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Effects of total fat intake on body weight (Review)

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TABLE OF CONTENTS

[Intervention Review]

Effects of total fat intake on body weight

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ABSTRACT

Background

In order to prevent overweight and obesity in the general population we need to understand the relationship between the proportion of energy from fat and resulting weight and body fatness in the general population.

Objectives

To assess the effects of proportion of energy intake from fat on measures of weight and body fatness (including obesity, waist circumference and body mass index) in people not aiming to lose weight, using all appropriate randomised controlled trials (RCTs) and cohort studies in adults, children and young people

Search methods

We searched CENTRAL to March 2014 and MEDLINE, EMBASE and CINAHL to November 2014. We did not limit the search by language. We also checked the references of relevant reviews.

Selection criteria

Trials fulfilled the following criteria: 1) randomised intervention trial, 2) included children (aged ≥ 24 months), young people or adults, 3) randomised to a lower fat versus usual or moderate fat diet, without the intention to reduce weight in any participants, 4) not multifactorial and 5) assessed a measure of weight or body fatness after at least six months. We also included cohort studies in children, young people and adults that assessed the proportion of energy from fat at baseline and assessed the relationship with body weight or fatness after at least one year. We duplicated inclusion decisions and resolved disagreement by discussion or referral to a third party.

Data collection and analysis

We extracted data on the population, intervention, control and outcome measures in duplicate. We extracted measures of weight and body fatness independently in duplicate at all available time points. We performed random-effects meta-analyses, meta-regression, subgrouping, sensitivity and funnel plot analyses.

Main results

We included 32 RCTs (approximately 54,000 participants) and data from 25 cohorts. There is consistent evidence from RCTs in adults of a small weight-reducing effect of eating a smaller proportion of energy from fat; this was seen in almost all included studies and was highly resistant to sensitivity analyses. The effect of eating less fat (compared with usual diet) is a mean weight reduction of 1.5 kg (95% confidence interval (CI) -2.0 to -1.1 kg), but greater weight loss results from greater fat reductions. The size of the effect on weight does not alter over time and is mirrored by reductions in body mass index (BMI) (-0.5 kg/m^2, 95% CI -0.7 to -0.3) and waist circumference (-0.3 cm, 95% CI -0.6 to -0.02). Included cohort studies in children and adults most often do not suggest any relationship between total fat intake and later measures of weight, body fatness or change in body fatness. However, there was a suggestion that lower fat intake was associated with smaller increases in weight in middle-aged but not elderly adults, and in change in BMI in the highest validity child cohort.

Authors' conclusions

Trials where participants were randomised to a lower fat intake versus usual or moderate fat intake, but with no intention to reduce weight, showed a consistent, stable but small effect of low fat intake on body fatness: slightly lower weight, BMI and waist circumference compared with controls. Greater fat reduction and lower baseline fat intake were both associated with greater reductions in weight. This effect of reducing total fat was not consistently reflected in cohort studies assessing the relationship between total fat intake and later measures of body fatness or change in body fatness in studies of children, young people or adults.

PLAIN LANGUAGE SUMMARY

Effect of cutting down the fat we eat on body weight

The ideal proportion of energy from fat in our food and its relation to body weight is not clear. This review looked at the effect of cutting down the proportion of energy from fat in our food on body weight and fatness in both adults and children who are not aiming to lose weight. The review found that cutting down on the proportion of fat in our food leads to a small but noticeable decrease in body weight, body mass index and waist circumference. This effect was found both in adults and children. The effect did not change over time.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Low dietary fat compared with usual fat for controlling body fatness

Low dietary fat compared with usual fat for body fatness

Patient or population: children, young people and adults from the general population
Settings: general population
Intervention: low dietary fat
Comparison: usual fat

Methods: randomised controlled trials

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Usual fat	Low dietary fat				
Weight, kg (adults) body weight in kg Follow-up: 6 to 96 months	Median weight change -0.04kg[1]	The mean weight, kg (adults) in the low fat groups was **1.54 lower** (1.97 to 1.12 lower)	—	53,647 (30 RCTs)	⊕⊕⊕⊕ **high** [2,3,4,5,6,7,8]	—

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]The median weight change in the control groups over the course of each study was -0.04kg, ranging from -1.91kg to 2.13kg.
[2]While most studies were unblinded for participants and allocation concealment was often unclear (as randomisation was described poorly), RCT results in adults were remarkably consistent in their direction. Sensitivity analyses removing studies without clear allocation concealment did not lose the statistically significant relative weight reduction in the low fat arm, and neither did running fixed-effect (rather than random-effects) meta-analysis or removing studies with attention bias favouring those in the low fat arm, or those with other interventions alongside the fat reduction. The consistent weight loss was despite the fact that none of the studies included intended to alter weight in either arm, so that publication bias on this outcome is unlikely. Together this suggests that the risk of bias was low.
[3]The direction of effects in these RCTs was remarkably consistent - in almost every study participants eating lower total fat intakes were lower in weight (on average) at the study end than participants eating a higher percentage of total fat. The only inconsistency (where heterogeneity arose) was in the size of this effect. The heterogeneity was partly explained by the degree of reduction of fat intake, and by the level of control group fat intake, which together explained 56% of between-study variance (in meta-regression). The reduction in weight in those taking on lower fat diets was seen in very different populations and from six months to several years. It was also consistent when we excluded studies

that gave additional support, time or encouragement to the low fat arms, and where we excluded studies that delivered additional dietary interventions (on top of the change in dietary fats). The results were consistent in direction, and much of the heterogeneity in the size of the effect was explained by the selected factors.

