppressants, lipid-lowering resins, retinoids or fish oil supplements; systemic steroids (other than hormone replacement therapy) and insulin)*
Recruitment	N/R
Randomisation	Minimisation method: primary defined cardiovascular risk factor, study centre, and weight loss achieved during run-in period (≤1 kg or >1 kg).
Intervention (mode and intensity)	*12 months, contacted 11 times (baseline, twice in first month then monthly to month 6 then every 2 months to month 12).*
Duration of active intervention	12 months
Control (mode and intensity)	As above
Delivery of intervention/control (who)	All dietary advice given by a practice nurse (rather than a dietitian).
Dropout rates	*16% orlistat, 12% control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Rossner 2000 (in Avenell and O'Meara HTA) RCT	
Country and setting	Europe. Centres – no details.
Participants (included/excluded)	*Included if aged ≥18 years, BMI 28–43 kg/m^2, completed 4-week pre-treatment phase and 75% or more compliance (by capsule count).* *Excluded if pregnant, lactating, women of childbearing potential not taking adequate contraception, clinically significant conditions (excluding obesity) that might effect study outcome, >4 kg weight loss in previous 6 months,* stopped smoking in previous 6 months, *GI surgery for weight loss, history of post surgical adhesions or of bulimia or laxative abuse; any drug that might influence body weight or serum lipids taken in 8 weeks prior to screening; uncontrolled hypertension, drug- treated diabetes mellitus, history or presence of symptomatic cholelithiasis.*
Recruitment	N/R
Randomisation	Had to show ≥75% compliance in the run-in period. No other details.
Intervention (mode and intensity)	24 months, contacted 18 times (baseline, every 2 weeks for first 2 months then monthly up to month 6 then every 2 months to month 24).
Duration of active intervention	*24 months*
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	Participants received advice from a dietitian.

Dropout rates	*25% orlistat 60 mg, 26% orlistat 120 mg, 35% control at 12 months.* 42% orlistat 60 mg, 35% orlistat 120 mg, 44% control at 24 months.
Treatment of dropouts (return to baseline, or last measurement?)	Last value carried forward.

Sjöström 1998 (in Avenell and O'Meara HTA) RCT	
Country and setting	Europe. No further details.
Participants (included/excluded)	*Included if aged ≥18 years, BMI 28–47 kg/m^2, women of childbearing potential if using adequate contraception, >75% compliance during pre-treatment phase at end of year 1 in order to continue to year 2.* *Excluded if serious diseases including uncontrolled hypertension (DBP ≥105 mmHg) and pharmacologically treated diabetics, weight loss >4 kg in 3 months prior to screening, surgery for weight reduction, history of post surgical adhesions, bulimia or laxative abuse, use of any drug which might influence body weight or plasma lipids in last month; drug or alcohol abuse*
Recruitment	From hospital waiting lists or by local advertising.
Randomisation	Had to be >75% compliant. Stratified by weight loss during run-in period (≤2 kg or >2 kg
Intervention (mode and intensity)	Four weeks pre-treatment phase, 52 weeks treatment then reassigned for further 52 weeks treatment, contacted 25 times (baseline, every 2 weeks until week 12 then every month until month 12 then 8 visits in year 2).
Duration of active intervention	*24 months*
Control (mode and intensity)	*As above*
Delivery of intervention/control (who)	*N/R*
Dropout rates	18% orlistat, 24% control at 52 weeks, 16% orlistat, 19% control at 104 weeks.
Treatment of dropouts (return to baseline, or last measurement?)	LOCF

Additional studies (not in HTA Avenell or O'Meara)

Weight loss

Bakris 2002 RCT	
Aim	To investigate the hypothesis that weight reduction with orlistat plus mild energy restriction leads to better BP control than diet alone in obese individuals with inadequately controlled hypertension.
Participants	People with inadequately controlled hypertension who were overweight (BMI between 28 and 43 kg/m^2). Total 532 – 325 F, 207 M. Mean (SD) age 53.2 (0.5) years orlistat (*n*=267), 52.5 (0.5) years control (*n*=265). Mean (SD) BMI 35.8 (3.9) kg/m^2 orlistat , 35.4 (4.0) kg/m^2 control.
Intervention	*Diet: nutritionally balanced hypoenergetic diet (estimated energy requirements – 600 kcal/day) with no more than 30% of energy as fat.* Antihypertensive medication was continued as established prior to study entry. If the BP on any two visits and at any time during the study became uncontrolled, i.e. exceeded 179 mmHg systolic and/or 109 mmHg diastolic, modification of the hypertension medication was prescribed by the primary physician. Such modification of medication was also allowed if the BP exceeded 159/95 mmHg after 16 weeks. Uncontrolled hypertension did not necessitate study withdrawal. The primary physician was allowed to modify antihypertensive medications as needed according to his/her own judgment, with the exception of diuretic therapy, which had to remain stable for the duration of the study. *Activity: encouraged to participate in moderate physical activity as deemed appropriate by their physician.* *Lifestyle intervention literature was made available to all participants during the study and all met with a dietitian periodically to review dietary instructions and food records.* *Drug: orlistat 120 mg three times per day with meals.*
Control	*As above except* Drug: placebo three times per day with meals.
Length of follow-up	*12 months*
Results	*The trial design did not include a run-in period.* *At 12 months, mean weight change (SD) was –5.40 (6.40) kg in the orlistat group compared with –2.70 (6.40) kg in the control group. Mean weight change in the intervention group compared with control was –2.70 (95% CI –3.79 to –1.61).* *At 12 months, 45.7% of the orlistat group compared with 22.6% of the placebo group lost more than 5% of initial body weight (*p<*0.001).*
Quality and comments	*Blinded assessment not reported. ITT analysis done. Random allocation but no description of concealment.* *More women than men were in both groups, and most participants were white.*
Sponsor details	*None reported. Corresponding author based at Hoffman-La Roche.*

**NB: have included the 5% weight loss, but this is >5% NOT ≥5% as in other studies.

Derosa 2003 RCT	
Aim	To assess obese participants with hypercholesterolaemia who were prescribed a standardised diet, comparing the action of orlistat, fluvastatin, orlistat plus fluvastatin, and placebo on anthropometric measures, BP and lipid profile.
Participants	People who were obese (BMI >30 kg/m^2), aged >40 years of age, with TC of ≥6.15 mmol/l (240 mg/dl). Total 50 – 26 F, 24 M (overall 99). Mean (SD) age 51.6 (8.3) years orlistat (*n*=27), 52.4 (10.2) years control (*n*=23). Mean (SD) BMI 32.0 (1.3) kg/m^2 orlistat, 31.7 (1.0) kg/m^2 control.

Intervention	*Four week, single-blind placebo pre-treatment with a 1500 kcal/day diet (54% energy as carbohydrate, 24% as protein, 22% as lipids (6% saturated fat), 108 mg cholesterol, 35 g fibre). Also, physical aerobics activity (≥30 min, 4 days/week) by bicycle.* *Diet: continued from pre-treatment. Food diaries and discussion used to ensure dietary and exercise compliance.* *Activity: as pre-treatment.* *BT: behaviour modification programme – participant discussion and assessment of diaries (self-monitoring?).* *Drug: orlistat 120 mg three times per day after each meal (two placebo per day).*
Control	*As above except* Drug: placebo five times per day
Length of follow-up	*12 months*
Results	*Weight loss during run-in period not reported.* *At 6 months, mean weight change (SD) was –5.10 (7.36) kg in the orlistat group compared with –4.20 (7.10) kg in the control group. Mean weight change in the intervention group compared with control was –0.90 (95% CI –4.99 to 3.19).* *At 12 months, mean weight change (SD) was –8.60 (8.35) kg in the orlistat group compared with –7.60 (8.07) kg in the control group. Mean weight change in the intervention group compared with control was –1.00 (95% CI –5.65 to 3.65).* *5% and 10% responders not reported.*
Quality and comments	*Only results of orlistat and placebo group reported. Assume baseline to be after 4-week lead in period.* *Blinded assessment not reported. ITT analysis not done. Attempt at concealment, but chance of disclosure. Reported SDs very low so used HTA formula.*
Sponsor details	*None reported.*

Kelley 2002 RCT	
Aim	To assess the effects of orlistat on weight loss, glycaemic control, and cardiovascular risk factors in people who are overweight or obese with insulin-treated type 2 diabetes.
Participants	People who were overweight or obese (BMI 28 to 43 kg/m^2) with insulin-treated type 2 diabetes. Total 535 – 301 F, 234 M. Mean (SD) age 57.8 (8.2) years orlistat (*n*=266), 58.0 (8.2) years control (*n*=269). Mean (SD) BMI 35.8 (3.3) kg/m^2 orlistat, 35.6 (4.9) kg/m^2 control.
Intervention	Diet: nutritionally balanced energy-deficit diet designed to induce a weight loss of 0.25–0.5 kg per week. 30% of energy as fat, 50% as carbohydrate, and 20% as protein, with a maximum of 300 mg/day of cholesterol. Additional dietary instruction was provided at predetermined intervals during the study, and dietary compliance was monitored by the use of dietary intake records. At week 24, the prescribed energy intake was further reduced by 200 kcal/day (with a minimum energy intake of at least 1200 kcal/day) to compensate for reduced energy requirements induced by weight loss. BT: Lifestyle and behavioural modification literature were available throughout the study. Activity: encouraged to participate in moderate physical activity. *Drug: orlistat 120 mg three times per day.* *Investigators were instructed to try to maintain stable doses of insulin and other diabetes medications, but they had the option to adjust doses.*
Control	*As above except:* Drug: placebo three times per day.
Length of follow-up	*12 months*

Results	*A run-in period was not used.* *At 12 months, mean weight change (SD) was –3.89 (4.40) kg in the orlistat group compared with –1.27 (4.59) kg in the control group. Mean weight change in the intervention group compared with control was –2.62 (95% CI –3.38 to –1.86).* *At 12 months, 32.7% of the orlistat group compared with 13.0% of the placebo group lost 5% or more of initial body weight (*p<*0.0001).* *At 12 months, 10.2% of the orlistat group compared with 3.7% of the placebo group lost 10% or more of initial body weight (*p<*0.001).*
Quality and comments	*Calculated SDs from SEMs.* *Blinded assessment not reported. ITT analysis done. Random allocation but no description of concealment.*
Sponsor details	*Hoffman-La Roche*

Krempf 2003 RCT	
Aim	To determine the effect of orlistat on weight reduction and the long-term maintenance of this weight loss when associated with a continuous mildly energy-reduced diet.
Participants	People who were overweight (BMI ≥28 kg/m^2). Total 696 – 601 F, 95 M. Mean (SD) age 40 (11.1) years orlistat (*n*=346), 42 (11.2) years control (*n*=350). Mean (SD) BMI 36.0 (5.6) kg/m^2 orlistat, 36.2 (5.6) kg/m^2 control.
Intervention	*15 day placebo run-in period. Diet started at the beginning of the run-in period* *Diet: as per run-in, initial energy intake determined from food diaries and individually tailored diets (restricted energy by 20%, 30% of intake from fat).* *Intake reduced by 10% (never below 1200 kcal/day) if weight stable or gained.* *Drug: orlistat 120 mg three times per day.*
Control	*As above except:* Drug: placebo three times per day.
Length of follow-up	*18 months*
Results	*During the run-in period, weight loss was about 1.35kg (calculated from graph).* *At 12 months, mean weight change (SD) was –5.95 (8.00) kg in the orlistat group compared with –3.05 (6.78) kg in the control group. Mean weight change in the intervention group compared with control was –2.90 (95% CI –4.00 to –1.80).* *At 18 months, mean weight change (SD) was –5.05 (7.34kg in the orlistat group compared with –1.35 (6.30) kg in the control group. Mean weight change in the intervention group compared with control was –3.70 (95% CI –4.72 to –2.68)* *Mean weight regain between 12 and 18 months was lower in the orlistat group (1.2 vs 1.4 kg) but the difference was not statistically significant.* *At 12 months, 65.9% of the orlistat group compared with 46.4% of the placebo group lost 5% or more of initial body weight (*p<*0.0001).* *At 12 months, 32.9% of the orlistat group compared with 24.5% of the placebo group lost 10% or more of initial body weight (*p=*0.04).* *At 18 months, 58.3% of the orlistat group compared with 37.8% of the placebo group lost 5% or more of initial body weight (*p<*0.0001).* *At 18 months, 33.6% of the orlistat group compared with 16.8% of the placebo group lost 10% or more of initial body weight (*p<*0.0001).* *More people in the orlistat group maintained the ≥10% weight loss compared with placebo (28.1% vs 13.8%,* p=*0.0004).*
Quality and comments	*Calculated SDs from SEMs. People in the control group were significantly older than in the orlistat group (42 vs 40 years,* p=*0.04).* *Blinded assessment not reported. ITT analysis done. Random allocation but no description of concealment.* *Calculated from week 0 weight loss – assumed to be 1.35 kg (from graph). HTA formula used for SDs.*
Sponsor details	*Roche*

Miles 2002 RCT	
Aim	To assess the effect of orlistat on body weight, glycaemic control and cardiovascular risk factors in people with metformin-treated type 2 diabetes
Participants	People with metformin-treated type 2 diabetes and who were overweight (BMI of 28 to 43 kg/m^2). Total 504 – 242 F, 262 M. Mean (SD) age 52.4 (6.3) years orlistat (*n*=250), 53.7 (6.4) years control (*n*=254). Mean (SD) BMI 35.6 (4.7) kg/m^2 orlistat, 35.2 (3.2) kg/m^{2}control.
Intervention	*Diet: reduced-energy diet (about 600 kcal daily deficit) based on American Diabetes Association recommendations and containing 30% of energy as fat, 50% as carbohydrate, and 20% as protein, with a maximum cholesterol content of 300 mg/day. Energy content calculated from an estimate of initial energy requirements and was designed to promote a weight loss of 0.25–0.5 kg/week. Daily energy intake was reduced by an additional 200 kcal after 6 months to compensate for the reduction in energy requirements caused by weight loss, with a minimum intake of 1200 kcal/day. Participants received dietary counselling at baseline and at regular intervals throughout the study.* *Activity: encouraged to increase their level of physical activity.* *Other: multivitamin supplement prescribed to be taken daily at least 2 h before or after the evening dose of study medication. Diabetes medications were changed when hypoglycaemia occurred or when deterioration in glycaemic control was observed.* *Drug: orlistat 120 mg three times per day with main meals*
Control	As above except Drug: placebo three times per day with main meals
Length of follow-up	*12 months*
Results	*A run-in period was not used.* *At 12 months, mean weight change (SD) was –4.70 (7.25) kg in the orlistat group compared with –1.80 (3.02) kg in the control group. Mean weight change in the intervention group compared with control was –2.90 (95% CI –3.87 to –1.93).* *At 12 months, 39.0% of the orlistat group compared with 15.7% of the placebo group lost 5% or more of initial body weight (*p=*0.008).* *At 12 months, 14.1% of the orlistat group compared with 3.9% of the placebo group lost 10% or more of initial body weight (*p=*0.003).*
Quality and comments	*Calculated SDs from SEMs.* *Blinded assessment not reported. ITT analysis done. Random allocation but no description of concealment.*
Sponsor details	*Hoffman-La Roche*

Poston 2003 RCT	
Aim	To evaluate the effectiveness of a culturally appropriate lifestyle intervention combined with orlistat in producing weight loss in Mexican American women who were obese
Participants	Mexican American women who were obese (BMI ≤27 kg/m^2). Total 108 – all women. Mean (SD) age 42.4 (9.2) years orlistat (*n*=56), 43.7 (9.2) years control (*n*=52). Mean (SD) BMI 37.8 (6.2) kg/m^2 orlistat, 36.0 (5.2) kg/m^2 control.

Intervention	*Diet: instructed to lower energy intake by at least 500 energy/day to achieve a weight loss of about 0.45 kg (1 lb) per week. Fat intake limited to 30% of total energy intake. Used nutrition manual with 16 weight-loss lessons and 11 maintenance activities.* *Activity: to increase activity to minimum five times/week for 30 min per session for a total of ≥150 min/week. Primary exercise was walking. Also used exercise contracts and incentives to motivate participants.* *BT: classes which included nutrition component (food demonstrations of modified traditional dishes), problem-solving and role-playing (including identifying problem eating situations and setting exercise objectives), social support strategies, discussions on activity. Programme was culturally adapted with bilingual materials and instructor, modification of native diets, tailored rationales for diet and exercise (e.g. importance of family involvement, improving health rather than just appearance).* *Other: vitamin and mineral supplementation (one per day).* *Drug: orlistat 120 mg three times per day with meals.*
Control	Waiting list control.
Length of follow-up	*12 months*
Results	*A run-in period was not used.* *At 6 months, mean weight change (SD) was –5.20 (7.39) kg in the orlistat group compared with –1.00 (6.20) kg in the control group. Mean weight change in the intervention group compared with control was –4.20 (95% CI –6.77 to –1.63).* *At 12 months, mean weight change (SD) was –5.60 (7.50) kg in the orlistat group compared with –0.30 (6.00) kg in the control group. Mean weight change in the intervention group compared with control was –5.30 (95% CI –7.85 to –2.75).* *Significantly more women in the intervention group achieved 5% or more weight loss (*p*<0.000 for 6 and 12 months) and 10% or more weight loss (*p*=0.008 at 6 and 12 months) compared with waiting list control.*
Quality and comments	*Blinded assessment not reported. ITT analysis done. Random allocation but no description of concealment. SDs calculated using HTA formula. Open label study. Read 5/10% values off Figures 2 and 3 for analysis.*
Sponsor details	*Roche*

Swinburn 2005 RCT	
Aim	To compare the effect of orlistat and placebo on the predicted 10-year CVD risk in obese people with one or more cardiovascular risk factors treated for 12 months, in conjunction with a fat-reduced, but otherwise ad libitum, diet.
Participants	People who were overweight (BMI between 30 and 50 kg/m^2) with at least one cardiovascular risk factor Total 339 – 193 F, 146 M. Mean (SD) age 52.0 (7.5) years orlistat (*n*=170), 52.5 (7.4) years control (*n*=169). Mean (SD) BMI 37.6 (5.1) kg/m^{2}orlistat, 38.0 (4.9) kg/m^{2}control.
Intervention	*Pre-treatment 4-week, single-blind, placebo lead-in period with advice on reducing dietary fat and increasing physical activity levels (moderate-intensity physical activity of at least 30 min per day on most days). Received advice from a dietitian about identifying the sources of dietary fat (such as through label reading) and reducing them as much as possible by using a variety of strategies, including fat-reduced cooking methods. Aim to reduce daily dietary fat intake to between 25 and 30% of total daily energy intake or about 40 g/day.* *Diet: given further advice on maintaining a fat-reduced diet.* *Activity: given further advice on maintaining a regular physical activity.* *Other: diaries (self-monitoring) and goal setting.* *Drug: orlistat 120 mg three times per day.*
Control	As above except: Drug: placebo three times per day.
Length of follow-up	*12 months*

Results	*Weight loss during run-in period not reported.* *At 12 months, mean weight change (SD) was –4.70 (7.70) kg in the orlistat group compared with –0.90 (4.20) kg in the control group. Mean weight change in the intervention group compared with control was –3.80 (95% CI –5.12 to –2.48).* *5% and 10% responders not reported.*
Quality and comments	*Blinded assessment not reported. ITT analysis done. Random allocation but no description of concealment.* *Higher proportion of women in the orlistat group compared with control. Two people with left ventricular hypertrophy in the control group.*
Sponsor details	*Hoffman-La Roche*

Toplak 2005 RCT	
Aim	To determine the effect of two different levels of energy deficit on weight loss in obese people treated with orlistat.
Participants	People who were obese (BMI 30 to 43 kg/m^2, with a body weight of ≥90 kg and a WC of ≥88 cm (women) or ≥102 cm (men). Total 356 – 277 F, 79 M. Mean (SD) age 41.1 (12.1) years orlistat+1000 kcal/day deficit (*n*=141), 41.3 (11.0) years orlistat+500 kcal/day deficit (*n*=215). Mean (SD) BMI 37.4 (3.6) kg/m^2 orlistat+1000 kcal/day deficit, 37.3 (3.4) kg/m^2 orlistat+500 kcal/day deficit.
Intervention	*Diet: 1000 kcal/day deficit diet consisted of 30% of energy as fat, 50% as carbohydrate and 20% as protein. Energy intake prescribed for each individual on the basis of estimated daily maintenance energy requirements (1.3 × calculated basal metabolic rate).* *Activity: encouraged to increase physical activity.* *Drug: orlistat 120 mg three times daily.* *Participants who achieved ≥5% reduction in body weight after both 3 and 6 months eligible to continue treatment for the entire study period (12 months) and those who did not excluded from the study. After 6 and 9 months of treatment, energy intake restriction adjusted in order to maintain a 500 or 1000 kcal/day deficit.* *Allowed to continue with any antihypertensive medication during the study. If possible, dose of concomitant medication maintained constant throughout the course of the study. However, if clinically indicated, dose of concomitant medication could be titrated. Additionally, concomitant antihypertensive and lipid-lowering medications could be discontinued during the study if, during clinical assessment, it observed that such medications were no longer required.*
Control	As above except: Diet: 500 kcal/day deficit diet consisted of 30% of energy as fat, 50% as carbohydrate and 20% as protein. Energy intake prescribed for each individual on the basis of estimated daily maintenance energy requirements (1.3 × calculated basal metabolic rate).
Length of follow-up	*12 months*
Results	*No run-in period used.* *At 12 months, mean weight change (SD) was –9.52 (7.52) kg in the orlistat+1000 kcal group compared with –8.62 (6.61) kg in the orlistat+500 kcal group. Mean weight change in the intervention group compared with control was –0.90 (95% CI –2.51 to 0.71).* *(At 3 months, 75% of participants achieved 5% weight loss. Of these, 92% achieved 5% weight loss at month 6. Those who did not achieve a 5% weight loss at both months 3 and 6 were excluded from the study at month 6.)* *After 12 months of treatment with orlistat, 85% and 84% of participants in the 1000 and 500 kcal/day deficit groups, respectively, achieved 5% weight loss, and 53% and 50% respectively, achieved 10% weight loss compared with baseline. In addition, 21% and 23% in the 1000 and 500 kcal/day deficit groups, respectively, achieved 15% weight loss, and 11% and 7% respectively, achieved 20% weight loss compared with baseline.*

Quality and comments	*Blinded assessment not done. ITT analysis done. Good concealment of allocation – central randomisation.*
Sponsor details	*Hoffman-La Roche*

Torgerson 2004 RCT	
Aim	To determine the long-term effect of orlistat, in combination with lifestyle changes in reducing progression to type 2 diabetes and body weight over 4 years in obese, non-diabetic participants who had either normal glucose tolerance (NGT) or IGT. Also to determine the effect of orlistat treatment on weight-related metabolic abnormalities associated with increased risk for CVD and the safety and tolerability of orlistat over 4 years.
Participants	People who had NGT or IGT who were also obese (BMI ≥30 kg/m^2) Total 3277 – 1810 F, 1467 M. Mean (SD) age 43.0 (8.0) years orlistat (*n*=1640), 43.7 (8.0) years control (*n*=1637). Mean (SD) BMI 37.3 (4.2) kg/m^2 orlistat, 37.4 (4.5) kg/m^2 control.
Intervention	*Diet: reduced-energy diet (about 800 kcal/day deficit) containing 30% of energy as fat and not more than 300 mg of cholesterol per day. Prescribed energy intake readjusted every 6 months to account for any weight lost during the preceding months. Received dietary counselling every 2 weeks for the first 6 months and monthly thereafter.* *Activity: encouraged to walk at least 1 extra km per day in addition to their usual physical activity. Kept physical activity diaries.* *Drug: orlistat 120 mg three times per day with meals.*
Control	As above except: Drug: placebo three times per day with meals.
Length of follow-up	*4 years*
Results	*No run-in period used.* *At 12 months, mean weight change (SD) was –10.60 (8.91) kg in the orlistat group compared with –6.20 (7.67) kg in the control group. Mean weight change in the intervention group compared with control was –4.40 (95% CI –5.02 to –3.78).* *At 48 months, mean weight change (SD) was –5.80 (7.56) kg in the orlistat group compared with –3.00 (6.76) kg in the control group. Mean weight change in the intervention group compared with control was –2.80 (95% CI –3.55 to –2.05).* *At 12 months, 72.8% of the orlistat group compared with 45.1% of the placebo group lost 5% or more of initial body weight (*p<*0.001).* *At 12 months, 41.0% of the orlistat group compared with 20.8% of the placebo group lost 10% or more of initial body weight (*p<*0.001).* *At 48 months, 52.8% of the orlistat group compared with 37.3% of the placebo group lost 5% or more of initial body weight (*p<*0.001).* *At 48 months, 26.2% of the orlistat group compared with 15.6% of the placebo group lost 10% or more of initial body weight (*p<*0.001).*
Quality and comments	*Blinded assessment not reported. ITT analysis done for time to diabetes only?* *Attempt at concealment but possibility of disclosure (sealed envelopes).* *HTA formula used.*
Sponsor details	*Hoffman-La Roche*

Other outcomes

Bakris 2002 RCT	
Results	*At 12 months, mean (SD) TC change in mmol/l was –0.36 (0.94) in the orlistat group, and –0.04 (0.79) in the control group. Mean TC change in the intervention group compared with control was –0.32 (95% CI –0.47 to –0.17).* *At 12 months, mean (SD) LDL change in mmol/l was –0.31 (0.76) in the orlistat group, and –0.11 (0.70) in the control group. Mean LDL change in the intervention*

	group compared with control was –0.20 (95% CI –0.32 to –0.08). *Changes in HDL-cholesterol and TAG were not significant but details were not reported.* *At 12 months, mean (SD) DBP change in mmHg was –11.40 (8.30) in the orlistat group, and –9.20 (8.40) in the control group. Mean DBP change in the intervention group compared with control was –2.20 (95% CI –3.62 to –0.78).* *At 12 months, mean (SD) SBP change in mmHg was –13.30 (15.20) in the orlistat group, and –11.00 (15.00) in the control group. Mean SBP change in the intervention group compared with control was –2.30 (95% CI –4.87 to 0.27).* *Significant reductions in insulin levels were seen in both groups (–41.2 vs –26.7 pmol/l) but these were not significantly different between the groups.* *A 30% reduction in cardiovascular risk score occurred significantly more frequently in the orlistat group than in the placebo group (36.1 vs 24%,* p<*0.05).* *The reduction in sitting diastolic BP was significantly greater in people with diabetes randomised to receive orlistat (–15.3±2.1 vs –6.4±1.0 mmHg,* p=*0.028).* *Among those with diabetes who completed 52 weeks, a significantly greater percentage of those randomised to orlistat reached goal BP (10/11; 91%) than of those receiving diet only (3/9; 33%;* p=*0.009). Weight loss in orlistat-treated vs placebo-treated people with diabetes was not statistically different (–9.1±1.5 vs –4.3±0.8 kg,* p=*0.092).* *Overall, BP medication changes occurred in 131 participants during the trial. In 18 orlistat-treated people, medications were reduced at 23 weeks (mean) compared with 11 placebo participants where medication reduction occurred at 22 (mean) weeks. Medication increases occurred in 42 orlistat-treated vs 40 placebo-treated participants. These changes occurred at 22±3 weeks in the orlistat group vs 25±6 weeks in placebo (not significant). Finally, medications were substituted in eight orlistat-treated and four placebo-treated individuals at 25±6 and 33±8 weeks, respectively (not significant).* *Those participants in whom medication could be reduced had significantly greater weight loss (–11±11%) than those in whom an increase in medication was deemed necessary (–5±6%,* p=*0.009).* *No analysis of outcomes independent of weight loss was reported.*
Quality and comments	…

Derosa 2003 RCT	
Results	*At 6 months, no significant changes were seen in SBP, DBP, TC, LDL, HDL or TAG levels.* *At 12 months, mean (SD) DBP change in mmHg was –4.00 (8.30) in the orlistat group, and –2.00 (8.30) in the control group. Mean DBP change in the intervention group compared with control was –2.00 (95% CI –6.70 to 2.70).* *At 12 months, mean (SD) SBP change in mmHg was –6.00 (12.70) in the orlistat group, and –4.00 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –2.00 (95% CI –9.19 to 5.19).* *When the 12-month lipid and TAG figures were converted to mmol/l, the values appeared very different (for example –1 mmol/l for TC level) so have not added to analysis. But authors reported significant % changes in TC and LDL levels from baseline for both groups, and for the orlistat group for TAG (*p<*0.05). Significant differences were seen between groups for TC and LDL (*p<*0.05).* *No analysis of outcomes independent of weight loss was reported.*
Quality and comments	Could not add 6 months results to meta-analysis as no SDs reported. For 12-month results, assumed SDs to be similar to those of other studies. Results for completers only.

Kelley 2002 RCT	
Results	*At 12 months, mean (SD) TC change in mmol/l was –0.30 (0.58) in the orlistat group, and 0.08 (0.59) in the control group. Mean TC change in the intervention group compared with control was –0.38 (95% CI –0.48 to –0.28).* *At 12 months, mean (SD) LDL change in mmol/l was –0.38 (0.42) in the orlistat*

	group, and –0.08 (0.42) in the control group. Mean LDL change in the intervention group compared with control was –0.30 (95% CI –0.37 to –0.23). *At 12 months, mean (SD) HDL change in mmol/l was 0.02 (0.08) in the orlistat group, and 0.05 (0.09) in the control group. Mean HDL change in the intervention group compared with control was –0.03 (95% CI –0.04 to –0.02).* *At 12 months, mean (SD) TAG change in mmol/l was 0.18 (1.33) in the orlistat group, and 0.31 (1.10) in the control group. Mean TAG change in the intervention group compared with control was –0.13 (95% CI –0.34 to 0.08).* *At 12 months, mean (SD) HbA_{1c} % change was –0.62 (0.66) in the orlistat group, and –0.27 (0.68) in the control group. Mean TAG change in the intervention group compared with control was –0.35 (95% CI –0.46 to –0.24).* *At 12 months, mean (SD) DBP change in mmHg was –2.30 (5.83) in the orlistat group, and –1.00 (4.24) in the control group. Mean DBP change in the intervention group compared with control was –1.30 (95% CI –2.16 to –0.44).* *At 12 months, mean (SD) SBP change in mmHg was –1.20 (8.32) in the orlistat group, and –0.90 (8.47) in the control group. Mean SBP change in the intervention group compared with control was –0.30 (95% CI –1.71 to 1.11).* *At 12 months, mean (SD) FPG change in mmol/l was –1.63 (2.49) in the orlistat group, and –1.08 (2.54) in the control group. Mean FPG change in the intervention group compared with control was –0.55 (95% CI –0.97 to –0.13).* *HbA_{1c} improvements remained significant after adjustment for weight loss. Similarly for changes in TC and LDL levels.* *A greater reduction in insulin dose was associated with orlistat than with placebo treatment (–8.1 vs –1.6 units/day,* p=*0.007). A greater proportion of people achieved ≥5% reduction of insulin dose in the orlistat treatment group compared with placebo (41 vs 31%,* p<*0.001), whereas fewer of those in the orlistat than in the placebo group increased their insulin dose by ≥5% (12 vs 26%,* p<*0.001). More orlistat- (41.3%) than placebo-treated participants (30.9%) decreased the dose or discontinued at least one oral diabetes medication during the study; conversely, dose increase or the addition of at least one new diabetes medication occurred less frequently in orlistat- (14.7%) than in placebo-treated people (31.7%) (*p<*0.0001). There was a greater reduction in sulfonylurea dose in the orlistat group compared with placebo. Changes in metformin dose were not different between groups.*
Quality and comments	SDs calculated from SEMs, but seem high for TAG and FPG.

Krempf 2003 RCT	
Results	*At 18 months, TC levels were reduced by ≥20% in 10.1% of the orlistat group, compared with 2.6% of those in the placebo group. LDL levels were reduced by ≥20% in 19.9% of the orlistat group, compared with 6.6% of the placebo group (no* p *values reported).* *In those participants classified as at risk (FPG ≥6.05 mmol/l, LDL ≥3.36 mmol/l, HDL <0.90 mmol/l, TAG ≥2.54 mmol/l, SBP ≥140 mmHg, and DBP ≥90 mmHg), significant changes in the orlistat group compared with placebo were seen at 18 months for FPG (–0.86 vs –0.29 mmol/l,* p<*0.05), %LDL-cholesterol (–13.0 vs –7.0%,* p<*0.001). No significant differences were seen for HDL or TAG levels, or for SBP and DBP, but all the changes were in the right direction.* *No analysis of outcomes independent of weight loss was reported, although the authors did note 'beneficial changes in lipid levels that were greater than could be expected by weight loss alone'.* *Food intake reported only overall, not by groups. However, there was no statistical difference for energy and nutrient intakes between the two groups.*
Quality and comments	…

Miles 2002 RCT	
Results	*At 12 months, mean (SD) TC change in mmol/l was –0.27 1.08) in the orlistat group, and 0.06 (1.08) in the control group. Mean TC change in the intervention*

	group compared with control was –0.33 (95% CI –0.52 to –0.14). *At 12 months, mean (SD) LDL change in mmol/l was –0.25 (0.74) in the orlistat group, and 0.05 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.30 (95% CI –0.43 to –0.17).* *At 12 months, mean (SD) HDL change in mmol/l was 0.09 (0.29) in the orlistat group, and 0.10 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.01 (95% CI –0.06 to 0.04).* *At 12 months, mean (SD) TAG change in mmol/l was –0.25 (0.96) in the orlistat group, and 0.03 (0.96) in the control group. Mean TAG change in the intervention group compared with control was –0.28 (95% CI –0.45 to –0.11).* *At 12 months, mean (SD) %HbA_{1c} change was –0.75 (0.66) in the orlistat group, and –0.41 (0.65) in the control group. Mean TAG change in the intervention group compared with control was –0.34 (95% CI –0.45 to –0.23).* *At 12 months, mean (SD) SBP change in mmHg was –2.10 (12.70) in the orlistat group, and –0.30 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –1.80 (95% CI –4.02 to 0.42).* *At 12 months, mean (SD) FPG change in mmol/l was –2.00 (1.61) in the orlistat group, and –0.70 (1.63) in the control group. Mean FPG change in the intervention group compared with control was –1.30 (95% CI –1.58 to -1.02).* *Compared with placebo treatment, orlistat therapy was associated with reductions in both daily metformin dose (–16± 24 vs 49±24 mg/day,* p=*0.013) and relative sulfonylurea dose, expressed as percent change, with doses standardised to a percentage of maximum daily dose (–11.5±3.6 vs –0.9±2.6%,* p=*0.027). Twice as many people in the orlistat than in the placebo group either reduced or discontinued one or more diabetes medications (17.1 v. 8.2%). More placebo- than orlistat-treated participants required additional or increased dosages of diabetes medication (21.7 vs 12.2%). These changes in diabetes medication usage were significantly different between treatment groups (*p=*0.0004).*
Quality and comments	Assumed SDs similar to other studies.

Poston 2003 RCT	
Results	*Women in the intervention group had significant improvements in TC (*p=*0.029) and LDL-cholesterol (*p=*0.006) (not sure of the time point). No other (usual) outcomes were significant.* *No analysis of outcomes independent of weight was reported.*
Quality and comments	Did not use SDs from other trials for analysis as this trial was very different and similar effects could not be assumed.

Swinburn 2005 RCT	
Results	*At 12 months, mean (SD) TC change in mmol/l was –0.08 (0.73) in the orlistat group, and 0.16 (0.68) in the control group. Mean TC change in the intervention group compared with control was –0.24 (95% CI –0.39 to –0.09).* *At 12 months, mean (SD) LDL change in mmol/l was –0.12 (0.65) in the orlistat group, and 0.11 (0.62) in the control group. Mean LDL change in the intervention group compared with control was –0.23 (95% CI –0.37 to –0.09).* *At 12 months, mean (SD) HDL change in mmol/l was 0.04 (0.18) in the orlistat group, and 0.08 (0.19) in the control group. Mean HDL change in the intervention group compared with control was –0.04 (95% CI –0.08 to 0.00).* *At 12 months, mean (SD) TAG change in mmol/l was 0.01 (0.73) in the orlistat group, and 0.06 (0.57) in the control group. Mean TAG change in the intervention group compared with control was –0.05 (95% CI –0.19 to 0.09).* *At 12 months, mean (SD) %HbA_{1c} change was –0.04 (0.60) in the orlistat group, and 0.15 (0.60) in the control group. Mean TAG change in the intervention group compared with control was –0.19 (95% CI –0.32 to –0.06).* *At 12 months, mean (SD) DBP change in mmHg was –2.96 (8.01) in the orlistat group, and –1.37 (8.59) in the control group. Mean DBP change in the intervention group compared with control was –1.59 (95% CI –3.36 to 0.18).* *At 12 months, mean (SD) SBP change in mmHg was –4.05 (13.00) in the orlistat*

	group, and –0.51 (14.70) in the control group. Mean SBP change in the intervention group compared with control was –3.54 (95% CI –6.49 to –0.59). *At 12 months, mean (SD) FPG change in mmol/l was –0.19 (1.13) in the orlistat group, and 0.29 (1.42) in the control group. Mean FPG change in the intervention group compared with control was –0.48 (95% CI –0.75 to –0.21).* *No analysis of association with weight loss was reported.* *Vitality (SF-36) was the only domain to have a statistically significant (*p=*0.006) difference between the two groups at 52 weeks with the orlistat group having a higher score.* *In people taking medication for diabetes, lipids or hypertension, there were significant changes towards fewer or lower-dose medications for diabetes (*p=*0.026) and hypertension (*p=*0.0062), but not for lipids (*p=*0.42).* *The baseline (week 0) median 10-year risk of a CVD event (Framingham score) was moderately low at about 10%. At week 52 the median 10-year CVD risk was 0.083 (range: 0.008 to 0.304) in the orlistat group and 0.100 (range: 0.013 to 0.386) in the placebo group. This difference in the changes between the two groups was non-significant (*p=*0.091).*
Quality and comments	…

Toplak 2005 RCT	
Results	*At 12 months, mean (SD) DBP change in mmHg was –3.80 (8.50) in the 1000 kcal deficit group, and –2.60 (9.60) in the 500 kcal deficit group. Mean DBP change in the 1000 kcal deficit group compared with 500 kcal deficit was –1.20 (95% CI –3.28 to 0.88).* *At 12 months, mean (SD) SBP change in mmHg was –6.00 (13.90) in the 1000 kcal deficit group, and –6.00 (13.00) in the 500 kcal deficit group. Mean SBP change in the 1000 kcal deficit group compared with 500 kcal deficit was –0.00 (95% CI –3.07 to 3.07).* *At 12 months, mean (SD) FPG change in mmol/l was –0.20 (0.60) in the 1000 kcal deficit group, and 0.00 (1.90) in the 500 kcal deficit group. Mean FPG change in the 1000 kcal deficit group compared with 500 kcal deficit was –0.20 (95% CI –0.53 to 0.13).* *Changes in %TC, %LDL, %HDL, were all significantly different from baseline for both 1000 kcal deficit and the 500 kcal deficit groups, apart from %TAG which were not significantly different from baseline in either group.* *When a subgroup of analysis of people with risk factors at baseline was done, all changes were significant from baseline (*p<*0.001) apart from %HDL-cholesterol (only significant from baseline in the 1000 kcal deficit group +16.9%,* p<*0.05 and NS from baseline for the 500 kcal deficit group, +8.2%) Similarly for %TAG (–37.4%,* p<*0.001 in the 1000 kcal deficit group vs –11.1% in the 500 kcal deficit group, NS).* *No analysis of association with weight loss was reported.* *Reported difference in energy intake, as determined by self-reported participant food diaries, was –111 kcal deficit/day at month 6 (1511 vs 1400 kcal/day;* p=*0.0083) and –95 kcal/day at month 12 (1564 vs 1469 kcal/day;* p=*0.0580).* *Reported difference in fat intake at 12 months was approximately 2 g/day (53 vs 51 g,* p=*0.6151).*
Quality and comments	

Torgerson 2004 RCT	
Results	*At 12 months, mean (SD) TC change in mmol/l was –0.51 (1.08) in the orlistat group, and –0.08 (1.08) in the control group. Mean TC change in the intervention group compared with control was –0.43 (95% CI –0.51 to –0.35).* *At 12 months, mean (SD) LDL change in mmol/l was –0.42 (0.74) in the orlistat group, and –0.06 (0.74) in the control group. Mean LDL change in the intervention group compared with control was –0.36 (95% CI –0.42 to –0.30).* *At 12 months, mean (SD) HDL change in mmol/l was 0.04 (0.29) in the orlistat*

	group, and 0.10 (0.29) in the control group. Mean HDL change in the intervention group compared with control was –0.06 (95% CI –0.08 to –0.04). *At 12 months, mean (SD) TAG change in mmol/l was –0.12 (0.96) in the orlistat group, and –0.12 (0.96) in the control group. Mean TAG change in the intervention group compared with control was 0.00 (95% CI –0.07 to 0.07).* *At 12 months, mean (SD) DBP change in mmHg was –3.60 (8.30) in the orlistat group, and –2.60 (8.30) in the control group. Mean DBP change in the intervention group compared with control was –1.00 (95% CI –1.62 to –0.38).* *At 12 months, mean (SD) SBP change in mmHg was –7.30 (12.70) in the orlistat group, and –5.20 (12.70) in the control group. Mean SBP change in the intervention group compared with control was –2.10 (95% CI –3.05 to –1.15).* *At 12 months, mean (SD) FPG change in mmol/l was 0.10 (1.35) in the orlistat group, and 0.20 (1.35) in the control group. Mean FPG change in the intervention group compared with control was –0.10 (95% CI –0.20 to 0.00).* *At 48 months, all changes were significantly different between groups (*p<*0.01) except for %TAG.* *No analysis of outcomes independent of weight loss was reported.* *During 4 years of treatment, orlistat plus lifestyle changes significantly decreased the progression to type 2 diabetes compared with placebo plus lifestyle changes (*p=*0.0032). Cumulative incidence rates after 4 years were 6.2 vs 9.0%. The hazard ratio (0.627, 95% CI 0.455 to 0.863) corresponded to a 37.3% decrease in the risk of developing diabetes with orlistat compared with placebo.* Exploratory analyses: In people with IGT at baseline, orlistat plus lifestyle changes significantly decreased the progression to type 2 diabetes when diagnosed on the basis of a single test (*p*=0.0024). Cumulative incidence rates after 4 years were 18.8 vs 28.8%, corresponding to a 45% risk reduction (hazard ratio 0.551). In addition, orlistat plus lifestyle changes significantly decreased the progression to type 2 diabetes when diagnosed by repeat positive testing in this subgroup with IGT (*p*=0.0171). Cumulative incidence rates after 4 years were 8.3% with orlistat vs 14.2% with placebo, corresponding to a 52% risk reduction (hazard ratio 0.482). *In people with NGT at baseline, the progression rate to type 2 diabetes with placebo was very low (2.7% over 4 years) and insufficient to detect a statistically significant difference compared with orlistat (2.6% over 4 years).* *Independent of orlistat or placebo treatment, the relative risk of developing type 2 diabetes was greater in participants with IGT than in those with NGT, in men than in women, in older than in younger individuals, and in individuals with a higher BMI.* *Weight loss was significantly greater with orlistat than placebo in both participants with IGT at baseline (5.7 kg with orlistat vs 3.0 kg with placebo;* p<0*.01) and participants with NGT (5.8 vs 3.0 kg, respectively;* p<*0.001).* *There was no difference in the progression rate from NGT to IGT over 4 years between orlistat- and placebo treated individuals (27.6 vs 30.5%,* p=*0.1521).* *There were statistically significant decreases in the orlistat group compared with the placebo group after 4 years of treatment for all assessed fat-soluble vitamins (vitamin A –0.22 vs 0.19 µmol/l,* p<*0.05; 25-hydroxycholecalciferol –17.2 vs –13.0 nmol/ml,* p<*0.001; vitamin E –2.8 vs 0.4 µmol/l,* p<*0.001; and vitamin* K_1 *–0.08 vs 0.07 µg/l,* p<*0.001), with the exception of 1,25-hydroxycholecalciferol (–15.8 vs –14.0 pmol/ml). However, the mean level of each assessed vitamin remained well within its reference range at all times during the 4-year study for both the orlistat and placebo groups. Decreases were seen early and then were maintained over the treatment period. In people with normal baseline vitamin levels, the proportions with two subsequent, consecutive abnormally low values was similar in the orlistat and placebo groups for vitamin A (5.5 vs 4.4%, respectively) and notably different only for vitamin E (3.2 vs 0.5%, respectively). Proportions for all other vitamin levels were <1% and similar between treatment groups*
Quality and comments	Used % change to calculate absolute changes from baseline. Assumed SDs as for other studies. Could not add 48-month data to analysis as no SDs from other studies at that time point.

Reported harms

Bakris 2002 RCT	
Harms	At least one adverse event was reported by more participants in the orlistat-treated group (89%) than in the placebo group (71%). This difference was due primarily to the greater number of adverse events involving the GI system in the orlistat-treated group compared with the placebo-treated group. GI adverse effects were reported by 72.5% in the orlistat-treated group, compared with 43.6% in the placebo-treated group. The adverse GI effects occurred early during therapy, and their frequency tended to decrease with continued treatment. 15 of 200 (7.5%) of those who developed GI symptoms on orlistat stopped the medication for this reason, vs six of 120 (5.0%) in the control group. In the majority, the symptoms resolved without sequelae despite continued therapy. No deaths occurred during the study. Serious adverse events (necessitating or prolonging hospitalization) were reported in 29 people, of whom 14 were in the orlistat-treated group. In these people with insufficiently controlled hypertension, two in the orlistat group suffered a myocardial infarction, two had chest pain and one had an episode of atrial fibrillation. There were no episodes of uncontrolled BP reported in the orlistat-treated group. In the placebo-treated group, one had accelerated hypertension, one suffered a myocardial infarction, one had a worsening of atherosclerotic coronary artery disease and two had an episode of chest pain. A ductal carcinoma in situ was reported in one placebo-treated participant. One participant in the orlistat group and four in the placebo group withdrew from the study because of a serious adverse event. A reduction in study drug dosage occurred after a serious adverse event in eight orlistat-treated people and in nine receiving placebo.
Quality and comments	…

Derosa 2003 RCT	
Harms	*Only 3.0% of all participants experienced side effects (no details by group). Three people withdrew due to adverse events related to orlistat (two in the orlistat group, and one in the orlistat+fluvastatin group).*
Quality and comments	Less detailed reporting than other studies. Also far less GI events experienced/reported.

Kelley 2002 RCT	
Harms	GI events were the most commonly reported adverse event in both groups and were reported more frequently in the orlistat- (80%) than in the placebo-treated group (62%; $p<0.05$). Most people with GI events reported a single episode, and most GI events in both treatment groups were of mild to moderate intensity. Episodes of hypoglycaemia occurred in a greater proportion of orlistat- than placebo-treated participants (16.9 and 9.7%, respectively, $p<0.05$). In the majority of people, hypoglycaemic symptoms were mild to moderate, with blood glucose levels ranging from 2.2 to 6.9 mmol/l. Only four (one in the placebo and three in the orlistat group) required medical intervention due to hypoglycaemia. The incidence of adverse events related to other organ systems was similar in placebo- and orlistat-treated participants. More orlistat- (13%) than placebo-treated participants (8%) discontinued treatment because of an adverse event, whereas a lower percentage of orlistat- than placebo-treated participants (37 vs 46%) withdrew for other reasons.
Quality and comments	…

Krempf 2003 RCT	
Harms	*Overall proportion of people with at least one adverse event was higher in the orlistat group (86.1 vs 72.3%,* p*<0.001). The percentage of people experiencing GI events was higher again in the orlistat group (63.3 vs 36.3%). These GI events*

	occurred primarily during the first month of treatment and resolved spontaneously. 6.9% of the orlistat group and 3.4% of the placebo group (23 people overall) withdrew because of adverse events. Five events in the orlistat group and four in the placebo group were serious – seven of which were deemed 'doubtfully related' to the treatment. Non-clinically relevant changes in safety parameters occurred at a similar incidence in both groups.
Quality and comments	…

Miles 2002 RCT	
Harms	More people in the placebo group withdrew prematurely from the study than in the orlistat group (44 vs 35%, $p<0.05$). Of these, more orlistat- than placebo-treated participants (10 vs 5%, $p<0.05$) discontinued treatment because of an adverse event. Adverse event profiles were similar in the two treatment groups, with the exception of a higher incidence of GI events associated with orlistat. A total of 83% of people in the orlistat group experienced at least one GI event compared with 62% in the placebo group. More than 75% of those who had GI events reported only a single episode. The majority of GI events were mild, transient, and occurred during the early phase of treatment. Hypoglycaemic episodes occurred in 10% of orlistat-treated people compared with 4% of placebo-treated participants. None required medical intervention for hypoglycaemia, with symptoms reported as mild to moderate in intensity in both groups.
Quality and comments	…

Poston 2003 RCT	
Harms	Only adverse events for the orlistat group were reported. No adverse events were reported by participants that required trial termination. At 6 months, 37 (expected) GI events were reported, and 32 (expected) GI events at 12 months.
Quality and comments	…

Swinburn 2005 RCT	
Harms	One hundred and thirty-five participants (39.8%) reported adverse events before randomisation. The GI system was most frequently involved with 18.3% of these participants reporting adverse events. After randomization, almost all participants in each treatment group experienced at least one adverse event: 94.7% in the orlistat group and 93.5% in the placebo group. Almost all of these were minor with only 9.4% (orlistat) and 7.1% (placebo) experiencing more serious adverse events. The most frequently affected body system for any adverse event was the GI system with 82.4% in the orlistat group (mainly related to fatty/oily stools), compared with that with 60.4% in the placebo group ($p=0.0005$). In general, adverse events were mild to moderate in intensity. For all other events reported in more than ten participants in either treatment group, there were no statistically significant differences between the two treatment groups. There were five participants (2.9%) in the orlistat group and two participants (1.2%) in the placebo group who withdrew because of adverse GI events.
Quality and comments	…

Toplak 2005 RCT	
Harms	The adverse event profile was similar between the treatment groups. The most frequent adverse events in both the groups were GI in nature and were considered related to the pharmacological action of orlistat. Headache (18%) and nasopharyngitis (19%) were the most common non-GI events in both the groups.

	The majority of adverse events were mild or moderate in intensity. Of 19 people reporting serious adverse events, only four were considered treatment-related. In one participant in the 500 kcal/day deficit group, abdominal pain and cholelithiasis were considered possibly related to treatment; pancreatitis (500 kcal/day group, *n*=1), chest pain (*n*=1) and anal fissure (*n*=1) (1000 kcal/day group) were considered remotely related to treatment. Treatment was discontinued due to adverse events in 20 participants (eight in the 500 kcal/day deficit group and 12 in the 1000 kcal/day deficit group). In ten of these, adverse events, in most cases GI, were considered treatment-related. There were no significant changes in vital signs or laboratory parameters in the safety population, which included all participants who received at least one dose of study medication and had at least one safety evaluation taken before and after the treatment.
Quality and comments	…

Torgerson 2004 RCT	
Harms	Orlistat was well tolerated during the study. The overall incidence of adverse events was similar in the two treatment groups, with the exception of a higher incidence of GI events. Most GI events were mild to moderate in intensity and occurred during the early phase of treatment. During the first year of treatment, the proportion of participants experiencing at least one GI event with orlistat or placebo was 91 vs 65%, respectively. This compares with 36 vs 23% for orlistat or placebo, respectively, during the 4th year. Over the 4-year period, a similar proportion of placebo-treated participants had at least one serious adverse event as compared with orlistat-treated participants (13 vs 15%). Similar proportions of serious GI events occurred in the placebo (*n*=32; 2%) and orlistat (*n*=32; 2%) groups. No deaths were attributed to study medication. Overall, 4% of placebo participants and 8% of orlistat participants withdrew from the study because of adverse events or laboratory abnormalities; the difference was primarily due to GI events.
Quality and comments	…

Generalisability

Bakris 2002 RCT	
Country and setting	USA. Referral centres – assumed to be hypertension clinics?
Participants (included/excluded)	Included if BMI between 28 and 43 kg/m^2, were taking at least one antihypertensive medication and had a sitting DBP between 96 and 109 mmHg on two consecutive visits. Antihypertensive medication dose(s) had to be stable for at least 12 weeks preceding study entry. Individuals with easily controlled and stable diabetes were allowed to participate. Excluded if unstable medical and/or psychiatric illness, recent (within 12 weeks before study entry) initiation or change in diuretic therapy, previous GI surgery for weight reduction, and any active GI disorders such as malabsorption syndrome except more than mild lactose intolerance, diarrhoea or constipation, history of bulimia or laxative abuse, substance abuse, including alcohol, and unwillingness or inability to comply with protocol requirements. Pregnant or lactating women, women of childbearing potential not using acceptable contraceptive methods. The use of nicotine replacement therapy, appetite suppressants, fish-oil supplements, oral retinoids, chronic systemic steroids other than sex hormone replacement and gonadotropin releasing hormone was prohibited during the study, as was acute antidepressant or anxiolytic therapy.
Recruitment	No details other than from referral centres.

Randomisation	No details other than participants were randomised.
Intervention (mode and intensity)	*Baseline visit and 11 follow-up visits spread over the 52-week duration of the study*
Duration of active intervention	12 months
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Participants met with the study dietitian at each follow-up visit.
Dropout rates	*42% orlistat, 62% placebo at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	In the final analysis of each group, LOCF for endpoint analysis, irrespective of its actual timing during the study.

Derosa 2003 RCT	
Country and setting	Italy. University (lipids?) clinic
Participants (included/excluded)	Included if aged over 40 years, BMI >30 kg/m^2, had TC ≥6.15 mmol/l, SPB <140 mmHg, DBP <90 mmHg, non-smokers, normal thyroid function. No details of exclusions.
Recruitment	Selected from clinic database.
Randomisation	Weight change in the 4-week lead-in period was used to stratify for randomisation (a measure of weight loss potential).
Intervention (mode and intensity)	*12 months – assessed 3 monthly, met with dietitian 3 monthly*
Duration of active intervention	12 months
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Met with dietitian for counselling and behaviour modification programme (recording food intake) every 3 months.
Dropout rates	*7% orlistat, 0% placebo at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

Kelley 2002 RCT	
Country and setting	USA. (Diabetes care?) centres
Participants (included/excluded)	Included if aged 40–65 years, BMI 28–43 kg/m^2 and a stable weight (<3 kg weight change) for 3 months before study entry, treatment with a stable daily dose (±10%) of insulin for 6 weeks before study entry, and an HbA_{1c} of 7.5–12.0% at screening. Women with childbearing potential were required to have a negative serum pregnancy test at screening and to use an acceptable form of contraception throughout the study. Excluded if diabetes treatment included a thiazolidinedione or if diabetic medications, with the exception of insulin, had changed during the 12 weeks before screening. Other exclusion criteria were medical history or presence of renal, hepatic, or endocrine disorders that could affect the results of the study, previous bariatric surgery, use of approved or experimental weight reduction medications or treatments, presence of malabsorption syndrome, presence of bulimia or laxative abuse, or presence of disorders that could affect compliance with the requirements of the study.
Recruitment	No details reported.
Randomisation	Stratified by %HbA_{1c} levels (≤10%).
Intervention (mode and intensity)	*2 week screening, followed by 52 week intervention – seen at 2–4 weekly intervals*
Duration of active intervention	12 months

Control (mode and intensity)	As above
Delivery of intervention/control (who)	At the baseline visit, participants received diet instructions from a registered dietitian. Also seen at pre-determined (no details) intervals for additional dietary instructions.
Dropout rates	*50% orlistat, 54% control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	All efficacy variables were analysed using the LOCF technique.

Krempf 2003 RCT	
Country and setting	France. Hospital centres.
Participants (included/excluded)	Included if aged 18 to 65 years, BMI ≥28 kg/m^2. Excluded if serious eating disorder, type 1 or type 2 diabetes, pregnant or lactating women, smoking one or more pack of cigarettes per day or intention to stop smoking during the trial, previous surgery for obesity, known or suspected substance abuse, significant thyroid, renal, hepatic, GI or immune disorders, or concomitant use of medication that alter body weight, appetite or the absorption of food.
Recruitment	N/R
Randomisation	N/R
Intervention (mode and intensity)	*18 months – clinic visit every month for assessment.*
Duration of active intervention	18 months
Control (mode and intensity)	As above
Delivery of intervention/control (who)	N/R
Dropout rates	*39% orlistat, 43% placebo at 18 months*
Treatment of dropouts (return to baseline, or last measurement?)	Analysis by observed results only, and by LOCF.

Miles 2002 RCT	
Country and setting	US and Canada. (Diabetes) centres – no details.
Participants (included/excluded)	Included if type 2 diabetes, aged 40–65 years, BMI of 28–43 kg/m^2, maintained stable weight for ≥3 months, HbA_{1c} between 7.5 and 12.0%, and had received metformin treatment at 1000–2550 mg/day for at least 6 weeks. Sulfonylurea therapy in combination with metformin was permitted as long as the sulfonylurea dose was stable for 12 weeks before study entry. Excluded if receiving insulin, thiazolidinediones or alpha-glucosidase inhibitors, any clinical condition that might affect study endpoints, including renal, hepatic, or endocrine disorders, poorly controlled hypertension (SBP ≥160 mmHg or DBP ≥100 mmHg), active GI disease, previous bariatric surgery, a history of bulimia, substance abuse, or the use of any weight loss medications. Women who were pregnant, lactating, or of childbearing potential were also excluded.
Recruitment	N/R
Randomisation	No details reported.
Intervention (mode and intensity)	*Initial screening visit – clinic visits at weeks 0, 2, 4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 52.*
Duration of active intervention	12 months
Control (mode and intensity)	As above

Delivery of intervention/control (who)	N/R
Dropout rates	*35% orlistat, 44% placebo at 12 months*
Treatment of dropouts (return to baseline, or last measurement?)	N/R

Poston 2003 RCT	
Country and setting	USA. No details of setting – community based?
Participants (included/excluded)	Included women of Mexican origin, BMI ≥27 kg/m^2. Women with borderline/definite hypertension with physician's consent. Excluded if serious medical conditions that precluded participation, physician unwilling to consent, not going to reside in Houston area for full 12 months of the study.
Recruitment	N/R
Randomisation	No details reported.
Intervention (mode and intensity)	*Twenty-four weekly classes, six bimonthly, and three monthly maintenance classes (each 60 min) .*
Duration of active intervention	12 months
Control (mode and intensity)	Waiting list control
Delivery of intervention/control (who)	Classes led by a bilingual instructor with training in cognitive behavioural modification. Activity encouraged by an 'instructor', assumed to be as for behavioural modification.
Dropout rates	*43% orlistat, 34% control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	ITT analysis used LOCF. All reported data used actual observed values (not those derived using last observed values), unless specifically noted.