[4]All included RCTs directly compared (and randomised participants to) lower versus usual fat intake; therefore there was no indirectness in intervention. All studies were conducted in industrialised countries so the potential to generalise to other cultural contexts is limited. Nonetheless there is no reason to believe that the effect would be different in different populations. There are changes in diets in many countries around the world, which are resulting in greater similarity in diets in developed and developing countries. Additionally, the industrialised countries represented included a wide variety of baseline (or control group) fat intakes, and the effect was apparent at all of these levels. The studies all addressed weight directly and did not use proxy measures.

[5]Imprecision was unlikely, as over 40,000 participants were included in RCTs of at least six months duration, and effect sizes were highly statistically significant. There was little imprecision. If the true effect on weight was at either end of the 95% CI we would see the effect in the same way.

[6]The funnel plot did not suggest publication bias.

[7]Subgrouping supported the presence of a dose response gradient in that studies that altered the total fat intake between intervention and control by less than 5% of energy had a negligible effect on weight, while greater differences in total fat intake were associated with statistically significant differences in weight. This was supported by the meta-regression, which suggested a statistically significant relationship between the degree of fat reduction and of weight loss.

[8]The effects on body weight are supported by similar effects on BMI in adults (-0.50 kg/m^2, 95% CI -0.74 to -0.26, 10 RCTs, > 45,000 participants), waist circumference in adults (-0.30 cm, 95% CI -0.58 to -0.02, one RCT, > 15,000 participants) and BMI reduction in the one RCT in children.

BACKGROUND

The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) expert consultation on fats and fatty acids in human nutrition debated optimal intakes of total fat in 2008. In light of the rising levels of overweight and obesity, particularly in low- and middle-income countries undergoing rapid nutrition transition, this consultation agreed that any effect of total fat intake on body weight was pivotal in making global recommendations on total fat intake. Overweight and obesity are associated with increased risk of many cancers, coronary heart disease and stroke (Manson 1990; Song 2004; WCRF/AICR 2009).

A previous systematic review found no randomised controlled trials (RCTs) of lower total fat intake that aimed to assess effects on body weight (Kelly 2006), but we were aware of RCTs that had randomised participants to low fat versus usual fat diets, and measured weight or BMI as a process measure (Hooper 2012a). Additionally, meta-regression within a systematic review assessing RCTs on the effects of step I and II diets (diets designed by the National Heart, Lung and Blood Institute national cholesterol education programme to reduce the risk of cardiovascular disease in the general population and those at increased cardiovascular risk, respectively), found a strong relation between total fat intake and body weight (Yu-Poth 1999). This review, however, included studies that were as short as three weeks in duration and studies in which weight loss was a goal of the intervention, which may have overstated any relation because the advice was to lower both fat and energy intake. It also excluded many trials of reduction in total fat intake that did not fit the step I or II criteria.

More recent reviews that have explored the long-term effects of low fat diets either did not explore weight or body fatness as an outcome (Schwingshackl 2013), or looked at low fat intake as part of a wider health promotion intervention (Ni 2010). Other systematic reviews have explored the relationship between fat intake and body fatness but were either limited to the effect low fat dairy versus high fat dairy consumption (Benatar 2013), or investigated it as part of looking at the overall dietary patterns (Ambrosini 2014), or diet quality (Aljadani 2015).

In order to aid the WHO's understanding of the relation between total fat intake and body weight with a view to updating their guidelines on total fat intake, the WHO Nutrition Guidance Expert Advisory Group (NUGAG) subgroup on diet and health (http://www.who.int/nutrition/topics/advisory_group/nugag_dietandhealth_topics/en/) was requested to assess the relationship. The expert advisory group aimed to generate a recommendation on the population impact of total fat intake in the development of obesity. The NUGAG group agreed to exclude studies of populations recruited specifically for weight loss and interventions intended to result in weight loss. These studies were potentially confounded by the implicit objective of reducing calorie intake to produce weight loss and might therefore lead to an overemphasis on studies carried out in highly selected obese populations in North America and Europe, which may have limited transferability to non-obese populations or those in developing countries or in countries in transition.

To fulfil the requirements for the new guideline, a systematic review was needed of all available evidence of the longer-term effects of total fat intake on body fatness, in studies not intending to cause weight loss. The WHO therefore commissioned a systematic review and meta-analysis to assess the relationship between total fat intake and indicators of body fatness (including obesity, waist circumference and body mass index) using all appropriate RCTs and cohort studies in adults and children (Hooper 2012b), which has been updated in 2015.