Swinburn 2005 RCT	
Country and setting	Australia and New Zealand. Clinical research centres.
Participants (included/excluded)	Included if aged 40 to 70 years, BMI between 30 and 50 kg/m^2 and one or more of the following concomitant conditions: hypercholesterolaemia: serum TC of >5.5mmol/l and/or LDL-cholesterol of >3.5 mmol/l and clinically stable if on treatment; hypertension: SBP >140 mmHg and/or DBP >90 mmHg and clinically stable if on treatment; type-2 diabetes treated with dietary modification or any oral hypoglycaemic agent for at least 6 months and clinically stable (HbA_{1c} 6.5 to 10%). Excluded if history of significant cardiac, renal, hepatic, GI or endocrine disorders, uncontrolled hypertension, previous GI surgery for weight reduction, history of post-surgical adhesions, smoking, history or presence of substance abuse, bulimia, type-1 diabetes, psychiatric disorders or active GI disease.
Recruitment	N/R
Randomisation	Minimisation algorithm used, but no further details.
Intervention (mode and intensity)	*Clinic visits scheduled for initial screening and beginning and end of 4-week lead-in phase. During the 52-week treatment period, participants were examined fortnightly for the first month, then every month.*
Duration of active intervention	12 months
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Dietitian delivered dietary advice.

Dropout rates	*22% orlistat, 19% control at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Analyses were performed for both the 'observed' data and the data after the LOCF methods.

Toplak 2005 RCT	
Country and setting	Austria, Germany, Belgium, France, Switzerland, Canada, Brazil, Mexico and Australia. Medical departments of university and country hospitals.
Participants (included/excluded)	Included if BMI 30 to 43 kg/m^2, aged 18 to 70 years with a body weight ≥90 kg and WC ≥88 cm (women) or ≥102 cm (men). Excluded if change in body weight 3 kg in the 3 months prior to screening; presence of diabetes mellitus; uncontrolled hypertension; myocardial infarction within 6 months; surgical treatment for obesity; substance abuse; or participation in a weight loss/maintenance programme, diet or weight loss clinical study within the last 6 months. Co-administration of the following medications not allowed during this study: resins for lipid lowering, fish oil supplements, cyclosporin, systemic steroids, appetite suppressants, oral anticoagulants and antiarrhythmics.
Recruitment	N/R
Randomisation	No details.
Intervention (mode and intensity)	*Dietary counselling performed every 2 weeks for the first month, monthly until month 3 and every 3 months thereafter.*
Duration of active intervention	12 months
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Study dietitian evaluated individual's daily food diary (assumed to give dietary counselling?).
Dropout rates	*35% 1000 kcal/day deficit diet, 42% 500 kcal/day deficit diet at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Participants who subsequently withdrew from the study had their last observation carried forward.

Torgerson 2004 RCT	
Country and setting	Sweden. Medical centres.
Participants (included/excluded)	Included if aged 30–60 years, BMI≥30 kg/m^2, non-diabetic glucose tolerance as assessed by a 75-g OGTT performed at baseline using venous whole blood and the 1994 WHO criteria (2-h whole blood glucose <10.0 mmol/l and fasting whole blood glucose <6.7 mmol/l. People with IGT were also eligible for inclusion, and the criteria for IGT were fasting whole blood glucose <6.7 mmol/l and 2-h whole blood glucose 6.7–10.0 mmol/l. Excluded if a change in body weight >2 kg between the screening and baseline examinations and a BP above 165 mmHg systolic or 105 mmHg diastolic on the same two consecutive visits, diabetes mellitus, myocardial infarction within 6 months, symptomatic cholelithiasis, GI surgery for weight reduction or peptic ulcer, active GI disorder or pancreatic disease, malignancy, significant psychiatric or neurological disorder, abuse or previous participation in any trial of orlistat.
Recruitment	Advertisements in daily newspapers.
Randomisation	No details.
Intervention (mode and intensity)	*Dietary counselling every 2 weeks for the first 6 months and monthly thereafter.*
Duration of active intervention	4 years

Control (mode and intensity)	As above
Delivery of intervention/control (who)	N/R
Dropout rates	*10% orlistat, 21% control at 48 months. 48% orlistat, 66% control at 48 months*
Treatment of dropouts (return to baseline, or last measurement?)	LOCF

1.6.2 Sibutramine

Included in HTA (Avenell)

Weight loss

Apfelbaum 1999 (In Avenell HTA)	
Aim	*To determine the efficacy of long-term treatment with sibutramine in maintaining or improving weight loss in obese patients who had lost weight with a VLED.*
Participants	Included patients were aged 18 to 55 years, with a BMI greater than 30 kg/m^2. 160 patients entered the double-blind period, 82 of whom were randomly assigned to sibutramine and 78 to placebo.
Intervention	*Patients were enrolled in a 4±1 week, site-specific VLED (220–800 kcal daily) to provide substantial weight loss before randomisation. Patients who lost at least 6 kg after the VLED and still fulfilled the entry criteria entered the 12 months double-blind treatment phase of the trial. They were randomly assigned in blocks of four to receive either white capsules containing sibutramine (10 mg) or matching placebo capsules, once daily in the morning. The VLED was stopped at entry to the double-blind period. All patients received dietary counselling according to published French guidelines to decrease their total energy intake by 20% to 30% compared with their pre-VLED intake.*
Control	Placebo white capsules given once daily.
Length of follow-up	*4±1 plus 12 months.*

Results	Weight change in the two groups between screening and baseline (randomisation were as follows: 103.4±17.5 kg to 95.7±16.9 for the sibutramine group, and 105.1±20.3 kg to 97.7±19.7 kg for the placebo group. In an ITT analysis, mean (±SD) absolute weight change at 1 year (or study endpoint) was -5.2 (±7.5) kg in the 81 patients in the sibutramine group and +0.5 (±5.7) kg in the 78 patients in the placebo group (p=0.004). Significantly greater weight loss occurred with sibutramine than placebo at each monthly assessment (p<0.05). One month after stopping treatment the two treatment groups were comparable for mean weight gain: sibutramine 1.6 (±1.5) kg, compared with placebo, 1.0 (±2.1) kg. Three months after cessation, the mean weight gain was 4.3 (±3.1) kg in the sibutramine group, compared with 2.3 (±2.9) kg in the placebo group. At the end of the study at least 86% of patients in the sibutramine group had lost at least 5% of their screening body weight, compared with 55% of those in the placebo group (p<0.001). Similarly, 54% of those in the sibutramine group had lost at least 10% of their body weight compared with 23% in the placebo group (p<0.001). 17% of the patients in the sibutramine group had lost 20% or more of their body weight, compared with 3% in the placebo group (p<0.01).

Change from baseline	**Endpoint (end of trial or last observation)**		**Month 12**	
	Sibutramine (n=81)	**Placebo (n=78)**	**Sibutramine (n=54)**	**Placebo (n=45)**
Weight loss	74%*	38%	74%†	**40%**
No change	0%	3%	0%	**2%**
Weight gain	**26%**	**59%**	**26%**	**58%**

*p<0.0001
†p<0.001

Quality and comments	*RCT. No details of randomisation or blinding were given. Adequate concealment method.*
Sponsor details	*Study medication provided by Knoll Pharmaceuticals.*

McMahon 2000 (in Avenell HTA)	
Aim	*To investigate the effects of sibutramine 20 mg once daily or placebo on body weight in obese hypertensive patients* (hypertension well controlled)
Participants	224 obese (BMI 27–40 kg/m^2), hypertensive patients. Hypertension was well controlled with a calcium channel blocker, with or without concomitant thiazide diuretic therapy *Mean (SD) age 52.3 (10.0) years sibutramine (*n=*150), 52.9 (8.7) years placebo (*n=*74). Mean (SD) BMI 34.5 (3.4) kg/m^2 sibutramine, 34.0 (4.0) kg/m^2 placebo.*
Intervention	*Initial screening phase, a 2 to 10 week placebo run-in period,* *Patients were randomised to a 2:1 ration to either sibutramine or placebo treatment taken once daily. During the initial 6 weeks, patients given sibutramine had their doses increased from 5 mg to 20 mg per day in 5 mg increments every 2 weeks.* *37% of the patients in the sibutramine group were on concomitant diuretics, compared with 38% in the placebo group.* *Patients received brief general dietary counselling regarding weight reduction at the initial run-in visit only.*
Control	Placebo with dietary counselling as above.
Length of follow-up	*52 weeks continuous treatment.*

Results	For patients receiving sibutramine, weight loss occurred during the first 6 months of treatment and was maintained to the end of the 12-month treatment period. The mean change in body weight among patients receiving sibutramine at week 52 was –4.4 kg, corresponding to a 4.7% decrease. This was significantly different from that of patients receiving placebo (–0.5 kg; *p<0.*05). Patients receiving sibutramine also had significantly greater decreases in BMI, waist and hip circumferences, and waist-hip ratio compared with patients receiving placebo (*p*<0.05). Mean percentage change in body weight among African American patients receiving sibutramine (–4.0%) was comparable with that for white patients (–4.9%). Of those patients receiving sibutramine, 40.1% lost 5% or more of body weight (5% responders) and 13.4% lost 10% or more of body weight (10% responders) vs 8.7% and 4.3%, respectively, of patients receiving placebo (*p*<0.05).
Quality and comments	Randomised, placebo-controlled, parallel-group comparison. No details of randomisation, or concealment method provided. ITT done – LOTF. *SD values used as in HTA.*
Sponsor details	*Knoll pharmaceuticals*

Smith 2001 (In Avenell HTA)	
Aim	*To assess the long-term weight reduction efficacy, tolerability, and safety of sibutramine used once daily in conjunction with behaviour modification to treat mild to moderate obesity.*
Participants	Individuals aged 18 to 65 years old, who were mildly to moderately obese (BMI 27 to 40 kg/m^2).
Intervention	*Participants were given standardised dietary advice and advice sheets to be followed throughout the study. They were advised to include a variety of vegetables and fresh fruit, bread, cereal, potatoes or rice; and they were told to substitute low-energy foods such as fresh fruits and baked potatoes for sugary and fried foods such chocolate and biscuits.* *Eligible patients then entered a 2-week single-blind placebo run-in period. At the ed of this run-in period, those who still met the criteria entered a 12-month double-blind treatment phase. Entry was restricted to those able to follow dietary advice as determined by the investigator. Patients were randomised to once daily treatment with placebo or sibutramine 10 mg or 15 mg dispensed in identical capsules, which were pre-packaged and coded by the sponsor according to a computer-generated randomisation list.*
Control	Placebo once daily and dietary advice for 12 months
Length of follow-up	*12 months*
Results	Of 510 who entered the run-in period, 485 continued for the double-blind period. No weight loss figures were reported after the run-in period. Mean weight change (95% CI) after 12 months of treatment was as follows: –1.6 (–2.3 to–0.9) kg for the placebo group; –4.4 (–5.4 to –3.4) kg for the 10 mg sibutramine group; and –6.41(–7.4 to –5.3) kg for the 15 mg sibutramine group. (Overall level of significance for comparison of treatment groups: 10 mg sibutramine vs placebo, *p*=0.04; 15 mg sibutramine vs placebo *p*<0.001; 10 mg vs 15 mg sibutramine *p*>0.05). The percentage of participants that lost ≥ 5% baseline weight was as follows: 32 (20) for the placebo group; 60 (39) (*p*<0.001) for the 10 mg sibutramine group; and 87 (57) (*p*<0.001) for the 15 mg sibutramine group. The percentage of participants that lost ≥10% baseline weight was as follows: 11 (7) for the placebo group; 30 (19) (*p*<0.01) for the 10 mg sibutramine group; and 52 (34) (*p*<0.001) for the 15 mg sibutramine group.
Quality and comments	*Double-blind randomised trial. No details of blinding. Adequate randomisation and concealment process. High dropout rate.*
Sponsor details	*Knoll Laboratories*

STORM James 2000 (In Avenell HTA as STORM) (also Hansen 2001 and Van Baak 2003)	
Aim	*To determine the effect of sibutramine in weight maintenance after weight loss.*
Participants	Sex: 390 women, 77 men Age: mean (SD) 40.6 (10.1) Mean (SD) weight: 102.6 kg (15.5) BMI (kg/m^2): mean (SD) 36.6 (4.1) Baseline comparability: yes
Intervention	Description of intervention: a + b: 6-month open pre-treatment weight reduction phase consisting of 10 mg sibutramine daily plus 600 kcal/day deficit plus 30 min daily extra walking plus advice on behaviour modification a: 10 mg sibutramine daily b: placebo daily a + b: sibutramine (or placebo) increased to 15 mg if more than 1 kg weight regain occurred after pre-treatment phase or since last dose increase providing dose stable for minimum of 2 months, if further weight increases dose increased to maximum 20 mg daily, dose reduced by 5 mg each time if patient could not tolerate higher dose, activity and behavioural advice, 600 kcal/day deficit (EE=resting metabolic rate × physical activity level) consisting of 45–50% energy as carbohydrate, 30% as fat, 15–20% as protein Provided more than 5% weight loss with less than a 2 kg weight gain form months 4 to 6 was achieved, participants were then randomly assigned at 6 months, on a 3/1 basis to sibutramine or placebo.
Control	Placebo for 18 months. The taste of the capsule was identical provided they were swallowed whole.
Length of follow-up	*Initial 6 months and then for a further 18 months*
Results	Allocated: a: 352 b: 115 Completed: a: 206 b: 57 *At the weight maintenance baseline (after the 6 months of the weight loss period) the sibutramine group had a mean weight (SD) of 102.3 kg (15.0) and the placebo a mean weight of 102.1 (16.1) kg. At 24 months the mean weight change from baseline (SD) was –8.9 (8.1) kg in the sibutramine group and –4.9 (5.9) kg in the placebo group.* *Of those who entered the weight-maintenance phase on sibutramine, 69% maintained at least 5% weight loss 18 months later, 46% maintained at least 10% weight loss and 27% maintained full initial weight loss.*
Quality and comments	Randomisation: 3:1, computer generated list maintained centrally. Allocation concealment: A Assessor blinding: no details given
Sponsor details	*BASF Pharma*

Wadden 2001 (In Avenell HTA)	
Aim	*To assess the benefits of adding lifestyle modification to the pharmacological treatment of obesity.*
Participants	53 women with 47.2±9.8 years; weight 101.3±9.7 kg; height 164.1±6.0 cm; and BMI 37.7±3.6 kg/m^2.

Intervention	*Fifty-five women were assigned to one of three treatment groups:* *(1) (*n=*19) drug-alone: balanced diet of 1200–1500 kcal/day with approximately 15% of the energy as protein, 30% as fat, and 55% as carbohydrate. 10 mg/day of sibutramine was given at week 0, which was increased to 15 mg/day at week 8.* *(2) (*n=*17) drug-plus-lifestyle modification: lifestyle modification session (during the first 20 weeks. 10 mg/day of sibutramine were given at week 0, which was increased to 15mg/day at week 8.* *(3) (*n=*17) drug-plus-lifestyle with a portion-controlled diet: same treatment as those in the drug plus lifestyle and additionally for the first 16 weeks, and they were given a 1000 kcal/day portion-controlled diet. At week 17, participants gradually decreased their consumption of liquid supplement, so that at week 20 they were prescribed a 1200–1500 kcal/day diet of conventional foods.*
Control	Three treatment groups
Length of follow-up	*12 months*
Results	At month 12, patients treated with the drug alone lost (mean±SD) 4.1±6.3% of their initial body weight compared with significantly (*p*<0.05) larger losses in the drug-plus-lifestyle group of 10.8±10.3% and the combined treatment group of 16.5±8.0%. Women in the two lifestyle groups achieved a significantly (*p*<0.05) greater percentage of their expected weight loss than those in the drug-alone group.
Quality and comments	*No details on randomisation were given. No concealment or blinding methods applied.* *Values of other outcomes were not given by groups at 52 weeks, as the only one group data was reported.*
Sponsor details	*Novartis Nutrition for OPTIFAST, and Knoll Pharmaceutical CO for providing sibutramine.*

Other outcomes

Apfelbaum 1999 (In Avenell HTA)	
Results	*TAG levels were reduced and HDL-cholesterol levels were increased in the sibutramine group compared with the placebo group at 12 months (*p<*0.05). LDL-cholesterol levels increased in both groups from the levels at baseline.* *There were no statistically significant changes between treatment groups in SBP.*
Quality and comments	…

McMahon 2000 (in Avenell HTA)	
Results	*Treatment with sibutramine was associated with significant improvements in metabolic parameters compared with placebo at week 52, including serum levels of TAG, HDL-cholesterol, glucose and uric acid. Treatment with sibutramine was associated with significant improvement in several scales of the Impact of Weight on Quality of Life questionnaire compared with placebo (results not shown). At week 28 of treatment, all patients receiving sibutramine had significant improvement in mean scores for Mobility and Activities of Daily Living (*p<*0.05 vs all patients receiving placebo), and sibutramine 5% and 10% responders showed improvement in mean scores for Health, Mobility, and Activities of Daily Living (*p<*0.05 vs all patients receiving placebo). At week 52, sibutramine 5% and 10% responders demonstrated significant improvement in mean scores for Health and Activities of Daily Living; sibutramine 5% responders also showed significant improvement in mean score for Mobility (*p<*0.05 vs all patients receiving placebo).* Treatment with sibutramine was associated with a small numerical mean increase in SBP that was not statistically significantly different from that in the placebo group. The mean change in DBP (2.0 mmHg) for patients receiving sibutramine was significantly greater than that for patients receiving placebo (–1.3 mmHg; *p*<0.05).

	The proportion of patients receiving sibutramine who experienced a potentially clinically significant increase from baseline in SBP or DBP (>10 mmHg at three consecutive visits) was comparable with that among patients receiving placebo The incidence of these changes in SBP or DBP was similar among African Americans and whites. The proportion of patients experiencing an increase from baseline in pulse rate greater than ten per min for three consecutive visits was greater for patients receiving sibutramine than for patients receiving placebo.
Quality and comments	…

Smith 2001 (In Avenell HTA)	
Results	*There were statistically significant changes in triglycerides compared with placebo (+3.2%) at month 6 for the sibutramine 10 and 15 mg treatment groups (–10.8%,* p*<0.05 and –10.0%,* p*<0.01, respectively).* *There were no statistically or clinically significant differences between the treatment groups for change in either the Beck Depression Inventory of the State Anxiety Inventory.* *Differences in mean changes in BP were not statistically significant between the sibutramine and placebo groups, except for a mean increase in DBP in the sibutramine 10 mg treatment group.*
Quality and comments	…

STORM James 2000 (In Avenell HTA) (also Hansen 2001 and Van Baak 2003)	
Results	*There were decreases in levels of serum TAG, VLDL-cholesterol, insulin C-peptide, and uric acid, but not in levels of LDL-cholesterol, which were maintained for up to 2 years and were proportional to weight loss. On the other hand, HDL-cholesterol levels (baseline levels: 1.24±0.38 mmol/l for sibutramine and 1.24±0.35 mmol/l for the placebo group) increased significantly after month 6 (1.41±0.35 in the sibutramine group and 1.35±0.36 for the placebo group) and at month 24 the values were 1.48±0.38 for the sibutramine and 1.35±0.38 for the placebo group (*p*<0.001).*
Quality and comments	…

Wadden 2001 (In Avenell HTA)	
Results	*Women in the two lifestyle groups were significantly more satisfied with the medication and with changes in weight, health, appearance, and self-esteem (*p*<0.05 for all). Women in the two lifestyle groups were significantly (*p*<0.05) more satisfied with sibutramine at months 6 and 12 than were patients treated with sibutramine alone.* *Significant reductions were observed at 12 months in TAG and LDL-cholesterol levels but systolic and DBP both increased significantly (*p*<0.05 for all).* *Increases in BP in the 13 of the 43 patients who had baseline BPs of ≥130 mmHg and/or ≥85 mmHg were of the same magnitude as those in the normotensive patients.*
Quality and comments	…

Reported harms

Apfelbaum 1999 (In Avenell HTA)	
Results	*Adverse events were reported by 96.6% of participants in the sibutramine group and 87.8% in the placebo group. Headache was the most frequent adverse event: 28.1% in the sibutramine group and 23.0% in the placebo group. Also 20.5% of*

	participants in the sibutramine group reported dry mouth, compared with 0% in the placebo group. The majority of the events were mild to moderate severity. 6.2% reported serious adverse events in the sibutramine group (potentially two being caused by treatment) and 6.8% in the placebo group. *Pulse rate increased significantly in the sibutramine group, compared with the placebo group at all time points (*p*<0.05).*
Quality and comments	…

McMahon 2000 (in Avenell HTA)	
Results	*Most adverse events reported for patients receiving sibutramine or placebo were mild to moderate in severity and transient. The most commonly reported adverse events (occurring in 10% of patients in either treatment group) are shown in Table 5. With the exception of dry mouth and constipation, incidence rates of these adverse events were similar in patients receiving sibutramine and placebo. Of patients receiving sibutramine, 20.0% (*n*=30) were discontinued from the study owing to an adverse event compared with 10.8% (*n*=8) receiving placebo (Table 5). The most common adverse event resulting in discontinuation was hypertension, reported for 5.3% (*n*=8) of patients receiving sibutramine and 1.4% (*n*=1) of patients receiving placebo. Four of the patients receiving sibutramine who were discontinued from the study owing to hypertension met the protocol-mandated criteria for discontinuation (mean increase from baseline in DBP >15 mmHg or DBP >100 mmHg at a single visit); the other four patients were discontinued from the study at an investigator's discretion. Only two patients had a DBP >100 mmHg, and none had a DBP >110 mmHg. Overall, discontinuation rates were comparable between sibutramine and placebo (Table 5).*
Quality and comments	…

Smith 2001 (In Avenell HTA)	
Results	Dry mouth occurred significantly more frequently with 10 mg (19 patients) or 15 mg (21 patients) sibutramine than with placebo (two patients; $p<0.001$). Eight serious adverse events led to early withdrawal during the double-blind phase of the study (two in each sibutramine groups and four in the placebo group).
Quality and comments	…

STORM James 2000 (In Avenell HTA) (also Hansen 2001 and Van Baak 2003)	
Results	*Eighteen patients were withdrawn because of increases in BP. The mean BP increase over 2 years was 1.4 (SD 9.3) mmHg; SBP increased by 0.1 (12.9) mmHg; DBP by 2.3 (9.4) mmHg.*
Quality and comments	…

Wadden 2001 (In Avenell HTA)	
Results	*Eight women took reduced doses of sibutramine hydrochloride because of increased BP or pulse rate, and doses were reduced in two other women because of disturbed sleep and in a third women because of reports of severe heartburn.*
Quality and comments	…

Generalisability

Apfelbaum 1999 (In Avenell HTA)	
Country and setting	France. Hospital research centre
Participants (included/excluded)	Included patients were aged 18 to 55 years, with a BMI >30 kg/m^2. Exclusion criteria encompassed the following parameters: obesity of endocrine origin, patients with type 2 diabetes mellitus who were receiving insulin or who were poorly controlled, patients with a supine DBP >100 mmHg. Also patients with medical illness, electrocardiographic or laboratory abnormalities, and patients who had unsuccessfully followed a VLED in the previous 6 months. Patients could not be more than borderline depressed on the clinical global impression scale, and were also not allowed to take any other therapies that might alter body weight or interfere with the study medication.
Recruitment	From 12 medical centres in France that had a special interest in obesity or endocrinology.
Intervention (mode and intensity)	*At baseline and every 3 months for 1 year, each participant met with a dietitian. The patients' subjective assessment of ease in complying with the dietary advice was assessed using a visual analogue scale ('easy to follow diet' to 'unable to follow diet').*
Duration of active intervention	4±1 weeks followed by 12 months double-blind.
Control (mode and intensity)	Patients were enrolled in a 4±1 week, site-specific, VLED (220–800 kcal daily) to provide substantial weight loss before randomisation. Patients who lost at least 6 kg after the VLED and still fulfilled the entry criteria entered the 12 months double-blind treatment phase of the trial. Controls received white capsules (matching sibutramine) placebo capsules, once daily in the morning.
Delivery of intervention/control (who)	Only dietitian is mentioned for the assessment of compliance with the dietary advice.
Dropout rates	32%
Treatment of dropouts (return to baseline, or last measurement?)	ITT analysis was performed with the LOCF.

McMahon 2000 (in Avenell HTA)	
Country and setting	USA. Clinical research centre

Participants (included/excluded)	Inclusion criteria consisted of patients ≥18 years of age with a BMI between 27 and 40 kg/m^2, a diagnosis of hypertension for at least 12 months before screening, and adequate medical control of hypertension. Hypertension was to be controlled using a constant dose of a calcium channel blocker (amlodipine besylate, diltiazem hydrochloride, felodipine, etc.) for at least 60 days immediately preceding the screening visit and during the run-in period. Use of a single thiazide diuretic in addition to a calcium channel blocker for hypertension was allowed, provided that the dose of the thiazide diuretic was stable during the same period. Adequate control was defined as having a mean DBP of 95 mmHg or less during the run-in period; variations in mean DBP measured at three consecutive run-in visits and variations in individual measurements during each of these qualifying run-in visits had to be within 10 mmHg. Concomitant therapy with a single antilipidaemic agent, diuretic, or -adrenergic receptor antagonist was allowed, provided that the dose was stable for at least 60 days preceding screening. Female patients who were at least 2 years postmenopausal, had undergone surgical sterilisation, or were using adequate contraceptive measures were enrolled. All patients had to provide written informed consent and had to demonstrate compliance (by pill count) of at least 75% during the placebo run-in period. Patients were excluded if they had an elevated BP secondary to a concurrent medical condition (other than obesity), a pulse rate greater than 95 per min at baseline, or DBP greater than 95 mmHg at any run-in visit. Other exclusion criteria were a history of significant cardiac disease, endocrine abnormalities, impairment of a major organ system, convulsions, severe cerebral trauma or stroke, hypersensitivity to two or more classes of drugs, adverse reactions to central nervous system stimulants, and substance abuse within 2 years before screening. In addition, gastric surgery to reduce weight or participation in a formal weight-loss programme within 3 months before screening, previous administration of sibutramine at any time or use of another investigational drug within 30 days before this study, and concomitant therapy with other weight-loss products were reasons for exclusion. Patients were discontinued from the study if they had an increase from baseline in DBP >15 mmHg, an absolute DBP >100 mmHg, or a pulse rate of ≥105 per min at any visit.
Recruitment	Not stated.
Intervention (mode and intensity)	Clinic visits occurred every 2 weeks during the placebo run-in period and during the first 8 weeks following randomisation and then every 4 weeks during the remainder of the treatment period.
Duration of active intervention	52 weeks
Control (mode and intensity)	As above
Delivery of intervention/control (who)	Not clear
Dropout rates	47% in the sibutramine group and 45% in the placebo group.
Treatment of dropouts (return to baseline, or last measurement?)	LOCF

Smith 2001 (In Avenell HTA)	
Country and setting	UK. Primary care setting.

Participants (included/excluded)	Individuals who had not lost more than 3 kg of weight during the previous 3 months, whose obesity was not of endocrine origin, and who did not have diabetes mellitus. They had to have a seated pulse rate of 100 beats per min or lower and a seated DBP of ≤100 mmHg. Hypertensive patients were included only if the condition had been stabilised with medication for 6 months. Individuals receiving laxatives, anorectic agents, diuretics, bulking agents, antidepressants or any other medication that could alter body weight were excluded.
Recruitment	Patients identified by primary care physicians.
Intervention (mode and intensity)	
Duration of active intervention	12 months
Control (mode and intensity)	Placebo once daily for 12 months.
Delivery of intervention/control (who)	The investigator delivered dietary advice and compliance with the advice, and recorded patients' weight at each visit.
Dropout rates	Placebo (51%), sibutramine 10 mg (49%) and sibutramine 15 mg (42%)
Treatment of dropouts (return to baseline, or last measurement?)	All efficacy analyses used the LOCF.