OBJECTIVES

To assess the effects of proportion of energy intake from fat on measures of weight and body fatness (including obesity, waist circumference and body mass index) in people not aiming to lose weight, using all appropriate RCTs and cohort studies in adults, children and young people.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) of adults and children: trials of reduced fat intake compared with usual diet or modified fat intake with no intention to reduce weight (in any participants in either or both arms), continued for at least six months, unconfounded by non-nutritional interventions and assessing a measure of body fatness at least six months after the intervention was initiated.

Randomisation of individuals was accepted, or of larger groups where there were at least six of these groups (clusters) randomised. We excluded studies where allocation was not truly randomised (e.g. divisions based on days of the week or first letter of the family name were excluded) or where allocation was not stated as randomised (and no further information was available from the authors). We excluded cross-over studies (as previous weight gain or weight loss is likely to affect future weight trends) unless the first half of the cross-over could be used independently.

Cohort studies of adults and children: prospective cohort studies that followed participants for (and assessed final or change in body fatness) at least 12 months after assessment of total fat, and related baseline total fat intake to absolute or change in body fatness at least 12 months later.

Types of participants

We accepted studies of adults (≥ 18 years, no upper age limit) or children and young people (aged ≥ 24 months) at any risk of cardiovascular disease (with or without existing cardiovascular disease). Participants could be of either sex, but we excluded those who were acutely ill, pregnant or lactating. We excluded intervention studies where participants were chosen for raised weight or body mass index (as most appeared to aim to reduce body weight within interventions, even when this was not explicitly stated in the intervention goals).

Types of interventions

Interventions

We considered all randomised controlled trials (RCTs) of interventions stating an intention to reduce dietary fat, when compared with a usual or modified fat intake.

We considered a low fat intake to be one that aimed to reduce fat intake to ≤ 30% energy (≤ 30%E) from fat, and at least partially replace the energy lost with carbohydrates (simple or complex), protein or fruit and vegetables. We considered a modified fat diet to be one that aimed to include > 30% energy from total fats, and included higher levels of mono-unsaturated or poly-unsaturated fats than a 'usual' diet.

As we were interested in the effects of fat intake on body weight and fatness in everyday dietary intake (rather than in people aiming to reduce their body weight in weight-reducing diets) we excluded studies aiming to reduce the weight of some or all participants, as well as those that included only participants who had recently lost weight, or recruited participants according to a raised body weight or BMI. We excluded multifactorial interventions other than diet or supplementation (unless the effects of diet or supplementation could be separated, so the additional intervention was consistent between the intervention and control groups). We excluded Atkins-type diets aiming to increase protein and fat intake, as well as studies where fat was reduced by means of a fat substitute (like Olestra). We excluded enteral and parenteral feeds, as well as formula weight-reducing diets.

Examples

We included studies that reduced fats and encouraged physical activity in one arm and compared this with encouraging physical activity in the control. We excluded studies that reduced fats and encouraged physical activity in one arm and compared this with no intervention in the control. We included studies that reduced fats and encouraged fruit and vegetables in one arm and compared this with no intervention in the control.

We included all trials that intended to reduce dietary fat to ≤ 30%E in one arm compared to usual or modified fat intake (> 30%E from fat) in another arm regardless of the degree of difference between fat intake in the two arms (dose). We explored the effects of the difference in %E from fat between control and intervention groups, as well as the effects of fat intake in the control groups and dietary fat goals in the intervention groups, in subgrouping.

Exposures

For cohort studies total fat intake, in grams or as a percentage of dietary energy intake, had to be assessed at baseline and related to a measure of body fatness, or change in body fatness, at least a year later. For cohorts that used multiple dietary assessments to model later body fatness or change in body fatness more than half of the assessments included in the model had to be at least a year before the assessment of body fatness (or the final assessment for a change measure) used in the model.

Types of outcome measures

Primary outcomes

The main outcomes were measures of body fatness, including body weight, body mass index, waist circumference, skinfold thickness or percentage fat. Studies had to report at least one of these measures, or a change in these measures, to be included in the review.

Secondary outcomes

Secondary outcomes included other classic cardiovascular risk factors (systolic or diastolic blood pressure, serum total, low density lipoprotein (LDL) or high density lipoprotein (HDL) cholesterol and triglyceride) and quality of life measures (including informal outcomes such as feelings of health and time off work).

Tertiary outcomes

Tertiary outcomes were process outcomes and included changes in saturated and total fat intakes, as well as other macronutrients, sugars and alcohol.

This is not a systematic review of the effects of reduced fat on these secondary or tertiary outcomes, but we collated the outcomes from included studies in order to understand whether any effects on weight might be compromised by negative effects on secondary or tertiary outcomes.