STORM James 2000 (In Avenell HTA) (also Hansen 2001 and Van Baak 2003)	
Country and setting	Eight European specialist centres.
Participants (included/excluded)	Inclusion criteria: either sex, 17–65 years, BMI 30–45 kg/m^2, lost ≥5% initial weight in 6 month open weight reduction phase with <2 kg weight gain between months 4 and 5 or months 5 and 6; women of childbearing potential if using adequate contraception, hypertensive patients stabilised on therapy. Exclusion criteria: endocrine related obesity, recent weight changes (loss or gain >4 kg in past 3 months, specified disease e.g. myxoedema (hypothyroidism); Cushing's syndrome; diabetes mellitus; significant neurological or psychological illness such as epilepsy, schizophrenia or depression; or eating disorder such as bulimia, severe somatic disease, hepatic or renal dysfunction; a history of heart failure, ischemic heart disease, stroke, transient ischemic attacks or unstable hypertension (persistent DBP >95 mmHg or pulse rate >100 beats per min); those with significant abnormalities on ECG; patients on such drugs as anorectics, oral beta-blockers, agonists such as those used for treating asthma, steroids, thyroid preparations, or diuretics for non-hypertensive purposes
Recruitment	From local health centres and screened medically for their suitability for the trial.
Intervention (mode and intensity)	a + b: 6-month open pre-treatment weight reduction phase consisting of 10 mg sibutramine daily plus 600 kcal/day deficit plus 30 min daily extra walking plus advice on behaviour modification a: 10 mg sibutramine daily b: placebo daily *a + b: sibutramine (or placebo) increased to 15 mg if more than 1 kg weight regain occurred after pre-treatment phase or since last dose increase providing dose stable for minimum of 2 months, if further weight increases dose increased to maximum 20 mg daily, dose reduced by 5 mg each time if patient could not tolerate higher dose, activity and behavioural advice, 600 kcal/day deficit (EE=resting metabolic rate × physical activity level) consisting of 45–50% energy as carbohydrate, 30% as fat, 15–20% as protein.*
Duration of active intervention	6 months plus 18 months

Control (mode and intensity)	As seen above
Delivery of intervention/control (who)	Dietitian and physician
Dropout rates	*Dropouts: a: 59% b: 50%*
Treatment of dropouts (return to baseline, or last measurement?)	*ITT: yes for weight outcome only*

Wadden 2001 (In Avenell HTA)	
Country and setting	USA. University research clinic
Participants (included/excluded)	Women who had a BMI of 30 to 45 kg/m^2 and who were free of physical contraindications including types 1 or 2 diabetes mellitus; uncontrolled hypertension; a history of cerebrovascular, cardiovascular, kidney or liver disease; the use of medications known to affect body weight; pregnancy or lactation; a weight loss of ≥5 kg and/or the use of anorectic agents in the previous 6 months; and the use of selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, or other medications contraindicated with the use of sibutramine. Additionally, contraindications were as follows: current psychotherapy; bulimia nervosa; major depression; as suggested by a score higher than 25 on the Beck Depression inventory; or other psychiatric illness that significantly disrupted daily functioning.
Recruitment	Selected from more than 300 respondents to advertisements in local newspapers.
Intervention (mode and intensity)	*The drug-alone group met with a physician. They were instructed to consume a balanced diet of 1200–1500 kcal/day with approximately 15% of energy from protein, 30% from fat and 55% from carbohydrate. They were also encouraged to gradually increase their exercise to four to five sessions per week for 30 to 40 min per session. 10 mg/day of sibutramine were given at week 0, which was increased to 15 mg/day at week 8.* *The drug-plus-lifestyle group had sibutramine delivered and had physician visits as scheduled with the drug alone group and also a weekly group lifestyle modification session (during the first 20 weeks) conducted by doctoral-level psychologists Traditional behavioural topics including stimulus control, slowing the rate of eating, social support, and cognitive restructuring were delivered.* *The combined treatment group received the same treatment as those in the drug plus lifestyle and additionally for the first 16 weeks, and they were given a 1000 kcal/day portion-controlled diet. At week 17, participants gradually decreased their consumption of liquid supplement, so that at week 20 they were prescribed a 1200–1500 kcal/day diet of conventional foods, similar to the patients in the other two conditions.*
Duration of active intervention	12 months
Control (mode and intensity)	Three treatment groups
Delivery of intervention/control (who)	Physician and doctoral level psychologists.
Dropout rates	31.6% dropped out in the drug alone group, as 23.5% in the drug-plus-lifestyle group
Treatment of dropouts (return to baseline, or last measurement?)	LOCF was used, in which patient's body weight at the time of attrition was included at the 6- and 12-month assessments. A more conservative ITT analysis was also conducted in which participants who discontinued treatment were assumed to gain 0.3 kg/month after leaving the study.

Additional studies (not in HTA Avenell, or in 'O'Meara as 'company submission')

Weight loss

Hainer 2005	
Aim	*To reveal whether baseline BMI, and psychobehavioural and nutritional markers, were significant predictors of the change in BMI observed after 4 and 12 months in obese women enrolled in a weight reduction programme, including LED, increased physical activity, cognitive behaviour therapy and sibutramine. The impact of changes in psychobehavioural and nutritional markers observed after 4 and 12 months of treatment on BMI changes was also investigated.*
Participants	Eighty eligible participants with a mean age of 43.9±10.6 years and a mean BMI of 36.7±4.8 kg/m^2.
Intervention	*All patients were given a 5–6 MJ/day diet, with approximately 50–60% of energy from carbohydrate, 15–20% from protein and 25–30% from fat. They were advised to distribute their daily intake over four to five meals.* *All patients, regardless of their baseline physical activity level, were instructed to increase their routine daily physical activity. A 30 min walking, 5 days/week, was recommended as a minimum increase in daily physical activity* *Drug: after the double-blind, placebo controlled 4-month phase, participants received either sibutramine (10 mg/day) or placebo. Subsequently, an open phase continued until month 12, in which sibutramine was administered to all participants.*
Control	Placebo
Length of follow-up	*12 months*
Results	n=*38 in sibutramine group and* n=*42 in placebo group.* *Weight loss (SD) in the sibutramine group was significantly higher than in the placebo group: 9.0 (8.4) vs 4.9 (7.3) kg (*p<*0.001). At month 12, a significant (*p<*0.001) body weight loss vs baseline values was shown in both groups. Significant decreases in BMI and WC were also registered, although results not shown.* *No values for 5% and 10% responders were reported.*
Quality and comments	*Randomised, double-blind, placebo controlled trial. No details on randomisation, concealment method or blinding were provided.* *HTA formula used to calculate SD values.* *No values for other outcomes were reported, thus not added in meta-analysis.*
Sponsor details	*Study grants COST and IGA.*

Hauner 2004	
Aim	To evaluate, in a primary care setting, the effect of a standardised non-pharmacological treatment programme and 15 mg sibutramine or placebo on long-term weight reduction in obese participants with a BMI ≥30 and <40 kg/m^2.
Participants	The ITT population consisted of 348 participants. The mean age of the ITT population was 42.7±11.7 years and the mean height 168.3±9.1 cm. The overall mean weight was 100.5±14.8 kg and the mean BMI 35.4±3.4 kg/m^2. Weight, age, height, BMI, WC and WHR at baseline were comparable for each treatment group, and there were less males in the sibutramine than in the placebo group (21.8 vs 29.3%, *p*<0.05).

Intervention	*Educational sessions: standardised information on the treatment programme including food choice, physical activity, motivational issues and behaviour modification.* *Diet: dietary counselling based on WHO formula for energy intake. Recommendations to achieve an energy deficit of at least 500 kcal, although not greater than 1000 kcal/day.* *Physical activity: to excess energy expenditure (exceeding 1000 kcal/week) by additional physical activity, such as low to moderate brisk walking, three to five times per week, for 30 min.* *Drug: 15 mg sibutramine once daily*
Control	*Placebo*
Length of follow-up	*54 weeks continuous therapy*
Results	n=*174 in the sibutramine and* n=*174 in the placebo group.* *Mean weight change (SD) was –8.1 kg (7.74) in participants under sibutramine treatment, and –5.1 (SD 6.73) kg in participants under placebo.* *Statistically significant more participants in the sibutramine group lost more than 5% and more than 10% of their baseline weight. In the active treatment group 62.6% of the participants experienced a 5% weight loss response against 41.4% in the placebo group (*p<*0.001) and 40.8% had a greater than 10% weight loss response compared with 10.0% of the patients receiving placebo (*p<*0.001).*
Quality and comments	*Randomised, double-blind, placebo-controlled trial. Details of randomisation and concealment not given. ITT analysis performed.* *SD values calculated from 95% CI*
Sponsor details	*Knoll Deutschland GmbH*

Kaukua 2004 (In O'Meara as Rissanen 1998)	
Aim	To evaluate the effects of 12-month treatment with sibutramine 15 mg daily compared with placebo on health-related quality of life (HRQL) in obese type II diabetes patients.
Participants	Obese (BMI ≥28 kg/m^2) type 2 diabetes patients (1985) aged 25–70 years
Intervention	The partcipants were enrolled in a 2-week single-blind run-in period with a modestly hypoenergetic diet (700 kcal daily deficit) and then randomised to receive either sibutramine 15 mg (*n*=114, 60% female) or placebo (*n*=122, 58% female) once daily with the hypoenergetic diet for 12 months.
Control	Placebo once daily with a 700 kcal hypoenergetic diet for 12 months.
Length of follow-up	*12 months*
Results	*No results for weight loss in run-in phase were given.* The mean weight change was greater in the sibutramine group (–7.1 kg) than in the placebo group (–2.6 kg, *p*<0.001).
Quality and comments	*No details of randomisation were given. Single-blinded in run-in phase then double blinded for rest of the trial. No details given. No concealment was reported.* *Values for other outcomes such as glycaemic control and haemodynamic variables did not provide SD, SEM or 95% CI, and for this reason were not included in meta-analysis.*
Sponsor details	*Knoll Laboratories*

McMahon 2002	
Aim	*To investigate the effects of sibutramine 20 mg once daily or placebo on body weight in obese hypertensive patients.*
Participants	220 obese (BMI 27–40 kg/m^2), hypertensive patients. Hypertension was well controlled with an ACE inhibitor, with or without concomitant thiazide diuretic therapy

Intervention	*Initial screening phase, a 2–10 week placebo run-in period,* *Patients were randomised to a 2:1 ratio to either sibutramine or placebo treatment taken once daily with 4oz (113 g) of water. During the initial 8 weeks, patients given sibutramine had their doses increased from 5 to 20 mg per day in 5 mg increments every 2 weeks. Treatment of hypertension continued for the 52 weeks of the study.* *48.5% of the patients in the sibutramine group were on concomitant diuretics, compared with 55.4% in the placebo group.* *All participants were given general dietary advice regarding weight reduction* *After week 52, patients attended a follow-up visit within 10–14 days; those who were withdrawn early attended a follow-up visit within 10–14 days after their last study visit.*
Control	Placebo group under general dietary advice regarding weight reduction and 55.4% were under concomitant diuretics.
Length of follow-up	*52 weeks continuous treatment. 10–14 days after treatment follow-up.*
for the un-in phase. *n*=146 to the sibutramine group a d *n*=74 to the placebo group. The silbtramine group had signifi antly (*p*≥0.05) greater significantly (*p*≥0.05) greater decreases from baseline in weight-related variables at week 52 compared with the placebo group. In the ITT analysis, patients treated with sibutramine lost a mean (SD) of 4.5 (7.19) kg of their body weight, compared with a mean of 0.4 (6.03) kg in patients treated with placebo (*p*≤0.05). Patients in the sibutramine group had a significantly larger mean reduction (5.3 cm) in WC, compared with patients treated with placebo (1.3 cm). The treatment differences in weight loss were statistically significant (*p*≤0.001) at all visits from week 4 onwards. *When compared with the placebo group, the sibutramine group had significantly higher percentages of 5% responders (42.8 vs 8.3%, respectively, LOCF) and 10% responders (13.1 vs 2.8%, respectively, LOCF) (p≤0.05).*	
Quality and comments	Randomised, placebo-controlled, parallel-group comparison. Although in study design it is mentioned that study is double-blinded, in the treatment schedule only single-blinded is mentioned. Trial. No details of randomisation, or concealment method provided. *SD values used as in HTA.*
Sponsor details	*Abbott Laboratories*

McNulty 2003 (In O'Meara as Williams)	
Aim	To evaluate the effects of sibutramine (15 and 20 mg/day) on weight, metabolic control, and BP in metformin-treated obese participants with type 2 diabetes.
Participants	Participants comprised 85 men (44%) and 109 women (56%) aged 27–69 years. There were no significant differences between centres in sex distribution, age, diabetes duration, or the dosage (mean 1250 mg/day) or duration of metformin treatment. At entry, 70 participants (36%) were hypertensive according to WHO criteria, and 56 (29%) were taking anti-hypertensive treatment, with 17 (9%) receiving lipid-lowering drugs
Intervention	Patients were given each centre's standard dietary advice by a dietitian and/or specialist nurse and returned within 4 weeks for random allocation to 15 or 20 mg/day sibutramine or placebo. For tolerability reasons, patients in the 20 mg sibutramine group took 15 mg sibutramine daily for the first 2 weeks. Patients were reviewed every 4 weeks, when dietetic advice was reinforced, medication compliance checked by capsule count, and adverse events and medication changes recorded. Glycaemic control was monitored 3-monthly by fasting glucose and HbA_{1c}. Metformin dosage was adjusted if necessary, but other antidiabetic drugs were not used.
Control	Placebo once daily for 12 months
Length of follow-up	*12 months*
Results	Sixty-eight patients were assigned to 15 mg/day sibutramine, 62 to 20 mg/day sibutramine, and 64 to placebo. Placebo-treated patients showed no weight change at any time; 88% of participants (56 of 63) either gained weight or lost <5%, whereas only 12% lost ≥5%, and none lost ≥10%. With 15 mg/day sibutramine, average weight fell over 6 months to 5.3 kg (about 6%) below baseline and was then maintained throughout treatment. The 20 mg dose caused greater weight loss, averaging 8 kg (about 8%) below baseline from 8 months to the end of treatment. Significantly more sibutramine-treated participants lost ≥5% weight (46 and 65% with 15 and 20 mg, respectively), whereas 14% of participants receiving 15 mg/day and 27% of participants taking 20 mg lost ≥10%
Quality and comments	*Double-blind RCT. No details of randomisation, blinding or concealment were given. Authors state that the dropout rate is unlikely to have influenced the outcome.* *SD values calculated with HTA formula (weight).* *SD values used from other HTA studies, except for HDL-cholesterol, as SD values quite different from trial to trial in the HTA report.*
Sponsor details	*Study medication provided by Knoll Pharmaceuticals.*

Porter 2004	
Aim	To evaluate the benefit of sibutramine hydrochloride monohydrate within a weight management programme
Participants	The mean (SD) weight in the drug group was 108.2 (22.7) kg compared with 103.5 (18.5) kg in the non-drug group (p=0.05). The mean (SD) BMI (kg/m^2) in the drug group was 38.6 (7.0) compared with 36.8 (5.6) in the non-drug group (p=0.01)
Intervention	*Participants were randomised to receive sibutramine or no drug treatment, but all participants were enrolled in the Kaiser Permanente Weight Management Program (KPWMP). The KPWMP is a physician-led, multidisciplinary programme. Drug: participants randomised to receive sibutramine received a prescription for 10 mg of sibutramine to be taken daily. If 1.8 kg was not lost in the first 4 weeks, the dosage was increased to 15 mg daily. The dosage was not increased in the participant lost more than 4.5 kg by the 4-week visit. The dosage was decreased by 5 mg daily if significant changes in BP or heart rate occurred or if intolerable adverse events were experienced. The dosage of sibutramine could be increased to 15 mg daily at 3 or 6 months, but not after 6 months.*

Control	Group with no drug treatment although enrolled in the KPWMP, as described above.
Length of follow-up	*12 months*
Results	n=*296 in the drug group and* n=*292 in the non-drug group.* *The mean weight change (SD) from baseline to 6 months was significantly greater in the drug group –6.8 (5.7) kg compared with –3.1 (6.15) kg in the non-drug group.* *In regard to BMI category of <35 kg/m^2, the mean (SD) percentage change in weight for the drug group was –6.7 (6.8)% compared with –1.5 (4.4) % for the non-drug group; and for BMI of ≥40 the percentage change was –5.2 (4.8)% for the drug group compared with –3.1 (7.6)% for the non-drug group.* *From 6 to 12 months the mean weight change (SD) 0.5 (3.9) kg in the drug group compared with 0.6 (4.3) kg in the non-drug group.* *BMI and percentage body fat did not significantly change between 6 and 12 months.* *Significantly more patients in the drug group experienced a 5% or greater weight loss at 12 months (47.3 vs 19.1%,* p*<0.001).*
Quality and comments	*RCT, with adequate concealment method although not blinded. Randomisation was completed using a computer-generated random numbers table. Study assignments were placed in envelopes that were opened at the end of the baseline visit by the study coordinator.* *Authors mention high dropout rate, although the exact value is not mentioned in text.* *ITT analysis was performed, with missing data being replaced by data from the last available recorded visit.* *Patients had financial commitments to participate in the study. Participants paid for the AHA classes ($140) and the KPWMP ($100). Participants who completed 6 months of the study received a $50 gift cheque. Participants who completed 12 months of the study received and additional $100 gift cheque.* *HTA formula used for SD calculations* *BP and blood chemistry values were not reported at 12 months. Therefore they were not included in the meta-analysis.*
Sponsor details	*Funding obtained from Abbott Laboratories*

Redmon 2003 and Redmon 2005	
Aim	*The aim of this study was to evaluate the effects of a combination weight loss programme, using intermittent LEDs, energy-controlled meal replacement products and sibutramine, on weight loss, diabetes control and cardiovascular risk factors in overweight or obese participants with type 2 diabetes. Two-year effects were assessed in Redmon 2005.*
Participants	Sixty-one participants were randomised to treatment groups.

Intervention	*Participants in both groups received individual counselling by a registered dietitian. At baseline, each subject's basal energy requirement was calculated, and resting energy expenditure was measured. Using these data and an estimate of the subject's typical activity level, the dietitian prescribed an individualised diet that would promote a 500–1000 kcal reduction in daily energy.* *Participants in both groups also received an individualised exercise prescription that included, at a minimum, walking for 30 min three times weekly in addition to usual activity. All participants received an educational programme of dietary, exercise, and behavioural strategies to facilitate weight loss using a commercially available dietary and lifestyle modification resource.* *Participants in the combination treatment group also received: (1) 10 mg sibutramine daily with the option to increase to 15 mg daily after 6 months if BMI remained >27 kg/m^2; (2) LEDs providing 900–1300 kcal/day made up exclusively of meal replacement products (meal shakes or meal bars, 220 kcal/serving, four to six servings daily) for seven consecutive days every 2 months; and (3) between LED weeks, use of one meal replacement product and one snack bar daily (120 kcal/snack bar) to replace one usual meal and snack and thereby facilitate achievement of the goal of a 500–1000-kcal/day reduction in energy intake.*
Control	Standard treatment as described above
Length of follow-up	*2 years*
Results	n=*29 in standard therapy group and n=30 in combination therapy group.* *At 12 months, mean weight change (SD) in the standard therapy group was –0.8 (4.8) kg and in the combination group was –7.3 (7.1) kg (p<0.001).* *At 12 months, mean BMI change (SD) in the standard therapy group was –0.3 (1.6) kg/m^2, whilst in the combination therapy group the change was –2.6 (14.2) kg/m^2 (p<0.001). Decreases in fat mass and lean body mass were also significantly greater in the combination therapy group than in the standard therapy group.* *At the end of the 2 years, weight change (SD) was –4.6±5.7 kg for the combination group (p=0.001) and in the standard therapy group weight change at 2 years was –8.1±8 kg (p<0.001).* *Mean weight loss was greatest at 10 months in the combination therapy group. There was then a slow regain over the subsequent 14 months.* *Women had a significantly greater weight loss than men after 12 months of combination therapy (8.6±1.5 vs 4.7±0.9%, p=0.03).* *No analysis was performed for the patients who lost more than 5% or 10% of their weight.*
Quality and comments	*Participants were randomly assigned to either a standard therapy or combination therapy group by a single study coordinator using a random allocation schedule provided by the study statistician. The study coordinator was blinded to the randomisation schedule. Randomisation was stratified by sex.* *Meal replacement products and snack bars were provided by Slim Fast Foods Company* *Redmon 2005 data was not included in meta-analysis, as data was not complete for both combined and standard groups.*
Sponsor details	*Resources and grants from Abbott Laboratories and Slim Fast Nutrition Institute.*

Sanchez-Reyes 2004	
Aim	*To assess the effect on body weight and glycaemic control of sibutramine in combination with glibenclamide in obese Hispanic patients with type 2 diabetes.*
Participants	Obese Hispanic patients who had type 2 diabetes for which they were receiving glibenclamide monotherapy.
Intervention	Drug: 10 mg daily for 12 months Diet: 30 kcal/kg ideal body weight, with 50% of energy from carbohydrate, 30% from lipids and 20% from protein. *Physical activity: patients were advised to walk for 30 min/day.*

Control	Placebo group. Participants of placebo group were given same diet, physical activity advice and glibenclamide.
Length of follow-up	*12 months continuous treatment*
Results	*86 participants;* n=*44 for sibutramine;* n=*42 for placebo.* In the sibutramine group, mean (SD) body weight was reduced from 73.9 (10.3) kg at baseline to 69.8 (10.6) kg at month 12; BMI decreased from 29.9 (2.6) to 28.2 (2.9) kg/m^2; WC was reduced from 94.9 (8.4) to 90.8 (8.4) cm. In the placebo group, the corresponding changes were from 74.5 (10.3) kg at baseline to 73.1 (11.2) kg at 12 months; from 30.1 (2.5) to 29.5 (2.9) kg/m^2; from 94.4 (7.3) to 93.1 (8.3) cm (*p*<0.05). Patients who received sibutramine had a significant loss in mean (SD) fat mass from baseline at 12 months (23.8 [7.2] vs 19.9 [6.8] kg; *p*<0.05,), whereas the change in fat mass was not significant in patients who received placebo (25.1 [8.1] vs 23.0 [6.4] kg). There was no difference in body fat between groups at the end of the study. The proportions of 5% and 10% responders were: 59.1% (26/44) and 25.0% (11/44) in the sibutramine group, compared with 16.7% (7/42) and 4.8% (2/482) in the placebo group (p<0.05), respectively.
Quality and comments	Randomised, double-blind, placebo-controlled Trial. No details of randomisation, or concealment method provided. *Could not calculate SD for meta-analysis.*
Sponsor details	*Abbott Mexico?*

Other outcomes

Hainer 2005	
Results	*Non-significant changes were reported in SBP and DBP and heart rate. Sibutramine induced a significant decline in plasma TAG and atherogenic index. Mean reported daily energy intake decreased by 1729 kJ (23%) (*p<*0.001). Reported fat intake decreased from 62.9 to 47.7 g/d (*p<*0.001) and % energy consumed as fat declined from 32.1 to 28.0 (*p=*0.004). Significant changes in all Eating Inventory parameters and in the Beck Depression Inventory score were demonstrated as a result of sibutramine treatment at month 4. Restraint increased whilst disinhibition and hunger decreased. Changes in all three parameters of the Eating Inventory at month 4 were significantly more evident in the sibutramine group than in the placebo group. The change in Beck Depression Inventory score at month 4 was not different between the two groups.*
Quality and comments	…

Hauner 2004	
Results	*Blood lipids: the mean change (SD) in TC was –0.06 (0.92) mmol/l in the participants of the sibutramine group and –0.04 (0.92) mmol/l in the placebo group. For LDL-cholesterol, the change in the participants receiving sibutramine was –0.16 (0.79) mmol/l and in the participants on placebo was –0.22 (1.1) mmol/l. In regard to HDL-cholesterol, participants receiving sibutramine had a significant change by 0.14 (0.26) mmol/l vs a change by 0.1 (0.40) mmol/l in the participants of the placebo group. TAG levels changed by –0.11 (0.79) mmol/l in participants on sibutramine treatment and changed by 0.19 (2.51) mmol/l in the placebo group. Nevertheless, the change was not significant between the two groups* *SBP decreased by (mean [SD]) 2.9 (14.7) mmHg in the sibutramine group and by 1.5 (16.4) mmHg in the placebo treatment group at 54 weeks. In DBP the decrease was 0.3 (10.5) mmHg in the sibutramine group and 1.3 (9.9) mmHg in the placebo group. There was no significant difference in BP decrease between the two treatment groups.*
Quality and	…

comments	

Kaukua 2004 (in O'Meara as Rissanen 1998)	
Results	*The scores on physical functioning and Health Change increased in both groups during the study, although no significant differences were reported between the two groups. The weight loss at 12 months was correlated with the increase in the scores of physical functioning (*p=*0.005) and health change (*p<*0.001). None of the other scales on RAND-36 showed statistically significant changes.* *The mean change in SBP was 4.1 mmHg in the sibutramine group and 3.6 mmHg in the placebo group (*p=*0.81). The mean change in DBP was 1.7 and –0.2 mmHg in the sibutramine and placebo groups, respectively.* *In the sibutramine group the change in DBP was inversely associated with the changes in the scores of physical functioning (*p=*0.035), vitality (*p<*0.001), mental health (*p<*0.026), general health (*p=*0.048) and health change (*p=*0.017). On the other hand, in the placebo group, there were no associations between changes in HRQL scores and haemodynamic variables.* *When HRQL changes were examined in categories of weight loss, the scores on physical functioning and health change increased with ≥5% weight loss, but the scores on vitality and general health increased only after ≥15% weight loss.* *There was no significant change in the glycaemic control in either study group during the trial (–0.2% to 0.3%, % for HbA_{1c}).* *Decrease in HbA1c was associated with increases in the scores of physical functioning, general health, vitality, mental health, and health change.*
Quality and comments	…

McMahon 2002	
Results	*At week 52 mean supine DBP was 82.8 mmHg with placebo treatment compared with 85.5 mmHg under sibutramine (*p=*0.004) and mean supine SBP was 130.4 mmHg with placebo compared with 133.1 mmHg with sibutramine (*p=*0.0497). Sibutramine group had greater decreases (–0.10 mmol/l) compared with (–0.06 mmol/l). Decreases in TAG, increases in HDL-cholesterol and decreases in VLDL-cholesterol were more visible in the sibutramine group than in the placebo group (*p≤*0.05).* *At week 28 of treatment, all undertaking sibutramine had significant improvement in mean scores for mobility and activities of daily living (*p<*0.05 vs all patients receiving placebo), and sibutramine 5% and 10% responders showed improvement in mean scores for health, mobility and activities of daily living (*p<*0.05 vs all patients receiving placebo). At week 52, sibutramine 5% and 10% responders demonstrated significant improvement in mean scores for health and Activities of daily living; sibutramine 5% responders also demonstrated significant improvement in mean score for mobility (*p<*0.05) vs all patients receiving placebo).*
Quality and comments	…

McNulty 2003 (In O'Meara as Williams)	
Results	HbA_{1c} concentrations did not change significantly among the treatment groups), but it fell significantly (0.7±0.3%, p<0.02) in participants who lost 5–10% of weight and significantly further (1.2±0.4%, p< 0.0001) in those losing ≥10%. Among the sibutramine-treated patients, percentage weight loss was significantly correlated with the fall in HbA_{1c} (r=0.43, p<0.001, for the 15 mg group and r=0.32, p<0.02, for the 20 mg group), but no correlation was seen in the placebo group, where average weight was unchanged (r=0.5, p=0.73). Fasting plasma glucose similarly showed no overall differences between the three treatment groups but fell significantly by 1.8 mmol/l (p<0.001) in patients (sibutramine-treated only) who lost ≥10%. Fasting plasma insulin showed no significant changes with 15 mg sibutramine or placebo, but the final concentration was significantly decreased with 20 mg sibutramine compared with placebo.

	Neither TC nor LDL-cholesterol showed any significant changes in any treatment group, but HDL-cholesterol showed slight but significant rises of 0.1 mmol/l with both 15 and 20 mg sibutramine. The TC:HDL cholesterol ratio showed a slight but statistically significant fall (10%) with 15 mg sibutramine but no significant change with 20 mg sibutramine. In participants who lost ≥5 or ≥10% weight, TC:HDL cholesterol ratio also showed modest but significant falls of 8% (p=0.011) and 16% (p=0.002), respectively. TAG levels did not alter significantly with placebo or 15 mg sibutramine but fell significantly by 0.2 mmol/l (9%) with 20 mg sibutramine. In participants losing ≥5 and ≥10% weight, TAG fell significantly by 0.3 mmol/l (13%, p<0.01) and 0.8 mmol/l (29%, p<0.01), respectively.
Quality and comments	…

Porter 2004	
Results	*The mean change in TC was 0.01 (95% CI –0.07 to 0.09) mmol/l in the drug group vs 0.05 (95% CI –0.04 to 0.13) mmol/ in the non-drug group (*p=*0.38). The mean change in TAG was –0.15 mmol/l (95% CI 0.24 to –0.05 mmol/l) in the drug group compared with –0.09 mmol/l (95% CI,–0.18 to 0.008 mmol/l) (*p=*0.35).* *The mean change in HDL-lipoprotein was 0.01 (95% CI –0.01 to 0.03) mmol/l in the drug group compared with 0.01 (95% CI, –0.02 to 0.04) mmol/l in the non-drug group (*p=*0.87). The mean change in LDL-cholesterol was 0.02 (95% CI –0.04 to 0.09) mmol/l in the drug group compared with 0.07 (95% CI –0.005 to 0.14) mmol/l in the non-drug group (p=0.39).* *The mean change in glucose was –0.04 (95% CI –0.21 to 0.12) mmol/l in the drug group compared with –0.1 (95% CI –0.3 to 0.02) mmol/l in the non-drug group (*p=*0.30).* *No significant changes occurred in BP from baseline to 6 months in either group, or at 12 months. Authors did not report values for 12 months, thus we could not include them in the meta-analysis.*
Quality and comments	…

Redmon 2003 and 2005	
Results	*HbA_{1c} decreased (SD) 0.6±1.6% in the combination therapy group, but was unchanged in the standard therapy group (*p=*0.05). Absolute values at 1 year were 8.2±0.2 and 7.5±0.3% in the standard therapy and combination groups, respectively.* *For the observed range of weight change (–10 to +4 kg), there was a significant positive linear association between change in weight at 1 year and change in HbA_{1c} (*p=*0.006).* *Changes in BP, pulse rate, and fasting plasma lipids did not differ between the two groups at 12 months.* *Only changes in systolic BP were significant, and only changes in the combination group were reported at year 2.*
Quality and comments	The authors contended that any effect of weight loss to reduce BP was offset by an effect of sibutramine to increase BP.

Sanchez-Reyes 2004	
Results	The fasting glucose concentration decreased (SD) from 7.8 (29.4) to 6.3 (32.0) mmol/l (all p<0.001) in the sibutramine group, and from 7.8 (25.2) to 6.9 (38.3) mmol/l (p<0.05) in the placebo group. In the sibutramine group, mean (SD) HbA_{1c} values were 8.9 (1.2)% at baseline, 8.3 (1.1)% at 6 months and 8.3 (1.2) % at 12 months (p< 0.01, 6 and 12 months vs baseline). Corresponding HbA_{1c} values in the placebo group (%) were 9.0 (1.2), 9.0 (1.2) and 9.1 (1.3), respectively; there were no significant changes from baseline. At 6 and 12 months, HbA_{1c} values were significantly lower in the sibutramine group compared with the placebo group (p<0.05).

	Small but significant decreases in mean BP were observed throughout the trial in both groups (p<0.05). Five patients in the sibutramine group and four in the placebo group had clinically significant increases in BP (>150/110 mmHg), and one patient in the sibutramine group had a clinically significant increase in heart rate to >100 beats per min.
Quality and comments	…

Reported harms

Hainer 2005	
Results	Side effects were rare in both groups, except for dry mouth, which was more frequently reported in the sibutramine group than in the placebo (20.0 vs 5.7%, p=0.027).
Quality and comments	…

Hauner 2004	
Results	*87.8% of participants in the sibutramine treatment group experienced adverse events, and 83.5% in the placebo group. These included: back pain, bronchitis, sinusitis and gastritis. Headache, dry mouth and constipation belong to the more specific adverse event profile of sibutramine and were more frequently reported in the sibutramine group when compared with the placebo group*
Quality and comments	…

Kaukua 2004 (In O'Meara as Rissanen 1998)	
Results	*In the sibutramine group the increase in DBP was associated with negative changes in HRQL.*
Quality and comments	…

McMahon 2002	
Results	*Adverse events were reported by 96.6% of participants in the sibutramine group, and 87.8% in the placebo group. Headache was the most frequent adverse event: 28.1% in the sibutramine group and 23.0% in the placebo group. Also 20.5% of participants in the sibutramine group reported dry mouth, compared with 0% in the placebo group. The majority of the events were mild to moderate severity. 6.2% reported serious adverse events in the sibutramine group (potentially two being caused by treatment) and 6.8% in the placebo group.*
Quality and comments	…

McNulty 2003 (In O'Meara as Williams)	
Results	Individual BP responses varied widely in all three treatment groups. A few sibutramine-treated patients showed marked BP rises, but systolic and DBP also rose in some placebo-treated patients, being higher at completion than at baseline in over 40% of cases. BP changes were influenced by weight change. With 15 mg sibutramine, systolic BP did not change significantly in participants who lost ≥5 or ≥10% weight, whereas the ≥5% responders with 20 mg sibutramine showed a mean placebo-subtracted fall of 4.6±2.0 mmHg (*p* =0.053 vs all placebo participants). Placebo-treated participants who lost ≥5% weight showed a systolic decrease of 3.3±1.4 mmHg. For >5% weight loss, mean placebo-subtracted diastolic changes were 2.0±1.5 with 15 mg sibutramine (NS vs placebo, 1.5±1.0 mmHg) and –0.9±1.4 mmHg (NS vs placebo) for 20 mg sibutramine. For >10% weight loss, mean

	placebo-subtracted changes were 1.7±2.2 and 1.0±1.8 mmHg, respectively (both NS vs placebo).
Quality and comments	…

Porter 2004	
Results	*Adverse events were significantly greater for patients under sibutramine treatment. 12.5% participants discontinued treatment as a result of 43 adverse events (2.0% with constipation, 2.0% with hypertension, 1.4% with tachycardia, 1.0% with headache, 1.0% with chest pain, 0.7% with insomnia, 0.7% with dizziness, 0.7% with haemorrhoidal or rectal events, 0.7% with rash, and 4.4% with miscellaneous events.* *Thirty-three serious adverse events were reported in 30 participants in the drug group, and 21 serious adverse events were reported in 18 participants in the non-drug group.*
Quality and comments	…

Redmon 2003 and 2005	
Results	*Dry mouth and constipation were reported by some participants whilst initiating the combination therapy, although these symptoms were not severe and did not require discontinuation of treatment.*
Quality and comments	…

Sanchez-Reyes 2004	
Results	*Twenty sibutramine patients experienced 39 adverse events, including increased BP in five patients. Besides alterations in BP, the most frequently occurring adverse events in the sibutramine group were hypoglycaemia (*n=*4) and constipation (*n=*3). Eighteen patients in the placebo group experienced 27 adverse events; the most frequently occurring events were hypoglycaemia (*n=*5), increased BP (*n=*4), upper respiratory tract infection (*n=*4), and dizziness (*n=*3).*
Quality and comments	…

Generalisability

Hainer 2005	
Country and setting	Czech Republic. Weight-reduction programme in obesity management centre.
Participants (included/excluded)	Participants were excluded if any of the following diseases were present: type 1 and type 2 diabetes mellitus; endocrine diseases; peptic ulcer; uncontrolled hypertension; cardiovascular, cerebrovascular, hepatic and renal diseases; psychiatric illnesses and eating disorders. Contraindications also included lactation and pregnancy; weight change >5 kg or the use of antiobesity drugs in the previous 6 months; administration of serotonin reuptake inhibitors or monoamine oxidase inhibitors as well as medications affecting body weight or contraindicated with the use of sibutramine.
Recruitment	Recruited from the obesity outpatient clinics
Intervention (mode and intensity)	*In monthly check-ups, a physician together with a psychologist and a dietitian assessed dietary and physical activity records and encouraged modifications in lifestyle according to cognitive behavioural modification techniques.*

Duration of active intervention	After the double-blind, placebo controlled 4-month phase, participants received either sibutramine (10 mg/day) or placebo. Subsequently, an open phase continued until month 12, in which sibutramine was administered to all participants.
Control (mode and intensity)	Same as treatment intervention, although with placebo.
Delivery of intervention/control (who)	Physician, psychologist and dietitian.
Dropout rates	16.25%
Treatment of dropouts (return to baseline, or last measurement?)	Not clear

Hauner 2004	
Country and setting	Primary care setting, general practice. Cologne-Dusseldorf, Germany.
Participants (included/excluded)	Participants were included if age was between 18 and 65 years, BMI between 30 and 40 kg/m^2, stable weight during the preceding 3 months (±2 kg), motivation and willingness to reduce weight and written informed consent for participation Participants were excluded if they had renal failure (serum creatinine > 2 mg/dl), hypercholesterolaemia (>160/95 mmHg, mean of three independent measurements), type 2 diabetes mellitus, coronary heart disease (CHD), clinically significant dysrhythmia, psychiatric diseases, childbearing potential without adequate contraception or use of medication that may alter appetite.
Recruitment	Participants were recruited in 33 general practices (general practitioners and family doctor internists).
Intervention (mode and intensity)	*All participants had a total number of 11 visits to the doctor's office.* *Diet: Individual dietary counselling for the first seven days. Second dietary counselling after 3 to 6 months for weight stabilising diet, and a third individual session held at the end of the study to develop weight regain prevention strategies, after discontinuation of drug.* *Educational sessions: during the first 4 weeks for 90 min.*
Duration of active intervention	*54 weeks*
Control (mode and intensity)	…
Delivery of intervention/control (who)	Trained dietitian, general practitioners and family doctor internists.
Dropout rates	*36.6% for sibutramine* *43% for placebo*
Treatment of dropouts (return to baseline, or last measurement?)	ITT analysis on all participants with at least one follow-up visit with weight measurement. LOCF technique was employed for the final analysis.

Kaukua 2004 (In O'Meara as Rissanen 1998)	
Country and setting	Finland. University research centre
Participants (included/excluded)	Participants were eligible for the study if treated by diet alone, had a relatively stable weight (<5 kg weight change in previous 3 months), and had no nephropathy, proliferative retinopathy, exudative masculopathy, or insulin deficiency (ketonuria or fasting C-peptide <0.3 mmol/l). Participants with significant illnesses such as uncontrolled hypertension, uncompensated heart failure, symptomatic coronary disease, and renal or hepatic failure were excluded.
Recruitment	From 11 Finnish primary medical care centres.
Intervention (mode and intensity)	See weight loss table

Duration of active intervention	12 months
Control (mode and intensity)	Placebo once daily and 700 kcal/day hypoenergetic diet for 12 months
Delivery of intervention/control (who)	N/R
Dropout rates	8% for the sibutramine group 11% for the placebo group.
Treatment of dropouts (return to baseline, or last measurement?)	Analysis were carried out in the completers population and in the ITT population.

McMahon 2002	
Country and setting	USA. Clinical research centre
Participants (included/excluded)	Participants had to have a history of hypertension that was controlled for ≥60 days preceding the screening visit with a constant dose of an ACE inhibitor, with or without a thiazide diuretic. The dose and nature of the medication used to control hypertension had to have been unchanged for ≥60 days preceding the screening visit. Patients were randomised if their hypertension was well controlled at each of three qualifying consecutive run-in visits, defined as a mean supine DBP ≤95 mmHg at each qualifying visit, with an overall difference of ≤10 mmHg between visits, without changes to the dose of the ACE inhibitor or thiazide diuretic. Exclusion criteria: increased BP secondary to concurrent medical condition or drug therapy; mean supine pulse rate >95 beats per min at baseline or mean supine DBP >95 mmHg at any run-in visit; clinically significant history of cardiac disease or any clinically significant abnormal cardiac condition other than hypertension; had been previously treated with sibutramine, or had gastric surgery to decrease obesity.
Recruitment	Not stated.
Intervention (mode and intensity)	As in weight loss table.
Duration of active intervention	52 weeks
Control (mode and intensity)	Placebo group given general advice regarding weight loss and 55.4% were on concomitant diuretic treatment.
Delivery of intervention/control (who)	Not clear.
Dropout rates	43% in the sibutramine group and 51% in the placebo group.
Treatment of dropouts (return to baseline, or last measurement?)	LOCF methodology was used in the intention-to-treat patient population (first analysis). Baseline data was not carried forward. A second analysis was an observed analysis that used only the actual data recorded for a patient; and the third analysis was on data for patients who completed the study.

McNulty 2003 (In O'Meara as Williams)	
Country and setting	Twenty-one primary and secondary care centres in England, Canada, France and Belgium.

Participants (included/excluded)	Inclusion criteria: type 2 diabetes (absence of ketonuria, rapid preceding weight loss, or need for insulin treatment), diabetes duration >6 months, BMI ≥27 kg/m^2, duration of metformin treatment of 3 months to 2 years, fasting serum glucose 7.0–15.0 mmol/l and age 25–70 years. Exclusion criteria encompassed the following: current or previous evidence of ischemic heart disease, heart failure, or stroke; seated pulse rate >100 beats per min; DBP >95 mmHg; total fasting serum cholesterol >7.8 mmol/l; fasting serum TAG >5.6 mmol/l; serum creatinine >120 µmol/l; serum liver enzymes or bilirubin levels that exceeded twice the upper limit of normal; weight change of >3 kg during the preceding 3 months; malignancy; and significant neurological or psychiatric disturbances, including alcohol or drug abuse. Excluded medications (within the previous 3 months) were anorectic agents, laxatives, beta-agonists (other than inhalers), cyproheptadine, phenothiazines, anti-depressants, anti-serotoninergics, barbiturates, antipsychotics, and oral corticosteroids. Antihypertensive and lipid-lowering drugs were permitted if treatment was stable for at least 3 months. Women were excluded if they were pregnant, lactating, or of childbearing potential while not taking adequate contraceptive precautions.
Recruitment	Suitable participants were identified from review of case notes and/or computerised clinic registers.
Intervention (mode and intensity)	*See weight loss table.*
Duration of active intervention	12 months
Control (mode and intensity)	Placebo once daily for 12 months.
Delivery of intervention/control (who)	Dietary advice for 4 weeks was given by dietitian and/or specialist nurse.
Dropout rates	There were 50 patients who withdrew prematurely (19 in the 15 mg/day sibutramine group, 13 in the 20 mg/day sibutramine group and 18 in the placebo group).
Treatment of dropouts (return to baseline, or last measurement?)	Analyses, performed by the Biostatistics Section, Knoll Limited, were based on the ITT populations using the LOCF.

Porter 2004	
Country and setting	USA. University weight management programme

Participants (included/excluded)	Included individuals were ≥18 years of age, willing to enrol in the KPWMP, willing and able to give informed consent, and had a BMI of ≥30 kg/m^2. Individuals with a BMI of 27 to 29.9 kg/m^2 were eligible for enrolment only if they had one or more of the following comorbidities: diabetes mellitus with or without drug therapy, hypertension treated with drug therapy, or hyperlipidaemia treated with drug therapy. Individuals were excluded if they had taken a prescription weight loss agent within 6 months; had a history of coronary heart disease, congestive heart failure, cardiac arrhythmia, or stroke; had uncontrolled hypertension (mean BP >145/95 mmHg, or isolated mean systolic BP >160 mmHg with diastolic BP <95 mmHg, or isolated DBP >95 mmHg with SBP <145 mmHg); a mean resting heart rate of greater than 100 beats per min; or one of the contraindications to sibutramine listed in the product labelling. Other exclusions included narrow-angle glaucoma, severe renal impairment, severe hepatic dysfunction, obesity of organic origin, seizures, other medical conditions that placed them at increased medical risk by participating in the study (as determined by the study physician), previous participation in the study, participation in KPWMP or any required American heart association classed within the past 6 months, and inability to read English. Individuals were also excluded if they were pregnant, planning a pregnancy during the study, or breastfeeding. Moreover, individuals taking: selective serotonine reuptake inhibitors, St John's wort, sumatripan succinate or related agents, ergotamine tartrate, lithium, fentanyl citrate, pentazocine, meperidine hydrochloride, dextromethorphan, tryptophan and cisapride
Recruitment	Individuals enrolled in the KPWMP.
Intervention (mode and intensity)	*Participants paid $100 for the programme consisting of five monitored care visits with a prevention specialist and two weight management seminars chosen from 20 possible seminars.* *Study visits for all patients occurred at baseline and at 3, 6, 9 and 12 months.*
Duration of active intervention	*12 months*
Control (mode and intensity)	No drug treatment although also enrolled in KPWMP
Delivery of intervention/control (who)	KPWMP was delivered by a physician
Dropout rates	*Not clear*
Treatment of dropouts (return to baseline, or last measurement?)	Last available recorded visit.

Redmon 2003 and 2005	
Country and setting	USA. Weight-loss programme at University research centre.
Participants (included/excluded)	*To be included, participants were required to have: age 30–70 years, diagnosis of type 2 diabetes with HbA_{1c} 7.0–10.0%, BMI 27–50 kg/m^2, stable weight for the previous 3 months, and constant doses of any oral diabetes, hypertension, and lipid medications for at least 1 month. Participants were excluded if they had: current use or use in the previous 6 months of insulin, prior use of sibutramine, use of any weight loss product or participation in any formal weight loss programme in the previous month, significant abnormality on screening tests, history of heart disease or stroke, prior bariatric surgery, lactose intolerance, and any chronic disease or therapy that would make adherence to the study protocol difficult.*
Recruitment	Not clear.

Intervention (mode and intensity)	*Participants in both groups received individual counselling by a registered dietitian. At baseline, each subject's basal energy requirement was calculated, and resting energy expenditure was measured. Using these data and an estimate of the subject's typical activity level, the dietitian prescribed an individualised diet that would promote a 500–1000 kcal reduction in daily energy.*
Duration of active intervention	12 months, with 10 mg sibutramine daily with the option to increase to 15 mg daily after 6 months if BMI remained >27 kg/m^2 and LEDs providing 900–1300 kcal for seven consecutive days every 2 months. After year 1, the standard therapy group was crossed over to combination therapy for the second year of the study. The combination therapy group continued combination therapy in the second year and therefore received 2 years continuous therapy.
Control (mode and intensity)	Intervention as described in weight loss table, although with no sibutramine.
Delivery of intervention/control (who)	Individual counselling by registered dietitian.
Dropout rates	8% At year 2 the dropout in the combination group was 23%, whilst in the standard therapy group was 14%.
Treatment of dropouts (return to baseline, or last measurement?)	Appears to be last measurement.

Sanchez-Reyes 2004	
Country and setting	Mexico. Endocrinology service, general hospital.
Participants (included/excluded)	Eligible participants were adult (age range 24–65 years) overweight or obese (BMI >27 kg/m^2) patients with type 2 diabetes who had stable fasting plasma glucose levels (<140 mg/dl) and had been receiving glibenclamide for at least 2 weeks. *Patients were excluded if they had endocrine diseases other than type 2 diabetes, uncontrolled hypertension (BP >140/90 mmHg), an autoimmune disease, ischemic heart disease, arrhythmia, or psychosis. Also excluded were those requiring medications acting on the central nervous system, cathartics, thyroid hormone replacement, or diuretics. Pregnant or lactating women were excluded.*
Recruitment	Unclear.
Intervention (mode and intensity)	All patients received individually tailored dietary advice and were counselled by a nutritionist and an endocrinologist at the monthly clinic visits. In general, it was recommended that patients adhere to a diet consisting of 30 kcal/kg IBW, with 50% of energy from carbohydrate, 30% from lipids and 20% from protein. Patients received a list of recommended foods, portions, and combinations. Patients were also advised to walk for 30 min each day.
Duration of active intervention	12 months
Control (mode and intensity)	Same as treatment group, although with placebo.
Delivery of intervention/control (who)	Physician performed medical assessment and part of monthly check. All patients received individually tailored dietary advice and were counselled by a nutritionist and an endocrinologist at the monthly clinic visits.
Dropout rates	45.5%
Treatment of dropouts (return to baseline, or last measurement?)	LOCF methodology was used.

1.7 Surgical interventions

Throughout, used data from Clegg and Maggard reviews for SDs, mean weight change etc…
Detailed evidence tables have only been done for comparative studies, and not single arm studies. We have adapted the Technology Evaluation Centre evidence tables for single arm studies, as appropriate.
We would like to acknowledge the work of the teams on both the Colquitt Cochrane review and the TEC review, as we have been able to use their detailed data extractions in our modified review.

1.7.1 Key systematic reviews and guidelines

Colquitt Cochrane Review 2005

- Types of studies
    - RCTs comparing surgical interventions with other surgical interventions.
    - RCTs, controlled clinical trials and prospective cohort studies comparing surgical interventions with non-surgical treatment (medical management or no treatment) were included as few RCTS were anticipated.
    - Short-term weight loss is common, therefore studies were only included if they reported measurements after a minimum of 1 year.
- Types of participants
    - Adults aged ≥18 years with morbid obesity defined as BMI >40 kg/m^2 or BMI >35 kg/m^2 with serious comorbid disease, in whom previous non-surgical interventions have failed. Different classifications for morbid obesity, such as percentage excess weight, were converted to BMI to confirm eligibility.
- Types of intervention
    - Comparisons of surgical procedures, performed either as open procedures or laparoscopically, including vertical banded gastroplasty, horizontal gastroplasty, gastric banding, GBP or biliopancreatic diversion.
    - Surgical procedures vs usual care (no treatment or medical management, for example VLED).
- Excluded comparisons
    - Comparisons of variations of surgical techniques rather than different procedures.
    - Jejunoileal bypass procedures: no longer recommended in Europe and the USA due to unacceptably high morbidity and mortality associated with the procedure.
- Types of outcome measures
    - Main outcome measures
    - Studies were included if they reported one or more of the following outcomes after at least 12 months follow-up: measures of weight change, fat content (for example BMI) or fat distribution (for example WHR).
    - Quality of life, ideally measured using a validated instrument.
    - Obesity related co-morbidities (for example diabetes, hypertension).

Lefevre 2005 TEC review

- Study selection
    - Full-length articles published in peer-reviewed journals in the English language between 1985 and May 2005.
- Patient population of adults with morbid obesity, as defined by: BMI >40 kg/m^2, BMI >35 kg/m^2 and at least one serious medical comorbidity, OR similar measure of defining morbid obesity (e.g. more than100% above IBW).
    - Patients treated with one of the bariatric surgical procedures of interest (i.e., open GBP, laparoscopic adjustable gastric banding, biliopancreatic diversion, long-limb GBP).

- At least 1-year follow-up (except for short term adverse events, for which this criterion did not apply)
- Reports on at least one relevant outcome: weight loss adverse effects of surgery (early morbidity/mortality of procedure, long-term adverse effects due to altered GI anatomy and physiology).
- Study design is:
    - Comparative study with one or more comparisons of interest: open GBP vs laparoscopic adjustable gastric banding, or open GBP vs biliopancreatic diversion/long-limb GBP for patients with super-obesity, and includes at least 25 evaluable patients per treatment arm;
    - OR: Single-arm study that reports on outcomes of laparoscopic adjustable gastric banding, or biliopancreatic diversion/long-limb GBP for patients with super-obesity, and includes at least 100 evaluable patients that were treated with particular procedure.
- For procedures intended for super-obese patients (biliopancreatic diversion, long-limb GBP), studies were sought for this specific population. However, due to the lack of studies that focused exclusively on this population, inclusion criteria were not limited to super-obese populations for these procedures.

Maggard 2005 meta-analysis (used for summary statistics)

- Focused on studies that assessed surgery and used a concurrent comparison group. This category included RCTs, controlled clinical trials and cohort studies. A brief scan of the literature showed that these types of studies were rare. Therefore, also elected to include case series with ten or more patients, since these studies could be used to assess adverse events and could potentially augment the efficacy data from comparative studies.

1.7.2 Surgery vs non-surgical interventions

Weight loss

Andersen 1984 (in Clegg TA Andersen 1988) RCT	
Aim	To compare the weight reducing effect of diet and gastroplasty with that of diet alone in people who were severely obese
Participants	*People who were severely obese (≥60% overweight)* *Total 57 (60 randomised) – 50 F, 7 M. Median (range) age 35 years (21 to 53 years) surgery+diet (*n=*27), 33 years (18 to 53 years) diet (*n=*30). Median (range) body weight 120 kg (94 to 166 kg) surgery+diet, 115 kg (98 to 206 kg).*
Intervention	*Surgery: gastroplasty (Gomez method)* *Diet (500 kcal, 34 g protein): started on seventh day after surgery. Five daily meals of 50 g each and 2l of low-energy drinks (in 50 ml portions) between meals. Food endangering stoma passage were avoided. Vitamin and mineral supplements were also given.* *Other: received 'careful' verbal and written instructions before start of treatment. Seen at weekly intervals initially, then every 2 weeks after three months.* In the long term (up to 5 years), if weight was regained, advised to return to previously prescribed diets. *After cessation of the primary weight loss, invited to a weekly open-house session.*

Comparison	Two alternating diets used. Diet (341 kcal, 35 g protein): For 8 weeks, special formula taken with orange juice, vitamin and mineral supplement (as above) and 3 g potassium chloride. Diet (900 kcal): From 2 weeks, natural high-protein, low-fat, low-carbohydrate foods. Allowed to take diethylpropion (reduces appetite) maximum 35 mg three times per day, but urged to do so only if hunger prevented compliance with the diet. Diets stopped when failed to lose weight for 2 months. Other: received 'careful' verbal and written instructions before start of treatment. Seen at weekly intervals initially, then every 2 weeks after three months. Also included visits to outpatient clinics and groups meetings. Group meetings were to repeat and elaborate the instructions, to discuss diet experiences, and to offer support in case of faltering compliance. After cessation of weight loss, participants seen for dietetic counselling every three months. In the long term (up to 5 years), if weight was regained, advised to return to previously prescribed diets. After cessation of the primary weight loss, invited to a weekly open-house session.
Length of follow-up	*5 to 6 years*
Results	At 3 months, mean weight change (SD) was –20.0 (no SD) kg in the surgery group compared with –15.0 (no SD) kg in the diet group (p<0.05). At 6 months, mean weight change (SD) was –25.0 (no SD) kg in the surgery group compared with –21.0 (no SD) kg in the diet group (p=NS). At 12 months, mean weight change (SD) was –22.0 (15.5) kg in the surgery group compared with –18.0 (15.5) kg in the diet group. Mean weight change in the surgery group compared with diet was –4.0 (95% CI –12.2 to 4.2). At 18 months, mean weight change (SD) was –18.5 (no SD) kg in the surgery group compared with –10.5 (no SD) kg in the diet group (p=NS). At 24 months, mean weight change (SD) was –30.5 (20.3) kg in the surgery group compared with –8.0 (20.3) kg in the diet group. Mean weight change in the surgery group compared with diet was –3.50 (95% CI –38.2 to –6.9). The median (range) time to maximum weight loss was 9 months (3 to 24 months) in the surgery group and 9 months (3 to 21 months) in the diet group (p=NS). Median maximum weight change was –26.1 kg in the surgery group and –22.0 kg in the diet group (p=NS). Median weight regain in the surgery group at 12 months was +10 kg compared with +12.5 kg in the diet group (p=NS). At 18 months, the diet group had regained significantly more weight than the surgery group (+21.5 vs +10 kg, respectively, p<0.05). At 5 years, 30 (95% CI 14 to 50) % of the surgery group had achieved weight loss of 10 kg or more compared with 17 (95% CI 6 to 35) %. Median weight change in those who had lost ≥10 kg did not differ between groups (–18.2 vs –26.8 kg, p=NS). Cumulative success rate was higher in the surgery group (16 vs 3%, respectively, p<0.05). *Excess weight not reported.*
Quality and comments	*During the study period, two diet only participants had gastroplasty elsewhere after having regained all weight lost.* From CR 2005: randomisation and concealment unclear. ITT not done. Blinded assessment not done. *Some discrepancies in reviews and original papers.* *Sugerman: horizontal, unbanded Gp is a flawed operation, and is no longer performed.*
Sponsor details	*Foundation grants. Formula and supplements provided by Oluf Mork Bio-Chemie.*

Mingrone 2002 RCT	
Aim	To investigate the consequence of weight reduction treatment in the modification of CHD risk in severely obese people.

Participants	People who were severely obese (not defined?). Total 79 – 52F, 27M. Aged 30 to 45 years (not reported by group). Mean (SD) weight 125.3 (12.8) kg surgery F (*n*=31), 151.8 (17.1) kg surgery M (*n*=15), 121.6 (24.1) kg diet F (n=21), 147.3 (26.8) kg diet M (*n*=12).
Intervention	*Surgery: biliopancreatic diversion.*
Comparison	Diet: 20 kcal/kg FFM, 55% carbohydrate, 30% fat, 15% protein. Modified 6 monthly in line with DEXA FFM.
Length of follow-up	*12 months*
Results	Women: At 12 months, mean weight change (SD) was –35.1 (no SD) kg in the surgery group compared with –7.1 (no SD) kg in the diet group (no *p* value). Men: At 12 months, mean weight change (SD) was –52.1 (no SD) kg in the surgery group compared with –9.1 (no SD) kg in the diet group (no *p* value). Changes in the surgery group for both women and men were significantly different from baseline ($p<0.0001$), and changes in the diet were not significant. *Excess weight not reported.*
Quality and comments	*Not sure how comparable the groups were – no baseline comparison.* From CR 2005: randomisation and concealment unclear. ITT and blinded assessment unclear.
Sponsor details	*None reported.*

SOS Matched control cohort study (in Clegg TA)	
Aim	To examine the effects of weight loss in people with severe obesity
Participants	Obese (BMI ≥34 kg/m^2 for men, ≥38 kg/m^2 for women) adults *Total – sample size differs with publication of different outcomes.* *Weight loss/diabetes/BP (at 8 years):* *Number: total 483, surgical 251, control 232* *Age (mean): surgical 46 (SD 6) years, Control 47 (SD 6) years.* *Sex: Surgical 65.9% female, Control 65.9% female.* *BMI: Surgical 41.6 (SD 3.9) kg/m^2, Control BMI 41 (SD 4.7) kg/m^2.* *HRQL:* *Number: total 974, surgical 487, control 487* *Age (mean): surgical 46.6 (95% CI 46.1 to 47.1) years, control 47.7 (95% CI 47.2 to 48.3) years.* *Sex: surgical 67% female, control 67% female.* *Lipid disturbances:* *Number: total 1479, surgical 767, control 712* *Age: surgical 47 (SD 5.8) years, control 48.6 (SD 6.3) years.* *Sex: surgical 69% female, control 68% female.* *BMI: surgical BMI 42.1 (SD 4.3) kg/m^2, control 39.8 (SD 4.6) kg/m^2.* *Gallstones, gallbladder disease and pancreatitis:* *Number: total 2682, surgical 1422, control 1260.* *Age, men: surgical 47.3 (5.7) years, controls 48.4 (6.1) years,* p=*0.005; women: surgical 47.1 (5.9) years, controls 48.3 (6.3) years,* p<*0.001.* *Sex (M:F): surgical 468:954, controls 418:842.* *BMI, men: surgery 41.2 (4.7) kg/m^2, control 38.8 (4.7)* kg/m^2, p<*0.001; Women: surgery 42.8 (4.1) kg/m^2, controls 40.6 (4.4) kg/m^2,* p<*0.001.* *Medication use:* *Number: total 965, surgery 510, control 455.* *Mean age: surgery 47.1 (5.8) years, control 48.6 (6.1) years.* *Sex, % of men: surgery 31.0, control 31.0.* *Mean BMI: surgery 41.8 (4.1)* kg/m^2, *control 39.9 (4.6)* kg/m^2. *Medication for CVD (%): surgery 29.4, control 27.5* *Diabetes: surgery 6.3, control 4.6.*

Intervention	*Surgery: vertical banded gastroplasty or gastric banding or GBP.* *Other: customary obesity treatment of the site at which the surgery was performed.*
Comparison	Conventional treatment: customary obesity treatment of the site at which registered. Ranged from sophisticated lifestyle and behavioural interventions, to no treatment.
Length of follow-up	*Differs with publication of different outcomes. Details reported by outcome.*
Results	Weight (kg), surgical (*n*=1210) vs control (*n*=1099): Baseline: difference 7 kg (95% CI 5.7 to 8.3) kg. 24 months: difference –21 kg (95% CI –23 to –19) kg. Weight loss after 24 months: Surgical 28 kg (23%), control unchanged, *p*<0.001. Weight changes at 8 years (surgical n=232, control n=251): Baseline: surgical 120.4 (SD 16.0) kg, control 114.7 (SD 17.8) kg. 8 years: surgical 100.3 (SD 17.8) kg, control 115.4 (SD 19.2) kg. Difference in weight change between groups at 8 years: 20.7 kg (*p*<0.001). Relative weight change at 8 years: surgical =–16.3 (SD 12.3)%, control =0.9 (SD 10.8)%. Weight at 8 years: GBP 92 kg vs vertical banded gastroplasty 100 kg (*p*=NS) vs gastric banding Weight loss at 2 years for subgroup with biliary disease data: Men: surgery 29.4 (15.3) kg, 21.9 (10.0) %, controls 0.3 (9.5) kg, 0.1 (7.4) %, *p*<0.001. Women: surgery 28.0 (13.8) kg, 23.9 (10.7)%, controls 0.6 (8.6) kg, 0.3 (7.9) %, *p*<0.001. Relative weight change, mean (SD) for subgroup with medication data: 2 years: surgery –22.6 (10.6)%, control –0.3 (7.9)%. 6 years: surgery –16.2 (11.5)%, control 0.8 (9.6)%. At 24 months, mean weight change (SD) was –28.0 (15.0) kg in the surgery group compared with 0.5 (8.9) kg in the non-surgery group. Mean weight change in the surgery group compared with non-surgery was –28.50 (95% CI –29.75 to –27.25) kg. At 8 years, mean weight change (SD) was –20.0 (16.0) kg in the surgery group compared with 0.7 (12.0) kg in the non-surgery group. Mean weight change in the surgery group compared with non-surgery was –20.70 (95% CI –23.21 to –18.19) kg. At 10 years, mean % weight change (SD) was –16.1% (no SD reported) in the surgery group compared with +1.6% (12) in the non-surgery group. Difference was –16.3 (95% CI –17.6 to –14.9) kg. The fractions of participants who, after completing 10 years of the study, had a loss of less than 5% of their initial weight were 72.7% (control group), 8.8% (GBP subgroup), 13.8% (vertical banded gastroplasty subgroup), and 25.0% (banding subgroup). The fractions of participants achieving 20% weight loss or more over the 10-year period were 3.8% (control group), 73.5% (GBP subgroup), 35.2% (vertical banded gastroplasty subgroup), and 27.6% (banding subgroup). Excess weight not reported.