Search methods for identification of studies

Electronic searches

The search to June 2010 is described in Hooper 2012b. We updated the searches to November 2014 and ran these in MEDLINE (Ovid, see Appendix 1). EMBASE (Ovid) and CINAHL (EBSCO host) searches were based on the MEDLINE search (Appendix 2; Appendix 3). The Cochrane Heart Group ran the update search for adult RCTs on 5 March 2014 in CENTRAL (2014, Issue 1) for a sister review, Hooper 2015 (Appendix 4), and we checked the references for this review.

Searching other resources

We searched the bibliographies of all related identified systematic reviews for further trials and cohort studies for the update, including Aljadani 2015, Ajala 2013, Aljadani 2013, Ambrosini 2014, Benatar 2013, Chaput 2014, Gow 2014, Havranek 2011, Hu 2012, Kratz 2013, Ni 2010, Schwingshackl 2013, Schwingshackl 2013a and Yang 2013.

Data collection and analysis

Selection of studies

We only rejected articles on the initial screen if the review author could determine from the title and abstract that the article was not a relevant RCT or cohort study. We rejected articles if they were not the report of a RCT; the trial did not address a low fat intake; the trial was exclusively in infants (less than 24 months old), pregnant women or the critically ill; participants were chosen for being overweight or obese; there was an intention to reduce weight in some or all participants; the trial was of less than six months duration; or the intervention was multifactorial. We rejected cohort studies where they were not prospective; where participants' total fat intake was not assessed; where they did not follow participants for at least 12 months after assessment of total fat; or where the relationship between total fat at baseline and a measure of absolute or change in body fatness at least 12 months later was not assessed.

When a title/abstract could not be rejected with certainty, we obtained the full text of the article for further evaluation. LH and AA assessed the inclusion of studies independently in duplicate, and we collected studies identified by either review author. LH and AA assessed the full texts collected for inclusion independently in duplicate, and discussed disagreements until agreement was reached.

Data extraction and management

We extracted data concerning participants, interventions or exposures and outcomes, and trial or cohort quality characteristics onto a form designed for the review. We extracted data on potential effect modifiers from RCTs (including duration of intervention, control group fat intake, sex, year of first publication, difference in % energy from fat between the intervention and control groups, type of intervention (food or advice provided), the dietary fat goals set for each arm, baseline BMI and health at baseline). Where provided, we collected data on risk factors for cardiovascular disease (secondary and tertiary outcomes).

All trial outcomes were continuous and where possible we extracted change data (change in the outcome from baseline to outcome assessment) with relevant data on variance for intervention and control arms (along with numbers of participants at that time point). Where change data were not available, we extracted data at study end (or other relevant time point) along with variance and numbers of participants for each arm. LH and AA extracted all data independently in duplicate.

Assessment of risk of bias in included studies

We carried out 'Risk of bias' assessment independently in duplicate. We assessed trial risk of bias using the Cochrane tool for assessment of risk of bias (Higgins 2011b). For included RCTs we also assessed whether trials were free of differences in diet (between intervention and control arms) other than dietary fat intake, and whether there was any systematic difference in attention or care or time given between the intervention and control groups, as we felt that these factors may also cause differences in weight. We used the category 'other bias' to note any further issues of methodological concern. Funding was not formally a part of our assessment of bias in RCTs as it is not a core part of the Cochrane 'Risk of bias' tool.

For cohort studies we assessed the number of participants lost to follow-up (with reasons), baseline similarity by total fat intake, funding, type of control group (internal or external), method of assessment of total fat intake, number of total fat assessments and factors adjusted for. We also noted factors not adjusted for (age, sex, energy intake, ethnicity, physical activity (and/or TV watching) and socioeconomic (including educational) status for adults and age, sex, energy intake, ethnicity, parental BMI, physical activity (and/or TV watching) and socioeconomic (including educational) status in children).

Measures of treatment effect

The effect measure of choice for continuous outcomes (all review outcomes were continuous outcomes) was the mean difference (MD).

Unit of analysis issues

We did not include any cluster-randomised or cross-over trials in this review.

Where there was more than one relevant intervention arm but only one control arm we pooled the relevant intervention arms to create a single pair-wise comparison (where the intervention arms were equivalently appropriate for this review) as described in Higgins 2011a. We excluded intervention arms that were not appropriate for this review, or less appropriate than another arm. When two arms were appropriate for different subgroups then we used the control group once with each intervention arm, but we did not pool the subgroups overall.

When weight or BMI were assessed at more than one time point we used the data from the latest time point available in general analyses, but we extracted data for all time points for use in subgrouping by study duration.

Dealing with missing data

Where included studies used methods to infer missing data (such as carrying the latest weight data forward) then we used these data in analyses. Where this was not done we used the data as presented.

Assessment of heterogeneity

We examined heterogeneity using the I^2 statistic and considered heterogeneity important where the I^2 was above 50% (Higgins 2003; Higgins 2011a).

Assessment of reporting biases

We drew funnel plots to examine the possibility of publication bias for measures of body fatness with at least 10 included comparisons (Egger 1997).

Data synthesis

All trial outcomes were continuous and where possible we extracted change data (change in the outcome from baseline to outcome assessment) with relevant data on variance for intervention and control arms (along with numbers of participants at that time point). Where change data were not available, we extracted data at study end (or other relevant time point) along with variance and numbers of participants for each arm. We did not use end data where the difference between the intervention and control groups at baseline was greater than the change in that measure between baseline and endpoint in both arms (instead we used change data in forest plots, but without standard deviations (SDs), so the data did not add to the meta-analyses but provided comparative information).

We combined data by the inverse variance method in random-effects meta-analysis to assess mean differences between lower and higher fat intake arms.

We planned to conduct separate meta-analyses of data from adult RCTs, data from child RCTs, data from adult cohort studies and data from child cohort studies, where data from separate studies were similar enough to be combined.

We created a 'Summary of findings' table assessing the effects of low dietary fat compared with usual fat for body weight in adults using RCT data.

Subgroup analysis and investigation of heterogeneity

For this update we classified all dietary interventions as low fat versus usual or modified fat. Pre-specified subgroups for body fat outcomes, to explore the stability of findings in different study subgroups, included:

- duration of intervention (6 to < 12 months, 12 to < 24 months, 24 to < 60 months, and 60+ months);

- control group total fat intake (> 35%E from fat, > 30%E to 35%E from fat, > 25%E to 30%E from fat);
- year of first publication of results (1960s, 1970s, 1980s, 1990s, 2000s, 2010s);
- sex (studies of women only, of men only, of men and women mixed);
- difference in %E from fat between control and reduced fat groups (up to 5%E from fat, 5%E to < 10%E from fat, 10%E to < 15%E from fat, 15+%E from fat, or unknown difference);
- type of intervention (dietary advice, advice plus supplements and diet provided);
- by total fat goal in the intervention arm (10%E to < 15%E from fat, 15%E to < 20%E from fat, 20%E to < 25%E from fat, 25%E to < 30%E from fat, 30%E from fat, and no specific goal stated);
- achieving fat goals (achieved 30%E from fat or less, did not achieve this);
- mean BMI at baseline (< 25, 25 to < 30, 30+);
- state of health at baseline (not recruited on the basis of risk factors or disease, recruited on the basis of risk factors such as lipids, hormonal levels etc., recruited on the basis of having or having had diseases such as diabetes, myocardial infarction, cancer, polyps);
- assessed energy reduction in the intervention compared with the control group during the intervention period (E intake the same or greater in the low fat group, E intake 1 to 100 kcal/d lower in the low fat group, 101 to 200 kcal/d lower in the low fat group, > 200 Kcal/d lower in the low fat group).

For subgrouping factors that appeared to suggest significant differences in effect size between subgroups we explored the effects using meta-regression on weight (we also intended to explore the effects on other outcomes, but no other outcome had more than 10 relevant comparisons). We performed random-effects meta-regression (Berkley 1995) using the STATA command metareg (Sharp 1998; Sterne 2001; Sterne 2009).

Sensitivity analysis

We carried out sensitivity analyses for primary outcomes, assessing the effect of:

- running fixed-effect meta-analyses (rather than random-effects) (Higgins 2011a);
- excluding the largest study (WHI with CVD 2006, WHI 2006);
- excluding studies that were not free of systematic differences in care (or unclear);
- excluding studies that were not free of dietary differences other than fat (or unclear);
- excluding studies with unclear or inadequate allocation concealment.

RESULTS

Description of studies

The study flow is shown in Figure 1. The perceived importance of obesity and overweight has increased over the past few years, therefore many trials of reduced fat diets now explicitly or implicitly aim at weight loss. To guard against inclusion of studies that intended weight loss without stating this clearly we decided to exclude RCTs that only included people based according to their BMI or weight classification (i.e. specifically including only people with a BMI > 25). For this reason (and to ensure consistency) we have excluded three RCTs included in the previous version of this review, Hooper 2012b, from this current review (CARMEN 2000; CARMEN MS sub-study; German Fat Reduced), while we have included an additional adult RCT (Diet and Hormone Study 2003).

Figure 1. Study flow diagram for this systematic review (update searches run November 2014).