Quality and comments	From CR 2005: baseline differences between groups including for confounders (but these were adjusted for). Unclear as to whether groups comparable for disease progression. Outcome assessment not blinded. Dropouts and reasons unclear. At inclusion, surgical group were younger than controls (p<0.001), had a higher prevalence of hypertension (p<0.05) and were more often smokers (not significant). Also reports higher BMI (p<0.001), BP (p<0.001) and energy intake (p<0.001) in surgical patients. Added weight loss data from Sjostrom 2004 for 10-year time point
Sponsor details	*Swedish Medical Research Council. Hoffman-La Roche. Others including Volvo Research Foundation, Skandia Insurance.*

Other outcomes

Andersen 1984 (in Clegg TA Andersen 1988) RCT	
Results	*None reported.*
Quality and comments	…

Mingrone 2002 RCT	
Results	*No significant changes were seen in the diet groups for ratios of TC:HDL, or levels of TC, HDL, LDL, TAG, or glucose (FPG?).* *Significant improvements were seen for women in TC:HDL (–2.0,* p<*0.01), TC (–0.88 mmol/l,* p<*0.0001), LDL (–0.74 mmol/l,* p<*0.01) and TAG (–0.5 g/l,* p<*0.0001).* *Significant improvements were seen for men in TC:HDL (–3.7,* p<*0.0001), TC (–1.78 mmol/l,* p<*0.0001), HDL (+0.68 mmol/l,* p<*0.0001), LDL (–2.04 mmol/l,* p<*0.0001), and TAG (–1.33g/l,* p<*0.0001), and glucose (–1.41mmol/l,* p<*0.01).*
Quality and comments	…

SOS Matched control cohort study (in Clegg TA)	
Results	HRQL (mean; 95% CI): Current health perception: 'general health rating index/current health scale ' Baseline: surgery 26.9 (26.1 to 27.7); control 29.4 (28.5 to 30.2). 2 years: surgery 34.3 (33.4 to 35.1); control 30.2 (29.4 to 31.1). Psychosocial functioning – 'obesity-related psychological problems': Change by 2 years (mean, 95% CI): Surgery males –1.01 (–1.14 to –0.87), females –1.10 (–1.19 to –1.00); Control males –0.07 (–0.17 to 0.03) (p=0.001); females –0.16 (–0.22 to –0.09) (p=0.001). 'Sickness impact profile/social interaction' Change by 2 years (mean, 95% CI): Surgery males –3.3 (–5.0 to –1.5), females –5.2 (–6.5 to –4.0); Control males 1.5 (0.2 to 3.2) (p=0.001); females 1.2 (0.2 to 2.2) (p=0.0001). Mental well-being scales – 'mood adjective checklist': Change by 2 years (mean, 95% CI): Pleasantness/unpleasantness: surgery 0.21 (0.16 to 0.26); control –0.04 (–0.09 to 0.01) (p=0.001); Activation/deactivation: surgery 0.32 (0.27,0.37); control 0.00 (–0.04 to 0.05) (p=0.001); Calmness/tension: surgery 0.20 (0.15,0.26); control –0.01 (–0.06 to 0.04) (p=0.001). Hospital Anxiety and Depression scale

Change by 2 years (mean, 95% CI):
Anxiety: surgery –1.7 (–2.0 to –1.4); control –0.6 (–0.9 to –0.2) (*p*=0.0001);
Depression: surgery –2.2 (–2.5 to –1.9); control –0.4 (–0.6 to–0.1) (*p*=0.0001);
At 24 months: improvement in surgical vs controls on all HQRL measures (*p*<0.0001).
Changes in all HRQL measures significantly related to magnitude of weight loss.

Type 2 diabetes:
2-year unadjusted incidence: controls 4.7%, surgical 0.0% (*p*=0.0012).
8-year unadjusted incidence: controls 18.5%, surgical 3.6% (*p*=0.0001).
Adjusted odds ratios of developing diabetes, 8 years:
Completers (*n*=437) 0.17 (95% CI 0.08 to 0.38).
All (ITT) (*n*=611) 0.16 (95% CI 0.07 to 0.36).

Hypertension:
2-year unadjusted incidence: controls 9.9%, surgical 3.2% (*p*=0.032).
8 year unadjusted incidence controls 25.8%, surgical 26.4% (*p*=0.91).
Adjusted odds ratios of developing hypertension, 24 months:
Completers (*n*=257) 0.27 (95% CI 0.07 to 0.99).
All (ITT) (*n*=377) 0.27 (95% CI 0.09 to 0.76)
Adjusted odds ratios of developing hypertension, 8 years:
Completers (n=257) 1.05 (95% CI 0.58 to 1.89).
All (ITT) (n=377) 1.01 (95% CI 0.61 to 1.67).

Lipids:
Adjusted odds ratios at 24 months (95% CI):
Hypertriglyceridaemia 0.10 (0.04 to 0.25), *p*<0.001.
Hypo HDL-cholesterolaemia 0.28 (0.16 to 0.49), *p*<0.001.
Hypercholesterolaemia 1.24 (0.84 to 1.8), *p*=NS.
Relative risks for recovery from disease:
Hyperinsulinaemia (n=221) 1.4 (1.2 to 1.7), *p*<0.00001.
Hypertriglyceridaemia (n=314) 1.9 (1.5 to 2.4), *p*<0.00001.
Hypo HDL-cholesterolaemia (n=216) 1.7 (1.4 to 2.1), *p*<0.00001.
Hypercholesterolaemia (n=531) 1.2 (0.95 to 1.5), *p*=NS.

Biliary disease and pancreatitis; frequencies over 2 years (%), Fisher's exact test and odds ratios (OR) (95% CI) adjusted for age and BMI at baseline:
Cholelithiasis, men: surgery 4.0, controls 1.2, *p*=0.011, OR 4.2 (1.5 to 12.0);
women: surgery 5.5, controls 4.5, p=0.328, OR 1.1 (0.7 to 1.8).
Cholecystitis, men: surgery 2.5, controls 0.7, *p*=0.058, OR 4.5 (1.2 to 17.1);
women: surgery 3.3, controls 2.5, p=0.379, OR 1.4 (0.7, 2.5).
Cholecystectomy, men: surgery 3.4, controls 0.7, *p*=0.008, OR 5.4 (1.5 to 19.6);
women: surgery 3.5, controls 2.3, *p*=0.191, OR 1.6 (0.9, 3.0).
Total biliary disease, men: surgery 4.1, controls 1.5, *p*=0.024, OR 3.5 (1.3 to 9.2);
women: surgery 6.8, controls 5.3, *p*=0.223, OR 1.2 (0.8, 1.9).
Pancreatitis, men: surgery 1.1, controls 0.2, *p*=0.219, OR 3.6 (0.4 to 31.2); women: surgery 0.7, controls 0.4, *p*=0.514, OR 1.8 (0.4 to 7.6).

Proportion on CVD medication, risk ratio (95% CI adjusted to mean values of sex, age and BMI at baseline):
Participants on medication at baseline, *n*: surgery 150, control 125.
Proportion on medication at:
2 years, %: surgery 61.7, control 91.2, RR 0.69 (0.60 to 0.80), *p*<0.05.
6 years, %: surgery 64.7, control 86.4, RR 0.77 (0.67 to 0.88), *p*<0.05.
Participants not on medication at baseline, *n*: surgery 360, control 330.
Proportion on medication at:
2 years, %: surgery 3.1, control 10.1, RR 0.28 (0.14 to 0.56), *p*<0.05.
6 years, %: surgery 13.3, control 16.7, RR 0.80 (0.56 to 1.16).

Proportion on diabetes medication, risk ratio (95% CI adjusted to mean values of

	sex, age, and BMI at baseline): Participants on medication at baseline, *n*: surgery 32, control 21. Proportion on medication at: 2 years, %: surgery 56.2, control 100.0, RR 0.56 (0.41 to 0.76), *p*<0.05. 6 years, %: surgery 68.8, control 100.0, RR 0.71 (0.56 to 0.89), *p*<0.05. Participants not on medication at baseline, *n*: surgery 478, control 434. Proportion on medication at: 2 years, %: surgery 0.2, control 3.7, RR 0.08 (0.01 to 0.58), *p*<0.05. 6 years, %: surgery 2.1, control 11.3, RR 0.20 (0.10 to 0.38), *p*<0.05. At 10 years, mean energy intake at the time of inclusion in the intervention study was 2882 kcal/ day among the surgically treated participants, as compared with 2526 kcal/day among the controls. The baseline adjusted energy intake was significantly lower in the surgery group than in the control group over the 10-year period (–20.7 vs –1.0%, *p*<0.001). Similarly, the fraction of participants physically active during leisure time was higher in the surgery group over the 10-year period, and the fraction of those physically active during work time was higher in the surgery group for the first 6 years of the intervention. *The WC was reduced more in the surgery group than in the control group after 10 years (–10.1 vs 2.8%,* p<*0.001). Glucose and insulin levels increased in the control group (+18.7 and +12.3%), whereas substantial decreases were seen in the surgically treated group after 10 years of observation (–2.5 and –28.2%,* p<*0.001 compared with control for both outcomes). Similarly, changes in uric acid, TAG and HDL-cholesterol levels were more favourable in the surgically treated group than in the control group 10 years. SBP was not significantly different at 10 years (0.5 vs +4.4%,* p=*NS). DBP (–2.6 vs –2.0%,* p<*0.001) and TC (–5.4 vs –6.0%,* p<*0.05) were reduced by more in the surgery group than in the control group after 10 years. The pulse-pressure increase was less pronounced in the surgery group than in the control group after 10 years (+10.8 vs +18.0%,* p<*0.05).* *The incidence rates of hypertriglyceridaemia (OR 0.61,* p=*0.03), diabetes (OR 0.25,* p<*0.001), and hyperuricaemia (OR 0.49,* p<*0.001) were markedly lower in the surgically treated group than in the control group 10 years. The incidence of low HDL-cholesterol was not significantly different in the surgical group after 10 years. The incidence of hypertension and hypercholesterolaemia did not differ between the groups over 10-year periods.* *Recovery from hypertension (OR 1.68,* p=*0.02), diabetes (OR 3.45,* p=*0.001), hypertriglyceridaemia (OR 2.57,* p<0*.001), a low HDL-cholesterol level (OR 2.35,* p=*0.001), and hyperuricaemia (OR 2.37,* p<*0.001) was more frequent in the surgical group than in the control group at 10 years. The rates of recovery from hypercholesterolemia did not differ between the two groups after 10 years.*
Quality and comments	…

Complications

Andersen 1984 (in Clegg TA Andersen 1988) RCT	
Harms	*No surgery participants needed to be re-operated.* *Perioperative complications (gastroplasty only,* n=*27): subphrenic abscess 7%; atelectasis/pneumonia 4%; wound infection 4%.* *Later complications (gastroplasty [*n=*27] vs VLED [n=30]): thrombophlebitis (4 vs 0%); nausea (15 vs 7%); heartburn (11 vs 0%); ructus (1 vs 0%); pain projected to left shoulder (15 vs 0%); epigastric pain (22 vs 10%); outlet obstruction (4 vs 0%); vomiting (52 vs 0%,* p<*0.05); cholesystectomy (7 vs 0%); obstipation (26 vs 13%); orthostatic hypotension (7 vs 27%); dizziness (7 vs 17%); transient loss of hair (15 vs 10%); headache (11 vs 17%); fatigue (30 vs 53%); irritability and low spirits (0 vs 33%,* p<*0.05); gout (0 vs 3%); staple line rupture (4 vs 0%), ventral hernia (4 vs 0%); abortion (4 vs 0%).*

	Two (6%) VLED patients had gastroplasty elsewhere having regained all weight lost on diet.
Quality and comments	…

Mingrone 2002 RCT	
Harms	None reported.
Quality and comments	…

SOS Matched control cohort study (in Clegg TA)	
Harms	*Postoperative mortality (at 8 years): four (0.2%) deaths, three due to leakage detected too late and one due to a technical laparoscopic mistake.* *Perioperative complications: 13% experienced complications. Bleeding 0.9%, thrombo-embolic events 0.8%, wound complications 1.8%, abdominal infection 2.1%, pulmonary symptoms 6.2%, miscellaneous 4.8%.* *Re-operation: 2.2%.* At 10 years, five of the 2010 participants who underwent surgery (0.25%) died postoperatively.
Quality and comments	…

Generalisability

Andersen 1984 (in Clegg TA Andersen 1988) RCT	
Country and setting	Denmark. Hospital obesity clinic.
Participants (included/excluded)	*Included consecutive patients referred for surgery assessed for eligibility and asked for consent.* *Excluded if less than 60% overweight (three), not aged between 18–54 years (14), not attempted previous treatments (three), chronic bronchitis (one), alcohol or drugs abuse (six), ongoing obesity treatment (two), unwillingness to co-operate or occupational or geographic factors impeding participation (21). Of 78 eligible, 11 refused surgical and three refused non-surgical treatment, four dropped out before random assignment, two refused after random assignment to gastroplasty, gastroplasty could not be performed in one patient due to hepatomegly.*
Recruitment	From participants referred for surgery.
Randomisation	No details.
Intervention (mode and intensity)	*Seen at weekly intervals initially, then every 2 weeks after 3 months. Also invited to weekly meetings after cessation of weight loss.*
Comparison (mode and intensity)	Seen at weekly intervals initially, then every 2 weeks after 3 months. Also invited to weekly meetings after cessation of weight loss.
Delivery of intervention/comparison (who)	Group meetings lead by clinical dietitians.
Dropout rates	*2% surgery and 2% diet in 2-year study. Further 2% from surgery during 5 years follow-up.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only?

Mingrone 2002 RCT	
Country and setting	Italy. No details.

Participants (included/excluded)	Included if aged 30 to 45 years. Excluded if pregnant; history or diagnosis of diabetes, heart disease, hypertension, or other chronic diseases; hormone replacement therapy; chronic steroid therapy; a history of alcohol or drug abuse; and glucose intolerance, defined as a 2 h glucose level of >140 mg/dl after a 75 g oral glucose load and of stable weight (within ±2 kg, 6 months before testing).
Recruitment	N/R
Randomisation	N/R
Intervention (mode and intensity)	N/R
Comparison (mode and intensity)	N/R
Delivery of intervention/comparison (who)	N/R
Dropout rates	*0% overall*
Treatment of dropouts (return to baseline, or last measurement?)	No dropouts and no crossing assumed.

SOS Matched control cohort study (in Clegg TA)	
Country and setting	Sweden. Multi-centre, primary care-based.
Participants (included/excluded)	Included if aged 37–60 years, BMI 38 kg/m^2 for women and 34 kg/m^2 for men. Excluded if previous bariatric surgery, gastric surgery for other causes in last 6 years, serious health problems including active malignancy and recent MI, bulimic eating pattern, drug or alcohol abuse, psychological problems likely to lead to poor co-operation, regular use of cortisone or NSAIDs.
Recruitment	Recruited through mass media and primary healthcare centres, and participants could volunteer for conventional or surgical treatment.
Randomisation	N/A
Intervention (mode and intensity)	*Varied.*
Comparison (mode and intensity)	Varied.
Delivery of intervention/comparison (who)	Varied – care provided by registered centre. No details.
Dropout rates	*27% surgical, 33% control at 8 years. 25% surgical, 26% control at 10 years.*
Treatment of dropouts (return to baseline, or last measurement?)	**Not sure of follow-up values?

1.7.3 Restrictive surgery

1.7.3.1 Laparoscopic (adjustable) gastric banding vs GBP

Comparative studies

Weight loss

Biertho 2003 (in TEC) case control

Aim	To compare the results of laparoscopic (adjustable) gastric banding (LAGB) and laparoscopic GBP.
Participants	Adults undergoing bariatric surgery Total 1261 – 997 F, 264 M. Mean (SD) age 41.7 (10.9) years LAGB (*n*=805), 40.2 (10.5) years laparoscopic GBP (*n*=456). Mean (SD) BMI (kg/m^2) 42.2 (4.9) LAGB, 49.4 (8.3) laparoscopic GBP.
Intervention	*Surgery: LAGB* *After the operation, followed in an outpatient clinic every 2 months for the first year, and then every 3 months for the following years. The gastric band was slowly inflated. Patients were evaluated every 3 months, and no inflation was done if a 1 kg weight loss had been noted in the past 3 months.*
Comparison	Surgery: Laparoscopic GBP After the operation, followed in an outpatient clinic every 3 months for the first year, and then every 6 months for the following years.
Length of follow-up	*18 months for key outcomes but TEC reported follow-up of 36.9 months?*
Results	% Excess weight loss (EWL)

Month	***3***	***5***	***12***	***18***
LAGB	*15*	*22*	*33*	*40*
Laparoscopic GBP	*36*	*52*	*67*	*75*

The EWL for patients in the laparoscopic GBP vs LABG groups at 12 months was 75 vs 37%, respectively, for patients with a BMI between 30 and 40 kg/m^2; 81 vs 40%, respectively, at 18 months for patients with a BMI between 40 and 50 kg/m2; and 69% vs 33%, respectively, at 18 months for patients with a BMI between 50 and 60 kg/m^2.
The weight loss analysis also showed an inverse correlation between preoperative weight and EWL: the heavier the patient, the smaller the EWL. This is illustrated by the inferior EWL for patients with a BMI between 50 and 60 kg/m^2 (69% in the bypass group and 33% in the LAGB group after 18 months) compared with patients with a BMI between 40 and 50 kg/m^2 (81 and 40%).
*In the laparoscopic GBP group, a super-super-obese group (BMI >60 kg/m^2) was available for analysis (*n=*40). In this group, the EWL was 36.1% at 3 months (*n=*35, 87.5%), 51.7% at 6 months (*n=*24, 60%), and 66.9% at 12 months (*n=*14, 35%).*

Quality and comments	*LGB group were significantly heavier than the LAGB group (135.4±26.3 kg vs 117±17.1 kg,* p=*0.0001). This difference was also expressed by a higher preoperative BMI (49.4±8.3 vs 42.2±4.9 kg/m^2,* p=*0.0001).* *Assessed by TEC: operations carried out in two different institutions in different countries, follow-up not reported, details of care not reported, ITT not done. Poor.*
Sponsor details	*N/R*

Weber 2004 (in TEC) case control

Aim	To define whether LAGB or laparoscopic Roux-en-Y GBP (LGBP) represents the better approach to treat patients with morbid obesity.
Participants	Adults undergoing bariatric surgery at one institution. Total 206 – 168 F, 38 M. Mean (SD) age 39.6 (10.1) years LAGB (*n*=103), 40.1 (9.9) years LGBP (*n*=103). Mean (SD) BMI (kg/m^2) 48.0 (6.3) LAGB, 47.8 (6.1) LGBP. Excess (SD) weight (kg) 73.0 (17.9) LAGB, 72.3 (17.6) LGBP.
Intervention	*Surgery: LAGB*
Comparison	Surgery: LGBP
Length of follow-up	*24 months*
Results	Weight loss was significantly different between both groups in favour of the bypass procedure. Already after 1 month and thereafter at every time point of follow-up, 3, 6, 9, 12, 18 and 24 months, BMI values differed significantly between the groups (*p*<0.02, range <0.001–0.012).

Months	0	1	3	6	9	12	18	24
LAGB	48.0	46.0	43.6	42.0	40.1	39.0	36.7	36.8
LGBP	47.8	43.7	39.3	36.2	33.8	33.1	33.2	31.9

The mean BMI decreased in the bypass group from 47.8 to 31.9 kg/m^2, whereas in the banding group the decrease was from 48.0 to 36.8 kg/m^2.

Regarding % excessive weight loss, similar findings with a significant difference at every time point of follow-up favouring the bypass procedure were seen.

Months	0	1	3	6	9	12	18	24
LAGB	0	8.2	16.4	24.9	30.7	35.1	41.9	42.1
LGBP	0	15.0	32.8	44.0	52.0	54.8	55.0	54.0

*The %EWL after 24 months was 54.0% in the LAGB group vs 42.1% in the LGBP group (*p<*0.05, range <0.001–0.043). After 12 months, body composition was routinely measured with an impedance analysis showing a mean fat mass loss of 38.8% for the bypass group vs 26.6% for the banding patients (*p<*0.001).*

Quality and comments	*First 50 patients with LAGB or LGBP were excluded to avoid a learning curve bias. Assessed by TEC: details of follow-up not reported. ITT not done. Fair.*
Sponsor details	*None reported.*

Other outcomes

Biertho 2003 (in TEC) case control

Results	*Postoperative stay after laparoscopic GBP was significantly less than after LAGB (3 vs 5 days,* p<*0.05), but this was probably related more to the differences in the health system in the two countries than to the operation itself.*
Quality and comments	…

Weber 2004 (in TEC) case control

Results	*The prevalence of comorbidities, such as arterial hypertension (60 vs 52%,* p=*0.35), diabetes mellitus type II (44 vs 37%,* p=*0.21), and dyslipidaemia (62 vs 74%,* p=*0.06), was comparable in the 2 groups (LAGB vs LGBP) before surgery. The frequency of all these comorbidities decreased in the follow-up period, with one exception of dyslipidaemia in the banding patients. The prevalence of hypertension dropped from 52 to 13% in the bypass group, and from 60% to 18% in the banding group. Diabetes declined from 37 to 6%, and 44 to 18%, respectively, leading to a significantly lower frequency in the bypass patients (*p=*0.007) in the follow-up. Dyslipidaemia was significantly lower in the bypass group after follow-up, than in the banding group (*p=*0.001).*

Quality and comments	…

Complications

Biertho 2003 (in TEC) case control	
Harms	Mortality: LAGB 0%, 0.44% laparoscopic GBP in first 30 days (*p*=NS). Major intraoperative complications: LAGB 10 (1.3)% – bleeding 4, liver haematoma 3, oesophageal perforation 1, haemorrhage from gastroepiploic artery 1, gas embolism 1; laparoscopic GBP 9 (2.0%) – major leakage of gastrojejunal anastomosis 3, Roux limb too short 3, revision of gastric pouch because of haematoma 1, end-to-end anastomosis pulled through stomach 1, nasogastric tube stapled 1. Conversion: LAGB 24 (3.0%) – difficulties with obesity 10, technical difficulties 7, hepatomegaly 4, splenectomy for bleeding 1, oesophageal perforation 1, haemorrhage from gastroepiploic artery 1: laparoscopic GBP 9 (2.0%) – excessive intraabdominal obesity 2, hepatomegaly 2, Roux limb too short 2, leakage of gastrojejunal anastomosis 1, end-to-end anastomosis pulled through stomach 1, nasogastric tube stapled 1. Note: in the LAGB group, most conversions occurred during the introduction of the technique. When last 400 cases were considered, conversion rate fell to 2% (*n*=8). Early major postoperative complications: LAGB 14 (1.7%) – pneumonia 8, pulmonary embolism 2, port haematoma 2, acute abdomen 1, port infection 1; laparoscopic GBP 19 (4.2%) - leakage of gastrojejunal anastomosis 6, deep vein thrombosis 4, gastric dilatation 2, intraabdominal bleeding 2, fistula on Roux limb 1, intestinal bleeding 1, paresia left arm 1, pneumonia 1. Late major complications: LAGB 46 (5.8%); laparoscopic GBP 37 (8.1%); LAGB Port-a-Cath+tube 23 (2.9%); LAGB others 4 (0.5%); LAGB total 73 (9.1%).
Quality and comments	…

Weber 2004 (in TEC) case control	
Harms	There was one conversion to open surgery in the bypass group because of a staple device malfunction, whereas in the banding group no conversion was necessary. The operation time was significantly longer for the bypass procedure than for the gastric banding (190 vs 145 min; *p*<0.001). The hospital stay was also significantly longer for the bypass procedure (8.4 vs 3.3 days; *p*<0.001). There was zero mortality in either group. Morbidity was reported as early complications within 30 days after surgery and late complications thereafter. To compare the severity of the complications, rates of re-interventions were reported and divided further to surgical re-operation and endoscopic dilatation. Early complications: 21 cases in the bypass group and 18 in the banding group (*p*=0.36). Re-interventions, including endoscopic dilatation, due to early complications were performed in 11 cases in the bypass group and once in the banding group (*p*=0.003). Surgical re-operations were indicated in 7 bypass patients and in 1 banding patient (*p*=0.033). Early complications were: LGBP wound/port site infections 8, intra-abdominal abscess 1, bleeding 1, stenosis at gastrojejunostomy 4, internal herniation 2, leakage at gastrojejunostomy 2, small bowel perforation 1, bleeding in remnant stomach 1, pulmonary embolism 1; LAGB wound/port site infections 16, intra-abdominal abscess 1, bleeding 1. Late complications: occurred in 14 patients in the bypass group and in 45 in banding group. Re-interventions were undertaken in 9 bypass patients and 26 banding patients (*p*=0.001). Late complications were: LGBP band slippage/pouch formation 1, stenosis at gastrojejunostomy 5, internal herniation2, gastrogastric fistula 1, incisional hernia at trocar site 1, pancreatitis 1, perisplenic abscess 1,

	cellulitis abdominal wall 1; LAGB band slippage/pouch formation 37, with oesophageal dysmotility 25, band leakage 4, band penetration 2, primary failure 1, port site infection 1. All 26 banding patients required surgery. Seventeen patients with banding were converted to a bypass, whereas no patient with a bypass was switched to another procedure. Four patients had their band replaced due to leakage of the band system, three patients due to secondary failure with pouch dilatation and weight gain, and one required a band repositioning for primary band failure. One port replacement was done. Surgery was necessary in only four of nine patients treated with GBP (p<0.001). Five patients underwent endoscopic dilatation.
Quality and comments	…

Generalisability

Biertho 2003 (in TEC) case control	
Country and setting	US and Switzerland. Specialist centres?
Participants (included/excluded)	Inclusion criteria for LAGB were a BMI >40 kg/m^2, or a BMI >35 kg/m^2 with at least one obesity-related morbidity, and failure of previous medical treatment. Patients with a BMI above 50 kg/m^2 were usually considered for a GBP, performed by laparotomy. The main indications for laparoscopic GBP were a BMI >40 kg/m^2 or >35 kg/m^2 with associated comorbidities. Patients with a BMI above 60 kg/m^2 were usually considered for a laparoscopic biliopancreatic diversion.
Recruitment	From referrals?
Randomisation	N/A
Intervention (mode and intensity)	*LAGB with follow-up in an outpatient clinic every 2 months for the first year, and then every 3 months for the following years. The gastric band was slowly inflated. Patients were evaluated every 3 months, and no inflation was done if a 1 kg weight loss had been noted in the past 3 months.*
Comparison (mode and intensity)	laparoscopic GBP with follow-up in an outpatient clinic every 3 months for the first year, and then every 6 months for the following years.
Delivery of intervention/comparison (who)	N/R.
Dropout rates	*3% LAGB, 13% laparoscopic GBP at 12 months.*
Treatment of dropouts (return to baseline, or last measurement?)	N/R – results for completers only.

Weber 2004 (in TEC) case control	
Country and setting	Switzerland. University hospital.
Participants (included/excluded)	Included for bariatric surgery if BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with comorbidities, history of obesity more than 5 years, failed conservative treatment of more than 2 years, and age between 18 and 60 years.
Recruitment	From clinic?
Randomisation	N/A
Intervention (mode and intensity)	*The choice for the type of surgery was based on the time when the operation was performed. In the first period of the study (from May 1995 until June 2000), preferentially performed laparoscopic banding procedures as bariatric operation. Based on the growing evidence progressively switched to LGBP after June 2000.*

Comparison (mode and intensity)	As above
Delivery of intervention/comparison (who)	Routine evaluation from MDT (nutritionist, endocrinologist, psychologist, surgeon) using standardised protocol.
Dropout rates	*Not clear.*
Treatment of dropouts (return to baseline, or last measurement?)	Not clear.