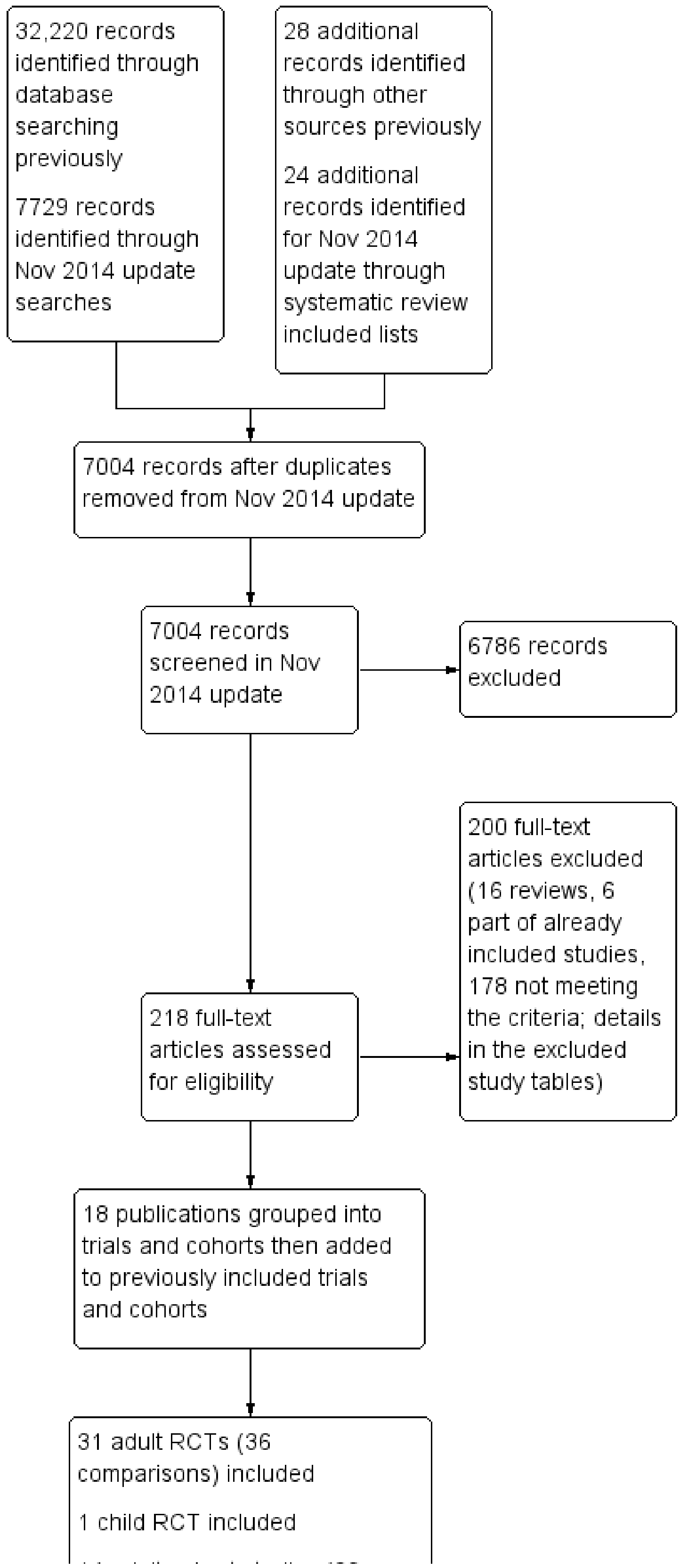
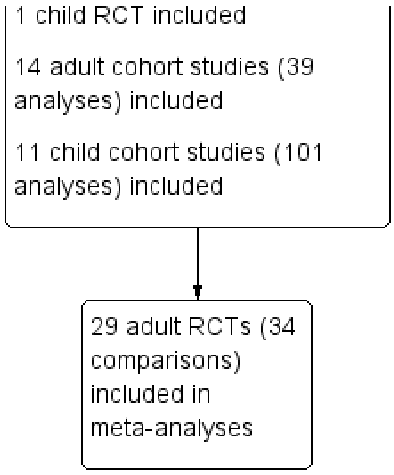


Figure 1. (Continued)



Results of the search

The search for RCTs and cohort studies in the original version of this review identified 32,220 titles and abstracts from the electronic searches plus 28 further potential studies from other sources. For this update the electronic searches identified 7729 possible titles and abstracts, plus we assessed a further 24 potential studies following our check of potentially relevant trials and cohort studies included in other systematic reviews. Of these 7753 potential update titles and abstracts, we assessed 218 full-text articles for eligibility (additional to the 465 assessed for the original review). We included a total of 32 RCTs (31 in adults, one in children) and 25 prospective cohort studies (17 sets of analyses of 14 cohorts in adults and 13 sets of analyses of 11 cohorts in children) (Figure 1). We included 29 adult RCTs (including 34 comparisons) in meta-analyses.

Included studies

Of the 31 RCTs in adults (36 comparisons, including roughly 53,626 participants - exact numbers depending on time point in study and endpoint used), 21 were from North America, nine from Europe and one from New Zealand, with none from developing or transitional countries. The duration of the trials varied from six months to more than eight years. In four trials the participants were all men, in 15 all women and in 12 both sexes (one of which reported outcomes by sex). Mean ages and states of health (low, moderate or high risk of cardiovascular disease or breast cancer) varied. The single trial in children analysed 191 Greek 12- to 13 -year old boys and girls, followed up for 17 months (VYRONAS 2009). See Characteristics of included studies for detailed characteristics of the RCTs in adults and young people.

When discussing the 31 RCTs, the de Bont study (de Bont 1981 non-obese; de Bont 1981 obese), DEER study (DEER 1998 exercise men; DEER 1998 exercise women; DEER 1998 no exercise men; DEER 1998 no exercise wom), and Kuopio study (Kuopio Reduced & Mod 1993; Kuopio Reduced Fat 1993) are each referred to and counted as a single study, although they appear as individual arms in analyses and in the validity table (suggesting 36 intervention arms).