Laparoscopic (adjustable) gastric banding

Single arm studies

Table 1 Study characteristics and weight loss outcomes

Study	Mean age (years)	Mean BMI (kg/m^2)	% Male	Follow-up (months)	No. enter/eval	No. at follow-up (years) and weight loss outcome(s)					Prosp/Cons[§]	Pre-operative workup
						1	2	3	4	5		
Lap-Band™												
Angrisani 2001	38	44.1	20	48	1265	NR BMI –9.0	NR BMI –13.9	NR BMI –12.0	NR BMI –12.6	…	…	…
Angrisani 2003	37.8	43.7	19.0	72 (maximum)	1893	NR BMI –10.0	NR BMI –8.9	NR BMI –9.6	NR BMI –11.0	NR BMI –8.9	Cons	…
Belachew 1998	35.5	42.9	21	36	350	NR EWL 50% BMI –10.9	NR EWL 58% BMI –11.9	NR EWL 77% BMI –16.9	…	…	Cons	…
Belachew 2002	34	42	22	48 (min)	763/687	NR EWL 40% BMI –10	NR EWL 50% BMI –12	NR EWL 60% …	NR EWL 52% …	NR EWL 66% BMI –12	…	…
Busetto 2002	37.6	46.6	28	36	260	252 EWL 40% BMI –8.6	247 … BMI –9.6	250 EWL 43% BMI –9.6	…	…	Cons	Yes
Cadiere 2000	40	45	24	24	652	NR EWL 38% BMI –10	NR EWL 62% BMI –12	…	…	…	Cons	…
Chevallier 2002	40.2	43.8	12	24	400	168 EWL 42% BMI –9.5	33 EWL 53% BMI –11.1	…	…	…	Prosp; cons	Yes
Dargent 1999	39.4	43	16	36	500	270 EWL 56%	96 EWL 65%	19 EWL 64%	…	…	Cons	…
Dargent 2004	39.5	43.3	15.4	108 (maximum)	1180	696 EWL 49%	573 56% EWL	434 EWL 57%	321 EWL 57%	190 54% (at 6 years, 86, 49% EWL, at 7 years, 14, 50% EWL)	Cons	…
Favretti 2002	37.9	46.4	22	84	830/805	660 BMI –9.1	479 BMI –10.0	305 BMI –9.6	185 BMI –9.8	74 BMI –10.0	Cons	Yes

[§] PROSP prospective study, CONS consecutive patients.

Study	Mean age (years)	Mean BMI (kg/m^2)	% Male	Follow-up (months)	No. enter/eval	No. at follow-up (years) and weight loss outcome(s)					Prosp/Cons[§]	Pre-operative workup
						1	2	3	4	5		
FDA data 2000	38.8	47.4	15	36	299	233 EWL 35% BMI –8.5	189 EWL 38% BMI –9.4	178 EWL 36% BMI –9.8	…	…	Prosp; cons	Yes
Frigg 2004	41	45	21	44 (mean)	295	243 EWL 40% BMI –8	200 EWL 46% BMI –10	155 47% EWL BMI –10	98 54% EWL BMI –11	…	Cons	…
Holloway 2004	NR	49	18	36 (maximum)	504	311 EWL 50% BMI –13	122 EWL 61% BMI –16	40 65% EWL BMI –16	…	…	Cons	Yes
Miller 1999	36	44	10	28 (mean)	166/156	NR BMI –10	NR BMI –14	NR BMI –16	…	…	Prosp; cons	Yes
O'Brien 2002	41	45	15	72	709	492 EWL 47% BMI –10	336 EWL 53% BMI –12	273 EWL 53% BMI –12	112 EWL 52% BMI –13	32 EWL 54% BMI –13 (at 7 years, 10, 54% EWL, and BMI –13)	Prosp; cons	Yes
Parikh 2005	43	55.3	30	36	180	158 EWL 35.3%	85 EWL 45.8%	31 49.5%	…	…	…	…
Spivak 2004	40	45.3	13	24 (maximum)	271	72 EWL 40% BMI –9	21 EWL 43% BMI –10.6	…	…	…	Cons	…
Vertruyen 2002	41	44	10	36 (mean)	543/521	NR EWL 38% BMI –10.8	NR EWL 61% BMI –12.7	NR EWL 62% BMI –13.9	NR EWL 58% BMI –12.6	NR EWL 53% BMI –12.8 (at 86 months, 52% EWL, and BMI –11.9)	Cons	Yes
Weiner 1999	35.2	47.8	11	24	184	112 EWL 58% BMI –15.8	53 EWL 87% BMI –19.2	…	…	…	…	…
Swedish adjustable gastric band												
Biertho 2005	43	42.4	22.8	39.6 (mean)	824	821 EWL 30%	744 EWL 42%	593 EWL 48%	380 EWL 52%	184 EWL 55%	Prosp; cons	…
Greenslade 2004	40.1	42.9	14	48 (maximum)	215	NR EWL 45% BMI –9.9	NR EWL 58% BMI –10.9	NR EWL 55% BMI –11.4	NR EWL 50% BMI –11.9	NR EWL 44%	Prosp; cons	Yes

Table 2 Adverse outcomes

Study	*n*	Perioperative complications (%)							Long-term complications (%)								
		Death	Perf	Conv	Throm	Card	Bleed	Wound	Reop	Rem	SI/Dil	Eros	Oesoph	Obstr	Port	Hern	GORD
Lap-Band™																	
Angrisani 2001	1265	0.6	0.4	1.7	0.2	0.2	0.4	–	3.2	0.6	5.2	1.9	–	–	4.3	–	–
Angrisani 2003	1893	0.3	…	3.1	…	…	…	…	…	0.9	…	1.1	4.8	…	4.1	…	…
Belachew 1998	350	0	0.3	1.4	0	–	–	0	13.4	2.6	13	–	–	–	–	–	–
Belachew 2002	763	0.1	0.6	1.3	–	–	0.1	0.1	11	3.1	8.0	0.9	–	–	2.5	0	–
Busetto 2002	260	0	0.8	4.2	–	…	4.6	…	4.2	1.9	12	0.8	–	–	29	–	–
Cadiere 2000	652	0.2	0.3	3.8	0	0.2	–	0	4.4	–	3.8	0.3	0.2	–	2.7	–	–
Chevallier 2002	400	0	1	3	0	1.8	–	–	8.8	5.8	8.5	0	–	–	7.5	0.5	–
Dargent 1999	500	0	0.2	1.9	–	–	–	0.6	5.2	1.4	5.0	0.6	–	–	–	–	–
Dargent 2004	1180	0.2	0.5	0.4	0.2	0.5	…	0.2	12.7	5.6	8.8	1.9	2.0	…	…	…	…
Favretti 2002	830	0	0.1	2.7	–	–	–	–	3.9	1.7	10	0.5	–	–	–	–	–
FDA data 2000	299	0	0.7	0.7	0.3	–	–	14	24	15	24	1.0	10	14	8.7	5.4	34
Frigg 2004	...	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
Holloway 2004	504	0.2	1.8	0.2	…	0.2	…	…	…	2.6	5.6	0.4	…	…	8.5	…	…
Miller 1999	166	–	0.6	1.9	–	–	0.6	0.6	7.0	3.2	1.3	0.6	1.3	–	2.5	–	–
O'Brien 2002	709	0	0.3	1.0	0.3	0.7	–	3.4	19	1.7	13	2.8	–	–	3.6	–	–
Parikh 2005	180	0	…	…	…	…	…	0.5	0.5	…	…	…	…	1.0	1.0	…	…
Spivak 2004	271	…	…	1.1	0.4	0.7	0.4	…	…	…	1.8	…	6.6	1.8	7.3	…	…
Vertruyen 2002	543	–	1.3	1.1	0.2	0.4	0.2	–	5.9	2.6	4.6	0.9	–	–	2.8	–	–
Weiner 1999	184	0	–	0	–	–	0.5	–	5.4	1.6	2.2	1.1	–	2.2	3.2	–	–
Swedish adjustable gastric band																	
Biertho 2005	824	0.1	0.1	8.3	…	…	…	…	14.7	…	4.2	…	7.5	…	6.7	…	…
Greenslade 2004	215	–	–	–	–	–	–	–	–	1.9	0	1.4	…	…	7.5	…	…

Bleed, bleeding complications; Card, cardiopulmonary complications, e.g. MI, congestive heart failure, pneumonia, respiratory failure; Conv, conversion from laparoscopic to open procedure; Death, death within 30 days of operation; Eros, erosion of adjustable band through oesophageal/stomach wall, or erosion into other visceral organ; GORD,; Hern, abdominal wall hernia at incision or port site; Obstr, bowel obstruction resulting from procedure; Oesoph, oesophageal abnormalities; Perf, perforation of bowel and/or visceral organ, including splenic injury; Port, complications at the port access site, including infection, dysfunction, and/or revisions; Rem, removal of band; Reop, re-operation resulting from a complication of the original procedure; Sl/Dil, slippage of adjustable band or dilation of proximal GI tract; Throm, thromboembolic complication; Wound, wound complications, including infection and dehiscence.

1.7.4 Restrictive/malabsorptive surgery

1.7.4.1 ***GBP***

Comparative studies

See other sections for comparison with LAGB and duodenal switch-bileopancreatic diversion (DS-BPD)

1.7.4.2 ***GBP (open)***

Single arm studies

Table 3 Study characteristics and weight loss outcomes

Study	Mean age (years)	Mean BMI (kg/m^2)	% Male	Follow-up (months)	No. enter/eval	No. at follow-up (years) and weight loss outcome(s)					Prosp/Cons[5]	Pre-operative workup
						1	2	3	4	5		
Avinoah 1992	36.1 (*n*=200)	…	29 (*n*=200)	80 (mean)	450/200	102 EWL 69%	198 65% EWL	103 (25 to 72 months) 48% EWL	…	88 (73 to 96 months) EWL 56%	…	…
Balsiger 2000	42 (median)	49 (median)	25.7	48	191	113 BMI –18	88 BMI –19	72 BMI –17	55 BMI –16	…	Prosp; cons	Y
Csendes 2005	38.5	46	22.3	36 (maximum)	400	115 BMI –18.3	55 BMI –18.4	14 BMI –18.3	…	…	Prosp	Y
Oh 1997	32.5	45.18	13.4	48	194/193	93 EWL 69% BMI –18	48 EWL 71% BMI –18.5	31 EWL 70% BMI –18	14 EWL 55% BMI –16.5	…	Prosp; cons	..
Pories 1995	37.3	49.7	16.8	168	608	506 EWL 69%	…	…	…	317 EWL 58% (at 10 years, 158, 55% EWL, at 14 years, 10, 49% EWL)	…	Y
Schoepel	41.7	50.2	13.1	24 (maximum)	168/85	85 EWL 51%	85 EWL 55%	…	…	…	…	…
Torres 1983	34	…	10.7	24 (maximum)	300	300 –48.5 kg	300 –52.0 kg	…	…	…	Cons	Y

[5] PROSP prospective study, CONS consecutive patients.

Table 4 Adverse outcomes

Study	*n*	Perioperative complications (%)								Long-term complications (%)							
		Death	Perf	Anas	Bleed	Obstr	Thromb	Card	Wound	Reop	Sten	Obstr	Ulcer	Nutr	N/V	Hern	Chol
Avinoah 1992	200	…	…	…	…	…	…	…	…	…	…	…	…	51% meat intolerance	…	…	…
Balsiger 2000	191	0.5	0.5	0.5	0.5	…	0.5	2.1	5.8	5	1	…	0.5	23% milk intolerance	4	17	0.5
Csendes 2005	400	0.5	…	2.5	0.75	0.25	…	…	1.25	…	…	2.0	…	…	…	10.2	…
Oh 1997	193	0	1.03	0	…	…	…	0.52	1.03	…	…	3.61	4.12	…	…	8.25	3.09
Pories 1995	608	1.5	2.5	3.0	…	…	…	…	14.6	2.8	…	…	…	40% vitamin B_{12} deficiency, 39% anaemia	…	23.9	11.4
Schoepel 2001	85	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
Torres 1983	300			0.7	2			0.3	2	12							

Anas, complication at one of the anastomic sites (stenosis, stricture, leak, staple line failure); Bleed, bleeding complications; Card, cardiopulmonary complications, e.g. MI, congestive heart failure, pneumonia, respiratory failure; Death, death within 30 days of operation; Chol, cholecystitis requiring cholecystectomy; Hern, hernial complications; Nutr, nutritional complications; N/V, nausea and/or vomiting; Obstr, bowel obstruction resulting from procedure; Perf, perforation of bowel and/or visceral organ, including splenic injury; Reop, re-operation resulting from a complication of the original procedure; stenosis;
Throm, thromboembolic complication; Ulcer, stomal, pouch, limb, near site of procedure; Wound, wound complications, including infection, necrosis and dehiscence.

1.7.4.3 GBP (laparoscopic)

Single arm studies

Table 5 Study characteristics and weight loss outcomes

Study	Mean age (years)	Mean BMI (kg/m^2)	% Male	Follow-up (months)	No. enter/eval	No. at follow-up (years) and weight loss outcome(s)					Prosp/Cons[6]	Pre-op workup
						1	2	3	4	5		
Ballesta-Lopez 2005	38.7	44.4	21	30 (maximum)	600	NR EWL 66% BMI –13	NR EWL 69% BMI –13	…	…	…	Cons	…
Higa 2001	13–73 (range)	35–78 (range)	18	36	1500/1497	572 EWL 69%	51 EWL 69%	19 EWL 62%	…	…	Cons	…
Schauer 2000	42	48.32	29	31 (maximum)	275	101 EWL 68.8% BMI – 16.75	19 EWL 83.2% BMI – 20.86	…	…	…	Prosp; cons	Y
Schauer 2003	48	50.4	25	48	240/191	97 EWL 59.9% BMI –16.2	42 EWL 66.5% BMI –16.8	33 EWL 59.1% BMI –15.0	11 EWL 52.1% BMI – 13.0	…	Prosp	Y
Wittgrove 2000	…	…	…	60 maximum	500	… EWL 77%	… EWL 81%	92 EWL 75%	36 EWL 75%	4 EWL 82%	Prosp; cons	Y

Table 6 Adverse outcomes

Study	*n*	Perioperative complications (%)							Long-term complications (%)								
		Death	Conv	Perf	Anas	Bleed	Obstr	Thromb	Card	Wound	Reop	Sten	Obstr	Ulcer	Nutr	N/V	Hern	Chol
Ballesta-Lopez 2005	600	1.1	0.5	0.3	3.8	1.6	…	…	0.1	0.1	1.8	0.1	0.6	1.2	…	…	…	0.6
Higa 2001	1497	0.2	1.3	0.3	0.7	0.8	0.2	0.2	0.1	0.1	0.1	5.6	…	0.8	…	…	2.5	2.1

[6] PROSP prospective study, CONS consecutive patients.

Study	*n*	Perioperative complications (%)									Long-term complications (%)							
		Death	Conv	Perf	Anas	Bleed	Obstr	Thromb	Card	Wound	Reop	Sten	Obstr	Ulcer	Nutr	N/V	Hern	Chol
Schauer 2000	275	0.4	1.1	…	8.4	3.3	1.1	1.1	0	9.1	9.8	…	0.3	0.7	23.8	12	0.6	1.5
Schauer 2003	191	0.5	1.6	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
Wittgrove 2000	500	0	…	…	2.2	0.8	…	…	1.4	5	0.03	1.6	0.6	…	…	…	…	…

Anas, complication at one of the anastomic sites (stenosis, stricture, leak, staple line failure); Bleed, bleeding complications; Card, cardiopulmonary complications, e.g. MI, congestive heart failure, pneumonia, respiratory failure; Conv, conversion from laparotomy to open; Death, death within 30 days of operation; Chol, cholecystitis requiring cholecycstectomy; Hern, hernial complications; Nutr, nutritional complications; N/V, nausea and/or vomiting; Obstr, bowel obstruction resulting from procedure; Perf, perforation of bowel and/or visceral organ, including splenic injury; Reop, re-operation resulting from a complication of the original procedure; Sten, stenosis; Throm, thromboembolic complication; Ulcer, stomal, pouch, limb, near site of procedure; Wound, wound complications, including infection, necrosis and dehiscence.

1.7.4.4 ***Laparoscopic vs open GBP***

Comparative studies

Weight loss

Lujan 2004 RCT	
Aim	To compare the results of open vs laparoscopic GBP in the treatment of severe obesity.
Participants	People who were severely obese (BMI >40 kg/m^2) without coexisting pathological disorders) or who were obese (BMI >35 kg/m^2) with coexisting pathological disorders. Total 104 – 81 F, 23 M. Mean (range) age 37 (18–64) years laparoscopic GBP (*n*=53), 38 (20–63) years open GBP (*n*=51). Mean (range) weight 130.70 (92–208) kg laparoscopic GBP, 137.57 (97–214) kg open GBP.
Intervention	*laparoscopic GBP*
Comparison	Open GBP
Length of follow-up	*36 months*
Results	*No statistical analysis of weight loss. From graph, laparoscopic and open GBP appeared to perform very similarly over time (36 months, mean follow-up 23 months) (described as 'similar' by the authors).* BMI (kg/m^2; estimated from figure), *p*=NS. 3 months: Laparoscopic 41, Open 47. 6 months: Laparoscopic 36, Open 41. 12 months: Laparoscopic 33, Open 37. 18 months: Laparoscopic 31, Open 36. 24 months: Laparoscopic 32, Open 35. 36 months: Laparoscopic 31, Open 35.5. (FROM CR)
Quality and comments	Blinded assessment not reported. ITT not stated, but probably as 0% loss to follow-up, and no mention of crossing groups.
Sponsor details	*None reported.*

Nguyen 2001 (in Clegg TA) RCT	
Aim	To compare outcomes, quality of life, and costs of laparoscopic and open GBP.
Participants	People who were severely obese (40>BMI (kg/m^2)<60). Total 155 – 139 F, 16 M. Mean (SD) age 40 (8) years laparoscopic GBP (*n*=79), 42 (9) years open GBP (*n*=76). Mean (SD) weight 131.1 (17.2) kg laparoscopic GBP 134.3 (20.0) kg open GBP.
Intervention	Laparoscopic GBP: Other: Pre-operative and post-operative antibiotics, antiembolic stockings and sequential pneumatic compression devices. Postoperative pulmonary care incentive spirometry and deep breathing exercises. Patient controlled analgesia using intravenous morphine.
Comparison	*Open GBP:* *Other: as above*
Length of follow-up	Up to 12 months
Results	*No weight loss data suitable to add to analysis.* Percentage excess body weight loss (not ITT): 3 months laparoscopic GBP (*n*=60) 37±1%; open GBP (*n*=56) 32±10% (*p*=0.01) 6 months laparoscopic GBP (*n*=45) 54±14%; open GBP (*n*=44) 45±12% (*p*=0.01) 12 months laparoscopic GBP (*n*=29) 68±15%; open GBP (*n*=25) 62±14% (*p*=0.07)

Quality and comments	From Clegg TA QA: blinded assessment not done.
Sponsor details	*None reported.*

Sundbom 2004 RCT	
Aim	To determine whether patients derive significant benefit from hand-assisted laparoscopic GBP in comparison to open surgery.
Participants	People who were referred for surgery? Total 50 – 45 F, 5 M. Median (range) age 37 (19 to 54) years laparoscopic GBP (*n*=25), 38 (24 to 54) years open GBP (*n*=25). Median (range) BMI (kg/m^2) 44 (36 to 54) laparoscopic GBP, 45 (34 to 54) open GBP.
Intervention	*Laparoscopic GBP: Roux-en-Y. Cholecystectomy done through a slightly enlarged incision for the hand-assisted device. Also, fenestration of an incidentally discovered large liver cyst was done in another patient.* *Other: antibiotic prophylaxis and thromboprophylaxis. Seen at outpatient clinic after 4–6 weeks. Also at 6 and 12 months.*
Comparison	Open GBP: Roux-en-Y Other: as above
Length of follow-up	*12 months*
Results	*At 4 to 6 weeks after surgery, median weight change was –13 kg in both groups. At 12 months, weight change was similar in both groups, –39 (–23 to –57) and –41 (–26 to –57) kg after hand-assisted and open surgery respectively. Accordingly, the reduction in BMI was 15 units, to 29 and 30 kg/m^2 respectively.*
Quality and comments	*Blinded assessment done. Sample size achieved (minimum 21 in each group). ITT done.* *Could not add weight loss to analysis as no SDs.*
Sponsor details	*None reported.*

Westling 2001 (in HTA) RCT	
Aim	To compare laparoscopic and open Roux-en-Y GBP with regard to postoperative pain, hospital stay, sick-leave, weight loss and complications.
Participants	*People who were severely obese (BMI >40, or BMI >35 kg/m^2 in the presence of significant comorbidity).* *Total 51 – 48 F, 3 M. Mean (SD) age 36 (9) years overall. Mean (SD) BMI (kg/m^2)42 (4) overall. Randomised* n=*30 laparoscopic GBP (including conversions), and 21 to open GBP.*
Intervention	Laparoscopic GBP: Roux-en-Y Other: antibiotic prophylaxis with intravenous cefuroxime and metronidazole, thromboprophylaxis with enoxaparine or preoperative dextron. Advice from specially trained nurse for advice and regular checks from dietitians and internists.
Comparison	*Open GBP: Roux-en-Y* *Other: as above*
Length of follow-up	12 months
Results	Mean BMI (1 year): laparoscopy 27±4 kg/m^2; open 30.6±4 kg/m^2. Mean change in BMI (1 year): laparoscopy 14±3 kg/m^2; open 13±3 kg/m^2 (*p*=NS).
Quality and comments	Baseline BMI was lower in the laparoscopic GBP group compared with the open GBP group (mean (SD) 41 (4) vs 44 (4) kg/m^2, *p*<0.05). From Clegg TA QA: proper sampling and blind assessment classified as substandard or incomplete, sample size not reported. *Not able to add weight loss to analysis.* *Sugerman: complication rate for laparoscopic GBP higher than other studies. Poss due to 'learning curve' affect. Laparoscopic GBP is classified as 'one of the most technically difficult of all laparoscopic procedures'. Also number of cases was 'profoundly lower' than most of the published observational studies.*

Sponsor details	None reported.

Other outcomes

Lujan 2004 RCT	
Results	*Mean operating time was 186.4 (125–290) min in the laparoscopic GBP group and 201.7 (129–310) min in the open GBP group (*p<*0.05).* *Mean hospital stay was 5.2 (1–13) days in the laparoscopic GBP group and 7.9 (2–28) days in the open GBP group (*p<*0.05)*
Quality and comments	…

Nguyen 2001 (in Clegg TA) RCT	
Results	Operative outcomes Operative time (min): laparoscopic 225±40, open 19±41, *p*<0.001; Estimated blood loss (ml); laparoscopic 137±79, open 395±284, *p*<0.001; Proportion requiring intensive care unit stay: laparoscopic 7.6%, open 21.1%, *p*=0.03; Median length of hospital stay (days): laparoscopic 3 (IQR 1), open 4 (IQR 2), *p*<0.001; Proportion requiring re-operation: laparoscopic 7.6%, open 6.6%, *p*=NS; Return to activities of daily living (days): laparoscopic 8.4±8.6, open 17.7±19.1, p<0.001; Return to work (days): laparoscopic 32.2±19.8, open 46.1±20.6, *p*=0.02; Intraoperative transfusion: laparoscopic 0, open 3.9% Conversion from laparoscopic to open: 2 (2.5%) due to failure of circular stapler; inability to insufflate abdomen safely. Quality of Life (not ITT) SF-36 Scores (mean ± SD) (pre-operative laparoscopic *n*=70, open *n*=73; 3 months laparoscopic *n*=54, open *n*=42) Physical functioning: pre-operative laparoscopic 46.5 (21.3), open 40.0 (24.4), *p*=NS; 1 month laparoscopic 60.9 (24.7), open 46.3 (24.7), *p*<0.05; 3 months laparoscopic 80.2 (19.1), open 67.8 (26.6), *p*=NS; US Norms 84.2 (23.3). Role-physical: pre-operative laparoscopic 47.2 (40.2), open 37.5 (37.9), *p*=NS; 1 month laparoscopic 29.7 (39.2), open 18.5 (32.3), *p*=NS; 3 months laparoscopic 80.7 (32.5), open 76.8 (33.3), *p*=NS; US Norms 81.0 (34.0) Bodily pain: pre-operative laparoscopic 51.0 (22.7), open 48.7 (24.1), *p*=NS; 1 month laparoscopic 59.2 (21.5), open 45.1 (24.4), *p*<0.05; 3 months laparoscopic 75.1 (24.7), open 68.1 (25.6), *p*=NS; US Norms 75.2 (23.7) General health: pre-operative laparoscopic 54.5 (21.6), open 52.9 (22.3), *p*=NS; 1 month laparoscopic 71.3 (18.0), open 64.0 (18.1), *p*<0.05; 3 months laparoscopic 77.2 (15.7), open 72.4 (16.5), *p*=NS; US Norms 72.0 (20.3) Vitality : pre-operative laparoscopic 38.5 (20.0), open 36.6 (19.9), *p*=NS; 1 month laparoscopic 45.4 (20.5), open 39.1 (18.9), *p*=NS; 3 months laparoscopic 65.8 (17.7), open 73.1 (95.2), *p*=NS; US Norms 60.9 (21.0) Social functioning: pre-operative laparoscopic 64.4 (26.3), open 61.6 (29.5), *p*=NS; 1 month laparoscopic 67.6 (24.5), open 51.9 (29.1), *p*<0.05; 3 months laparoscopic 87.3 (17.9), open 74.1 (30.0), *p*=NS; US Norms 83.3 (22.7) Role-emotional: pre-operative laparoscopic 49.1 (24.4), open 45.5 (27.2), *p*=NS; 1 month laparoscopic 78.5 (28.2), open 69.5 (33.5), *p*=NS; 3 months laparoscopic 83.0 (29.6), open 74.6 (40.7), *p*=NS; US Norms 81.3 (33.0) Mental health: pre-operative laparoscopic 73.0 (15.1), open 71.9 (17.3), *p*=NS; 1 month laparoscopic 76.8 (17.4), open 70.8 (19.4), *p*=NS; 3 months laparoscopic 82.9 (14.2), open 75.0 (19.2), *p*=NS; US Norms 74.7 (18.1) Morrehead-Ardelt Quality of Life scores (score of 0 =same as before, + score

	=positive changes, – score =negative change) (3 months laparoscopic *n*=47, open *n*=36; 6 months laparoscopic *n*=34, open *n*=28). Self-esteem (score range –1 to +1): 3 month laparoscopic 0.81 (0.3), open 0.73 (0.32) (p=NS); 6 months laparoscopic 0.84 (0.27), open 0.80 (0.28) (*p*=NS). Physical (score range –0.5 to +0.5): 3 month laparoscopic 0.48 (0.40), open 0.46 (0.44) (p=NS); 6 months laparoscopic 0.37 (0.17), open 0.34 (0.18) (*p*=NS). Social (score range –0.5 to +0.5): 3 month laparoscopic 0.31 (0.19), open 0.24 (0.21) (p=NS); 6 months laparoscopic 0.33 (0.19), open 0.29 (0.21) (*p*=NS). Labour (score range –0.5 to +0.5): 3 month laparoscopic 0.24 (0.19), open 0.13 (0.29) (p<0.05); 6 months laparoscopic 0.28 (0.21), open 0.21 (0.27) (*p*=NS). Sexual (score range –0.5 to +0.5): 3 month laparoscopic 0.20 (0.21), open 0.09 (0.24) (p<0.05); 6 months laparoscopic 0.26 (0.20), open 0.19 (0.26) (*p*=NS). Costs (mean $ ± SD) Direct costs: laparoscopic 7478 (2802); open 7,440 (4,661) (*p*=NS). Operative costs: laparoscopic 4922 (1927); open 3591 (1000) (p<0.01) Operative time and supplies: laparoscopic 4098 (1,538); open 2,788 (674) (*p*<0.01) Post-anaesthesia: laparoscopic 504 (487); open 525 (382) (*p*=NS) Hospital service costs: laparoscopic 2,519 (1,712); open 3,742 (3,978) (*p*=0.02) Diagnostic :laparoscopic 467(170); open 609 (402) (*p*<0.01) Nursing: laparoscopic 1,201 (821); open 1,975 (2,773) (*p*=0.03) Pharmaceutical: laparoscopic 418 (232); open 579 (413) (*p*<0.01) Therapeutic: laparoscopic 97 (249); open 146 (430) (*p*=NS) Other: laparoscopic 268 (213); open 423 (443) (*p*<0.01) Indirect costs: laparoscopic 6645 (2437); open 6,765 (4,077) (*p*=NS). Total costs: laparoscopic 14,087 (5237); open 14,098 (8,527) (*p*=NS).
Quality and comments	…

Sundbom 2004 RCT	
Results	*Post-operatively, all patients spent the first night after surgery in the surgical ward. Patient-controlled analgesia was satisfactory in all patients, and the amount of morphine required during the first 3 days after operation was similar for both procedures (Table 2). The systemic inflammatory response, measured by the C-reactive protein level, did not differ between the groups. Median length of hospital stay was 6 days in both groups.* *At 1-month follow-up (4 to 6 weeks), total sick leave, analysed in 40 patients, was 30 (15–59) and 37 (19–95) days after hand-assisted laparoscopic and open GBP respectively. The remaining ten patients were retired or on long-term sick leave.*
Quality and comments	…

Westling 2001 (in HTA) RCT	
Results	Pain – morphine dose (mg±sd): laparoscopy (*n*=29) 98 ±71.5) (*p*=NS); laparoscopy: conversions excluded (*n*=22) 69±46.4 (*p*<0.005); open (*n*=21) 140±90. Hospital stay (days): laparoscopy (n=29+) 4.5±1.2 (*p*=NS); laparoscopy: conversions excluded (*n*=22) 4±0.8 (*p*=0.025); open (n=21) 6±3.8. Sick leave (wks): laparoscopy (n=24+*) 3.9±2.1 (*p*=NS); laparoscopy: conversions excluded (*n*=18*) 2.8±1.8 (*p*=0.025); open (n=14*) 5±3.3 (**n* excludes people receiving pensions or who are unemployed). (*patient with malignant hyperthermia excluded) No correlation between pre-operative BMI and amount of morphine used post-operatively, length of stay or sick leave (no results reported). Patient satisfaction (1 year) All patients – 92% very satisfied, 8% satisfied. No difference between groups (no results reported).