We included 14 adult cohorts (20 published papers, cohorts presented their results in from one to eight main analyses, 39 analyses in total) which reported on baseline total fat intake and reported on a measure of body fatness at least one year later. Eleven cohorts reported change in weight, BMI and/or waist circumference over the course of the follow-up, while three cohorts reported absolute weight or BMI at follow-up. Follow-up was from one year to over 16 years (median five years). Most cohorts were of mixed sex, though one was men only and two women only. Recruitment included young people (13 years and over in one mixed cohort although most participants recruited were adults, 18 years and over in fully adult cohorts), middle aged and elderly adults (up to 75 years at baseline). Cohorts were recruited in North America (eight cohorts), Europe (five cohorts) and Australia (one).

The 11 included cohorts that recruited children and young people were followed for one to 23 years (median four years). They were reported in 13 published papers, and provided 101 separate analyses. The cohorts recruited children aged from two years to 14 years (although one study, Viva La Familia, may have recruited four- to 19-year olds, so included a few young people older than 14 at baseline), and followed up until later in childhood or early adulthood. Five were based in North America, three in Europe, two in Australia and one in Korea.

The table of characteristics of the adult cohort studies, along with their references, is found in Table 1, and of cohorts of children and young people in Table 2.

Excluded studies

Reasons for exclusion of the 345 adult RCTs that we read in full text but excluded from this review are found in Characteristics of excluded studies. Reasons for exclusion of child RCTs are found in Table 3, adult cohort studies in Table 4, and child cohort studies in Table 5, along with their references.

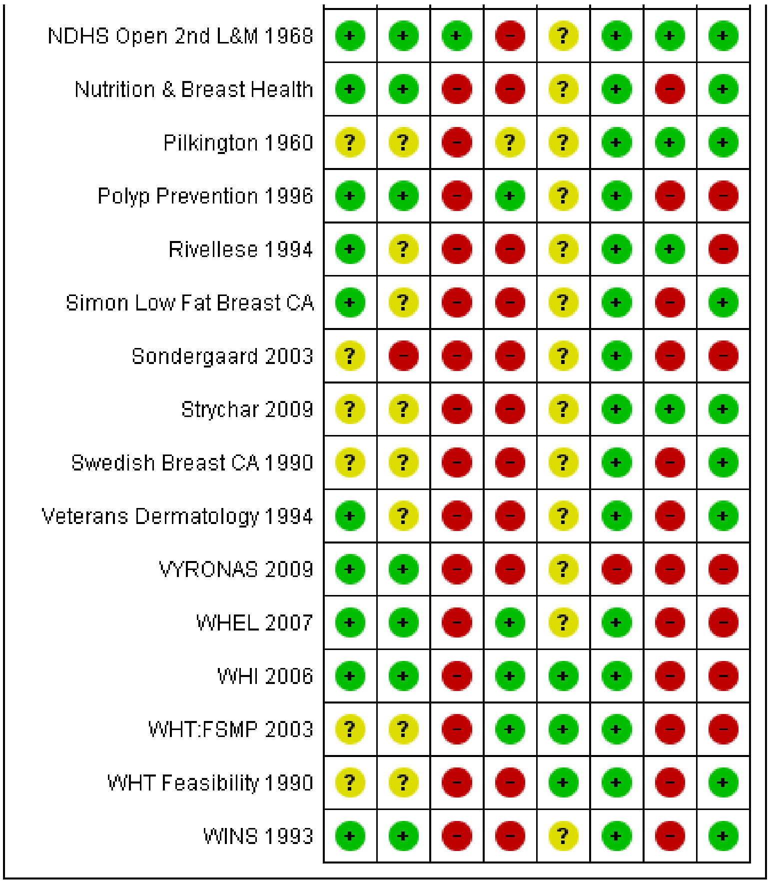
Risk of bias in included studies

To understand the risk of bias in the individual included RCTs in a visual way, see Figure 2. 'Risk of bias' assessments of included adult cohort analyses are found in Table 6, and of child and young people's cohort analyses in Table 7.