Quality and comments	…

Complications

Lujan 2004 RCT	
Harms	Laparoscopic GBP: conversion to laparotomy necessary in four patients (8%) due to extreme hepatomegaly, portal hypertension secondary to hepatic cirrhosis discovered during the operation, anaesthetic problems (hypercapnia), and splenic lesion during dissection of the angle of His. All the conversions occurred in the first 20 patients. Open GBP: intraoperative complications in four patients (8%): three splenectomies and one splenic vein tear requiring suture. Three patients died post-operatively, two in the laparoscopic GBP group, one case not related with the surgical procedure and one in the open GBP group. Early complications (<30 days): Twelve patients (22.6%) of the laparoscopic GBP group vs 15 patients (29.4%) of the open GBP group, with no significant differences. Of note in the laparoscopic GBP group were two asymptomatic leaks of the gastro-entero-anastomosis, diagnosed during a control intestinal transit performed in the immediate postoperative period. A further transit was performed at 6 days, with no evidence of leaks, and a liquid diet was started, with good patient progress. Two patients developed intra-abdominal bleeding revealed by blood in the drains, without haemodynamic repercussions or need for transfusion, which ceased spontaneously, probably because of bleeding of the gastric dissection line. Two patients presented with an upper GI haemorrhage, 1 requiring blood transfusion, with bleeding at the gastrojejunal anastomosis, which sclerosed with upper GI endoscopy. Another patient presented with a lower GI haemorrhage with no haemodynamic repercussions or need for transfusion, probably due to bleeding of the entero-anastomosis. Another patient presented with a stenosis of the gastro-entero-anastomosis, which required endoscopic dilatation. Four patients in the open GBP group presented with a subphrenic abscess, which was drained by radiological puncture. The origin of these abscesses is unclear, as all the patients presented with a normal GI transit; it cannot be ruled out that the origin was due to leaks occurring in the late postoperative period. Three had an upper GI haemorrhage, which evolved favourably with medical treatment without the need for transfusion, and 1 patient died of broncho-aspiration in the re-operation for evisceration secondary to coughing on the second postoperative day. Late complications (>30 days): 11% of the laparoscopic GBP group compared with 24% of the open GBP group, with statistically significant differences (p<0.05). Of note in the laparoscopic GBP group was a sudden death on postoperative day 32 due to a possible pulmonary thrombo-embolism (no autopsy) and three intestinal obstructions: one resolved with medical treatment and two requiring surgery: one was caused by a hernia through the mesocolon. Another patient presented with an internal hernia between the mesocolon and the mesentery of the small intestine (Peterson's space), which caused an obstruction of the alimentary loop leading to perforation of the gastrojejunal anastomosis with acute peritonitis. Undergoing surgery, the patient presented with multiorgan failure in the postoperative period and died at 48 h. In the open GBP group there was a subphrenic abscess, which was drained by radiological puncture, and an intestinal obstruction due to adhesions, which was operated on 8 months after surgery. The differences observed between the two groups are due to the presence of ten abdominal wall hernias in the open GBP group, three receiving surgery and seven awaiting operation.
Quality and comments	…

Nguyen 2001 (in Clegg TA) RCT	
Harms	*Complications* *Major complications: total laparoscopic 6 (7.6%), open 7 (9.2%) (p=0.78); anastomotic leak laparoscopic 1, open 1; gastric pouch outlet obstruction laparoscopic 0, open 1; hypopharyngeal perforation laparoscopic 1, open 0; jejunojejunostomy obstruction laparoscopic 3, open 0; pulmonary embolism laparoscopic 0, open 1; respiratory failure laparoscopic 0, open 1; GI bleeding laparoscopic 1, open 0; wound infection laparoscopic 0, open 2; retained laparotomy sponge laparoscopic 0, open 1.* *Minor complications: total laparoscopic 6 (7.6%), open 9 (11.8%) (*p=*0.42); GI ileus laparoscopic 1, open 0;* C. difficile *colitis laparoscopic 1, open 0; gastrogastric fistula laparoscopic 0, open 1; asymptomatic leak laparoscopic 0, open 1; GI bleeding laparoscopic 2, open 0; wound infection laparoscopic 1, open 6; deep venous thrombosis laparoscopic 1, open 1.* *Late complications: total laparoscopic 15 (18.9%), open 12 (15.8%) (*p=*0.52); anastomotic stricture laparoscopic 9, open 2; prolonged nausea/vomiting laparoscopic 1, open 2; small bowel obstruction laparoscopic 1, open 0; cholelithiasis laparoscopic 3, open 0; ventral hernia laparoscopic 0, open 6,* p=*0.01); anaemia laparoscopic 0, open 2; protein–energy malnutrition laparoscopic 1, open 0.* *125*
Quality and comments	…

Sundbom 2004 RCT	
Harms	One woman in the hand-assisted group experienced tachycardia, fever and general deterioration, and a contrast study revealed evidence of leakage at the gastrojejunostomy. Leakage near the gastrojejunostomy was confirmed at laparotomy and large-bore drains were placed. She made an uneventful recovery after a 2-day stay in the intensive care unit and was discharged after 14 days in hospital. There were no other re-operations. Respiratory symptoms that required prolonged antibiotic treatment and physiotherapy occurred in eight patients in the hand-assisted and five in the open group. No clinical deep venous thrombosis, pulmonary embolism or wound dehiscence was noted. One patient in each group received two units of blood because of postoperative anaemia. All patients tolerated solids at discharge. There were no deaths within the first 30 days after operation. One-month follow-up Eighteen patients complained of various grades of dysphagia. Gastroscopy revealed a narrow anastomosis in six patients, two in the hand-assisted group and four in the open group. All patients had successful balloon dilatation and no stomal ulcers were seen. One patient in each group had a wound infection with pus and four had abnormal secretions, all of whom were treated conservatively. One-year results All patients were taking regular supplements of vitamin B_{12} and multivitamins. Iron was given to all women, but two were anaemic and required intensive treatment. One patient in the open group had a symptomatic incisional hernia. Three patients in each group had required short-term treatment with a proton pump inhibitor. Gastroscopy revealed a small stomal ulcer in one patient in the open group. One patient died 11 months after operation from metastatic breast cancer. She received oncological treatment and conventional terminal care, which were not affected by her previous Roux-en-Y GBP.
Quality and comments	…

Westling 2001 (in HTA) RCT	
Harms	*Surgical outcomes* *Conversions: 7 (23%) of laparoscopic patients were converted to open due to either bleeding (*n=*4) or other operative concerns (*n=*3).* *Duration (min): laparoscopy (*n=*30) 245 (135–390); open (*n=*21) 100 (70–150).* *Preoperative bleeding (ml): laparoscopy (*n=*30) 250 (50–1500); open (*n=*21) 300 (200–500).* *Complications* *Deaths: one laparoscopy patient from malignant hyperthermia (family history).* *GI symptoms (dumping/vomiting/diarrhoea): 5% of all patients.* *Incisional hernia: one laparoscopy patient.* *6 (20%) laparoscopy patients without conversion re-operated: returned to hospital emergency department median 4 weeks (1–5 weeks) post-operation due to colicky pain and vomiting due to narrow stricture of tunnel through mesocolon (*n=*5), and to herniated Roux limb (*n=*1). Restriction was removed (*n=*5) or Roux limb closely adherent to pancreas and excluded stomach (*n=*1).* *One open suffered leakage due to failure of hand-sewn part.* *One laparoscopy had a small embolus.* *Jejunal ulcers: three laparoscopy, two open (p=NS)* *Stricture in gastrojejunostomy: one laparoscopic treated by endoscopic dilation.* *Superficial wound infection: three open.* *Readmission for unexplained fever (1), pneumonia (1), epigastric pain and/ or vomiting with normal gastroscopy (2).*
Quality and comments	…

Generalisability

Lujan 2004 RCT	
Country and setting	Spain. Department of surgery?
Participants (included/excluded)	Included if BMI >40 kg/m^2 without coexisting pathological disorders or BMI >35 kg/m^2 with coexisting pathological disorders. No exclusion criteria reported.
Recruitment	N/R
Randomisation	No details other than computer generated numbers in sealed, opaque, numbered envelopes.
Intervention (mode and intensity)	*Seen post-operatively at 15 days, then 3, 6, 12, 18, 24 months. Annually thereafter.*
Comparison (mode and intensity)	As above.
Delivery of intervention/comparison (who)	N/R
Dropout rates	*0%?*
Treatment of dropouts (return to baseline, or last measurement?)	N/R.

Nguyen 2001 (in Clegg TA) RCT	
Country and setting	USA. Department of surgery?

Participants (included/excluded)	Included all patients evaluated for surgical treatment of morbid obesity with BMI 40 to 60 kg/m^2, aged 21–60 years, failed previous non-surgical treatment. Excluded if previous obesity surgery, previous gastric surgery, large abdominal ventral hernia, history of venous thrombosis/ pulmonary embolism, severe cardiovascular, respiratory, hepatic or renal disease.
Recruitment	From clinic (all referrals).
Randomisation	Stratified by BMI (40 to 49, 50 to 60 kg/m^2).
Intervention (mode and intensity)	Assessed in outpatient clinic postoperatively at 7 days and at 1, 3, 6 and 12 months post-surgery and annually thereafter.
Comparison (mode and intensity)	As above
Delivery of intervention/comparison (who)	N/R
Dropout rates	People who withdrew consent or did not undergo GBP were excluded from the analysis. Nineteen eligible participants did not undergo randomisation; 13 requested laparoscopic GBP and six requested open GBP; two randomised to GBP were excluded after randomisation (one withdrew consent, one needed splenectomy).
Treatment of dropouts (return to baseline, or last measurement?)	ITT done – no details reported.

Sundbom 2004 RCT	
Country and setting	Sweden. Department of surgery?
Participants (included/excluded)	No details reported, other than not undergone previous bariatric surgery.
Recruitment	From hospital metabolic unit, but no details.
Randomisation	Stratified by sex.
Intervention (mode and intensity)	*Seen at outpatient clinic after 4–6 weeks. Also at 6 and 12 months.*
Comparison (mode and intensity)	As above.
Delivery of intervention/comparison (who)	Seen at 6 and 12 months by an internist and dietitian.
Dropout rates	*0% overall, but one woman died 11 months after the operation due to metastatic breast cancer.*
Treatment of dropouts (return to baseline, or last measurement?)	ITT done, no details but minimal dropout. Exclusion of protocol violations (cholecystectomy and liver cyst fenestration) did not alter the results substantially.

Westling 2001 (in HTA) RCT	
Country and setting	Sweden. Department of surgery?
Participants (included/excluded)	*Included if people with BMI >40 kg/m^2 or BMI >35 kg/m^2 with significant comorbidity; failed in various supervised non-surgical long term weight loss programs within hospital; fully informed of operation and consequences.* *Excluded 70 patients prior to randomisation as they were unsuitable for laparoscopy (*n=*21), had gallstones (*n=*7), or were scheduled for Roux-en-Y GBP as a revisional procedure (*n=*42).*
Recruitment	N/R
Randomisation	*Blocked 60% to laparoscopic GBP and 40% to open due to presupposed need for conversions. Stratified by gender, but not BMI.*

Intervention (mode and intensity)	*Seen at 4–6 weeks and 12 months after operation. Also encouraged to contact a specially trained nurse in-between scheduled appointments for advice on upcoming problems. Regular checks and support from dietitians and internists also given.*
Comparison (mode and intensity)	As above.
Delivery of intervention/comparison (who)	Specially trained nurse acted as contact after surgery, and dietitians and internists gave regular checks and support.
Dropout rates	*0%*
Treatment of dropouts (return to baseline, or last measurement?)	100% of participants were included.

1.7.5 Malabsorptive/restrictive surgery

Weight loss

Deveney 2004 (TEC) observational study

Aim	To compared weight loss (expressed as percentage of EWL) after 1 and 2 years in patients who underwent open Roux-en-Y GBP or DS-BPD performed by the same surgeons at one institution.
Participants	People who underwent open Roux-en-Y GBP or DS-BPD. Total 350 – 273 F, 77 M. Mean (SD) BMI DS-BPD 59 (11) DS-BPD (*n*=113), 55 (11) Roux-en-Y GBP, (*n*=237). Mean (SD) age 46 (10) years DS-BPD, 44 (11) years Roux-en-Y GBP.
Intervention	*Surgery: DS-BPD (open and laparoscopic)* *No further details of additional treatment.*
Comparison	Surgery: Roux en Y GBP (open and laparoscopic) No further details of additional treatment.
Length of follow-up	*24 months*
Results	*Change in body weight in kg was not reported.* *Only results for patients with 1- and 2-year follow-ups were reported.*

	DS-BPD (n=36)	***Roux-en-Y GBP (n=57)***
Mean age (years)	*44*	*45*
Mean (SD) BMI (kg/m^2)	*64 (9.5)*	*59 (10.9)*
Mean % EWL at 12 months	*53 (11)*	*54 (16)*
Mean % EWL at 24 months	*63 (21)*	*67 (18)*

	Statistically significant differences reported for baseline BMI only, and not for mean EWL at 12 or 24 months.
Quality and comments	*Baseline differences in BMI (heavier in DS-BPD group,* p<*0.05) and higher rates of diabetes (41 vs 30%,* p<*0.005) and hypertension (67 vs 56%,* p<*0.005) in the DS-BPD group.* *Retrospective review of records from patient database.*
Sponsor details	*None reported.*

Other outcomes

Deveney 2004 (TEC) observational study

Results	*None reported.*
Quality and comments	…

Complications

Deveney 2004 (TEC) observational study

Harms

	DS-BPD (n=113)	***Roux-en-Y GBP (n=237)***
Mean length of stay (days)	*8.7*	*5.9*
Wound infection	*25 (22%)*	*47 (20%)*
Postoperative anastomotic leak	*7(6%)*	*8 (3%)*
Mortality	*1 (0.9%)*	*2 (0.8%)*

Rates were similar apart from a higher length of stay for DS-BPD (*p*<0.05).

Quality and comments: …

Generalisability

Deveney 2004 (TEC) observational study	
Country and setting	USA. University centre?
Participants (included/excluded)	Included if underwent DS-BPD or roux-en-Y GBP between January 2000 and March 2003. Excluded if had previous failed bariatric procedures.
Recruitment	Retrieved records from database. Procedure chosen by surgeon and/or patient.
Randomisation	N/A
Intervention (mode and intensity)	*No details*
Comparison (mode and intensity)	No details.
Delivery of intervention/comparison (who)	No details.
Dropout rates	*68% DS-BPD, 76% Roux-en-Y GBP at 24 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.7.5.1 Duodenal switch (BPD)

Single arm studies

Table 7 Study characteristics and weight loss outcomes

Study	Mean age (years)	Mean BMI (kg/m^2)	% Male	Follow-up (months)	No enter/eval	No. at follow-up (years) and weight loss outcome(s)					Prosp/Cons[7]	Pre-operative workup
						1	2	3	4	5		
Anthone 2003	42.3	52.3	21.7	60 (maximum)	701	333 EWL 69% BMI –20.3	NR	71 EWL 73% BMI –21.3	NR	50 EWL 66% BMI –20.3	Prosp; cons	Yes
Biron 2004	38	48.4	21.5	94.8 (mean)	997	NR	NR	NR	NR	997 BMI –17.1 (not reported at specific time point)	Cons	…
Guedea 2004	38	54	15	67.9 (mean)	150/74	74 EWL 68% BMI –20	74 EWL 75% BMI –23	…	…	55 EWL 70% BMI –21	Cons	…
Hess 1998	39	50	22	18 (maximum)	440	NR EWL 74%	NR EWL 78%	NR EWL 77%	NR EWL 75%	NR EWL 73%	Cons	…
Marinari 2004	38	47	28.3	>60	858	…	800 EWL 67%	…	738 EWL 67%	659 (6 year) EWL 68%	…	…
Slater 2004	45	43	18	48 (maximum)	376	170 EWL 48%	59 EWL 68%	37 EWL 59%	28 EWL 59%	…	Cons	…
Totte 1999	35.8	48.8	20	36 (maximum)	180	118 EWL 57% BMI –16.8	…	72 EWL 70% BMI –20.0	…	…	Cons	…

Hess also reported rates of EWL of 70, 68, 70, 74 and 87% at 6, 7, 8, 9 and 10 years follow-up, respectively.

Table 8 Adverse outcomes

[7] PROSP prospective study, CONS consecutive patients.

Study	*n*	Perioperative complications (%)									Long-term complications (%)							
		Death	Perf	Leak	Bleed	Sten	SBO	Throm	Card	Wound	Reop	Sten	Obstr	Ulcer	Nutr	N/V	Hern	Chol
Anthone 2003	701	1.4	…	0.7	…	…	…	…	…	…	5.7	…	…	…	…	…	…	…
Biron 2004	997	1.0	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
Guedea 2004	74 (384)	0	…	2.7	…	…	…	…	…	6.8	2.7	4.1	…	10.8	…	…	33.8	…
Hess 1998	440	0.5	0.9	3.8	0.5	…	-	1.3	0.5	-	3.9	-	2.8	-	-	-	-	-
Marinari 2004	858	…	…	0.1	…	…	…	0.1	…	…	6.3	…	…	…	…	…	1.7	…
Slater 2004	Reported on nutritional outcomes, not complications	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
Totte 1999	180	0	-	1.1	-	…	-	1.1	-	5	3.9	-	1.1	11	1.1	-	18	-

Bleed, bleeding complications; Card, cardiopulmonary complications, e.g. MI, CHF, pneumonia, respiratory failure; Chol, cholycystectomy; Death, death within 30 days of operation; Hern, abdominal wall hernia at incision or port site; Leak, anastomitic leak; N/V, chronic nausea and/or vomiting, moderate or severe; Nutr, nutritional deficiencies, including vitamin deficiencies; Obstr, bowel obstruction resulting from procedure; Perf, perforation of bowel and/or visceral organ, including splenic injury; Reop, re-operation resulting from a complication of the original procedure; SBO, small bowel obstruction; Sten, stenosis; Throm, thromboembolic complication; Ulcer, mucosal ulceration occurring at or near site of procedure; Wound, wound complications, including infection and dehiscence.

1.7.6 Staged surgery

Detailed evidence tables were not needed for this section, as appropriate levels of detail are provided in the Narrative.

1.7.7 Competencies, training, and volume

Detailed evidence tables were not needed for this section, as appropriate levels of detail are provided in the Narrative.

1.7.8 Interventions in a UK clinical setting

Weight loss

Taylor 2003	
Aim	To compare the efficacy of an energy prescription diet with usual care (healthy eating diet)
Participants	Overweight (no definition) adults referred to a outpatient dietetic clinic. Total 53 – 18 M, 35 F. Mean (SD) age 48.9 (14.5) years diet (*n*=27), 44.5 (14.7) years healthy eating (*n*=26). Mean (SD) BMI (kg/m^2) 37.2 (9.0) diet, 37.0 (5.2) healthy eating.
Intervention	*Diet: 500 kcal/day deficit diet. No revisions made during study period.* *Seen at four sessions with a dietitian held at four weekly intervals up to week 12.*
Comparison	Healthy eating: based on Balance of Good Health. Seen as in intervention group.
Length of follow-up	*12 weeks*
Results	*At 4 weeks, mean (SD) weight change in kg was –1.7 (2.3) in the diet group, and –1.9 (2.5) in the control group. Mean weight change in the intervention group compared with control was 0.2 (95% CI –1.1 to 1.5).* *At 12 weeks, mean (SD) weight change in kg was –2.70 (3.8) in the diet group, and –3.1 (3.6) in the control group. Mean weight change in the intervention group compared with control was 0.4 (95% CI –1.7 to 2.4).*
Quality and comments	*Small, underpowered (needed 686 for 80% power) study. Quasi randomised (alternate allocation), but no further details. Blinded assessment not done. High dropout rate (almost 50%).*
Sponsor details	*None reported.*

Moore 2003	
Aim	To evaluate a training programme intended to improve the management of obesity, delivered to general practice teams.
Participants	General practices invited consecutive attending obese (BMI ≥30 kg/m^2) adults aged 16 to 64 years to participate. Total 843 – 220 M, 623 F. Mean (SD) age 48.4 (10.9) years intervention (*n*=415), 48.8 (12.2) years control (*n*=428). Mean (SD) BMI (kg/m^2) 37.0 (5.7) intervention, 36.9 (5.8) control.
Intervention	*4.5 h training programme promoting an obesity management model included* *Training: educational strategy was based on a previous nutrition training programme. All GPs and practice nurses to attend all three sessions.* *Model approach: incorporated best evidence and was perceived to be brief enough that primary care staff could deliver it to their patients. The training covered information on the clinical benefit of weight loss and effective treatment options, including reduction of dietary energy intake, increased physical activity, and pharmaceutical intervention.* *Organisation: seeing patients regularly (about every 2 weeks) until they had lost 10% of their original body weight and then less regularly (about every one to 2 months) for maintenance of weight over a sustained period. Current and target weight and dietary and activity targets were to be recorded in the patients' records to facilitate continuity of support across practice teams. Practices devised individualised weight management protocols based on the model.* *Diet: prescription of a moderate energy deficit diet was advocated. Diet sheets and supporting written resources facilitated the dietary prescription to patients.*
Comparison	Usual care
Length of follow-up	*18 months*

Results	*At 12 months, there was no difference between the intervention and control group patients with regard to weight (mean weight change +0.3 kg intervention vs 0.7 kg control,* p=*0.5).*
Quality and comments	*Cluster RCT, so contamination minimal. Randomisation done by statistician team, so assumed to be concealed allocation. Clustering accounted for. Results for completers only.*
Sponsor details	*NHS Executive (Northern and Yorkshire)*

Other outcomes

Taylor 2003	
Results	*No difference in mean satisfaction scores were seen between the groups (3.9 diet vs 3.6 healthy eating, no* p *value reported).*
Quality and comments	Satisfaction measured using a visual analogue scale of 1–5. No mention of whether validated scheme.

Moore 2003	
Results	*Patients in trained practices consulted, on average, on two more occasions than patients in control practices in the year after the delivery of the training. Trained practices were more likely to discuss weight (OR 2.0,* p=*0.003), and the records of patients from trained practices were more likely to include weight (OR 2.0,* p= *0.004), target weight (13.6,* p=*0.001) and dietary targets (4.5,* p=*0.02).*
Quality and comments	…

Harms

Taylor 2003	
Harms	None reported.
Quality and comments	

Moore 2003	
Harms	None reported.
Quality and comments	

Generalisability

Taylor 2003	
Country and setting	UK. Hospital outpatient dietetic clinic.
Participants (included/excluded)	Included if overweight adults referred to clinic over a 12-month period.
Recruitment	Consecutive referrals.
Randomisation	Alternate allocation
Intervention (mode and intensity)	*Seen at four sessions with a dietitian held at four weekly intervals up to week 12.*
Duration of active intervention	12 weeks
Comparison (mode and intensity)	As above
Delivery of intervention/comparison (who)	Dietitian
Dropout rates	*41% diet, 58% healthy eating at 12 weeks.*

Treatment of dropouts (return to baseline, or last measurement?)	N/R

Moore 2003	
Country and setting	UK. Primary care.
Participants (included/excluded)	Included adults with BMI ≥30 kg/m^2, aged 16 to 64 years. No exclusion criteria reported.
Recruitment	From consecutive attendees at a general practice.
Randomisation	Informed by practice and patient level characteristics.
Intervention (mode and intensity)	*Three 90 min sessions, intended to be delivered at intervals of no less than one week and no more than 2 weeks apart, to the 22 intervention practices* *Practitioners saw patients regularly (about every 2 weeks) until they had lost 10% of their original body weight and then less regularly (about every one to 2 months) for maintenance of weight over a sustained period*
Duration of active intervention	18 months, but training only during first 6 weeks maximum
Comparison (mode and intensity)	Usual care
Delivery of intervention/comparison (who)	Training by four dietitians trained in the standardised delivery of the training who then delivered the programme to small group, multidisciplinary general practice teams. Patient care by GPs and practice nurses.
Dropout rates	*38% intervention, 36% control at 18 months.*
Treatment of dropouts (return to baseline, or last measurement?)	Results for completers only.

1.7.9 Barriers and attitudes to the management of overweight and obesity in the clinical setting

Detailed evidence tables were not needed for this section, as appropriate levels of detail are provided in the Narrative.

1.7.10 Role of professionally organised therapies in the management of overweight and obesity

The evidence review was based on one systematic review only. No additional primary studies were identified.

1.7.11 Effectiveness of brief interventions in primary care and other general clinical settings in improving outcomes for people who are overweight and obese

Weight loss

Pritchard 1999 (in HTA) RCT	
Aim	To study the clinical and cost outcomes of providing nutritional counselling to people with one or more of the following conditions: overweight, hypertension, type 2 diabetes.
Participants	Men and women aged between 25 and 65 years with either hypertension, type 2 diabetes or were overweight (BMI >25 kg/m^2). 273 total – 198F, 75M. 199 participants were aged <50 years. Mean weight (kg) 91.7 in the dietitian led intervention group (*n*=92), 85.5 in the doctor and dietitian led intervention group (*n*=88), 89.1 in the control group (*n*=90). Majority were from disadvantaged socio-economic groups (58% most disadvantaged quartile and 20% more disadvantaged quartile).
Intervention (including details of diet)	*Counselling focused on principles of good nutrition and exercise and addressed problem areas in lifestyle and dietary patterns. Counselled on food, shopping, cooking, food selection, meal planning, exercise programmes. Advised to complete food records and diet history. Advised to reduce total energy intake and to reduce energy intake from fat to ≤30% (carbohydrate ≥50% and protein 20%). Discouraged from smoking and to have two or more alcohol-free days per week, with two or fewer alcoholic standard drinks for women and four for men.* *In the doctor and dietitian group, as well as counselling above, participants were seen by the GP at baseline and saw same GP on two other occasions during the 12 months for 5 min each time to encourage and monitor the participant.*
Control	Received results of initial screening and advised to discuss queries with the GP at appointment. Received usual care (including monitoring, advice and prescriptions) from GP but no dietitian counselling. Mailed to re-attend at 12 months.
Length of follow-up	*12 months*
Results	Only 12-month outcomes reported. In an intention to treat analysis, the doctor/dietitian group lost 6.7 kg or 7.3% of screening weight compared with the control group (95% CI 6.5 to 8.3) while the dietitian group lost 5.6 kg or 6.6 (95% CI 5.8 to 7.6)%. The doctor/dietitian group lost 1.1 kg or 0.7% more weight than the dietitian group but this was not statistically significant (95% CI - 0.42 to 1.82).

Quality and comments	*Control groups halved. ITT analysis done. Blinded assessment not done. Real possibility of disclosure of allocation, although some attempt made at concealment.*

Other outcomes

Pritchard 1999 (in HTA) RCT	
Results	*No effect was found on the subsequent use of medication between the intervention groups and control.* *The cost of an additional kg weight loss was AUS$9.76 in the doctor and dietitian group compared with AUS$7.30 in the dietitian group.*
Quality and comments	…

Reported Harms

Pritchard 1999 (in HTA) RCT	
Harms	None reported.
Quality and comments	…

Generalisability

Pritchard 1999 (in HTA) RCT	
Country and setting	Australia. University group general practice, in lower socioeconomic suburb.
Participants (included/excluded)	Included if aged between 25 and 65 years. Also if BMI >25 kg/m^2, or screened BP >140/90 mmHg and recorded BP >140/90 mmHg at least twice in medical records, history of type 2 diabetes. Excluded if mentally ill, intellectually handicapped, terminally ill, acutely ill, pregnant or participating in other health education programmes.
Recruitment	Participants were screened opportunistically when attending the GP. People with recorded diagnosis of overweight, hypertension or type 2 diabetes in their patient notes were invited to participate. People who appeared to be overweight on presentation at reception were also invited to participate.
Intervention (mode and intensity)	*Intervention lasted 12 months. Contacted seven times (baseline then six times by dietitian over 12 months). Also supplemented with baseline contact with GP and 25 min sessions with the GP in the doctor and dietitian group.*
Control (mode and intensity)	Contacted twice (baseline and 12 months).
Delivery of intervention/control (who)	Initial screening and counselling done by dietitian. Dietitian invited those allocated to the dietitian group to participate. GP invited those allocated to the doctor and dietitian group, after screening by the dietitian. Mailed invite to attend for final measurement in control group.
Dropout rates	*45% dietitian group, 29% doctor and dietitian group, and 29% control at 12 months. (As reported in original paper, not HTA.) Dropouts were significantly higher in the dietitian group (*p*=0.022) than either the doctor and dietitian group or the control.*
Treatment of dropouts (return to baseline, or last measurement?)	If missing data, the last measurement recorded was taken to populate subsequent data values.