Figure 2. 'Risk of bias' summary: review authors' judgements about each methodological quality item for each included adult and child RCT comparison.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Free of systematic difference in care?	Free of dietary differences other than fat?
Auckland reduced fat 1999	+	+	−	−	?	+	−	+
BDIT Pilot Studies 1996	?	?	−	−	?	+	−	+
beFIT 1997	+	?	−	?	−	+	−	+
Bloemberg 1991	+	?	−	+	?	+	−	+
BRIDGES 2001	+	+	−	−	?	+	−	−
Canadian DBCP 1997	+	+	−	−	?	+	−	+
de Bont 1981 non-obese	?	?	−	−	?	+	+	+
de Bont 1981 obese	?	?	−	−	?	+	+	+
DEER 1998 exercise men	+	?	−	−	?	+	−	+
DEER 1998 exercise women	+	?	−	+	?	+	−	+
DEER 1998 no exercise men	+	?	−	+	?	+	−	+
DEER 1998 no exercise wom	+	?	−	+	?	+	−	+
Diet and Hormone Study 2003	+	?	−	−	?	+	−	−
Kentucky Low Fat 1990	+	?	−	−	?	+	−	+
Kuopio Reduced & Mod 1993	+	?	−	+	?	+	+	+
Kuopio Reduced Fat 1993	+	?	−	−	?	+	+	+
Mastopathy Diet 1988	?	?	−	−	?	+	−	+
MeDiet 2006	+	?	−	+	?	+	−	−
Moy 2001	+	?	−	−	?	+	−	?
MSFAT 1995	+	+	−	−	?	+	+	+
NDHS Open 1st L&M 1968	+	+	+	−	?	+	+	+
NDHS Open 2nd L&M 1968	+	+	+	−	?	+	+	+

Figure 2. (Continued)



Validity of RCTs

Allocation

Twenty-two RCTs and the single child RCT, VYRONAS 2009, had low risk of bias from random sequence generation; the remainder were at unclear risk. Eleven adult RCTs and the single child RCT were at low risk of selection bias arising from poor or unclear allocation concealment or randomisation, one was at high risk (Sondergaard 2003), and the remaining RCTs were at unclear risk.

Blinding

There was a high risk of performance and detection bias due to lack of blinding (which is usual in dietary trials) in all included RCTs except the National Diet and Heart Studies (NDHS Open 1st L&M 1968; NDHS Open 2nd L&M 1968), which provided trial shops that blinded purchases of usual or low fat products.

Incomplete outcome data

For RCTs we assessed those studies that lost more than 5% of participants per year as at high risk of attrition bias; others were at low risk of attrition bias. Eight RCTs were at low risk of attrition bias, two were unclear and the remainder (including the one child RCT) at high risk.

Selective reporting

Most RCTs were at unclear risk of reporting bias (due to the paucity of accessible protocols, so that we could not assess reporting bias), but three adult RCTs were at low risk and one at high risk of bias. We examined the possible presence of reporting bias by using the list of included studies from a recent review of RCTs of the effects of reduced and modified fat on cardiovascular events (Hooper 2012b). Of 48 included RCTs in the other review, we included 21 in the current review. Of the remaining 27 RCTs, 10 did not compare reduced fat intake with usual fat intake (they were included as they modified fat compared with usual fat intake), 13 aimed to reduce weight in some or all participants and three included only participants with a high BMI. Only one trial was eligible for this review but was not included as no data were provided on any measure of body fatness (Toronto Polyp Prev 1994). The risk of reporting bias, related to the proportion of studies not included in a meta-analysis, seems minimal here (Furukawa 2007).

Other potential sources of bias

We considered all the adult RCTs to be at low risk of other types of bias, but the child RCT, VYRONAS 2009, was felt to be at high risk due to individual randomisation in a school setting, which raised the issue of contamination of the intervention between intervention and control children. Eight adult RCTs had low risk of systematic differences in level of care between the intervention and control groups, while 24 had high risk of such differences in care, as did the child RCT. Differences in attention, training, time from health professionals, number of health checks and/or group support could potentially alter feelings of self efficacy and increase contact with healthcare professionals offering various types of support, and alter participants' ability to look after themselves and maintain a healthy weight. Some dietary interventions to reduce fat also had specific goals around fruit, vegetables, fibre, alcohol etc., which raises the possibility that any changes in weight may result from these alterations, not from change in fat intake. Ten adult RCTs and the child RCT were at high risk of effects from dietary differences other than fat; the remaining 22 RCTs were at low risk of effects from other dietary advice.

Validity of cohort studies

We considered the cohort studies to be at either moderate or high risk of bias. Moderate risk of bias was suggested where less than 20% were lost to follow-up, two factors or fewer were unadjusted for in the design or analysis (of age, sex, energy intake, ethnicity, physical activity and/or TV watching and socioeconomic status (which includes educational status for adult cohorts), and diet was assessed using a 24-hour recall or diet diary. For child cohorts factors assessed for adjustment included age, sex, energy intake, ethnicity, parental BMI, physical activity and/or TV watching) and socioeconomic factors, including educational status. We considered all other studies to be at high risk of bias.

We considered all adult cohort analyses to be at high risk of bias, apart from the MONICA study analysis. We likewise considered all cohort studies of children and young people to be at high risk of bias, except for Davison 2001, which was at moderate risk of bias. Cohort studies overall suffered from high dropout rates, lack of complete adjustment for relevant potential confounders and poor assessment of total fat intake.

Effects of interventions

See: **Summary of findings for the main comparison** Low dietary fat compared with usual fat for controlling body fatness

A 'Summary of findings' table assessing the effects of low dietary fat compared with usual fat for body weight in adults using randomised controlled trial (RCT) data is presented (Summary of findings for the main comparison).

Effects of reducing dietary fat on weight and body fatness in adults (as seen in RCTs)

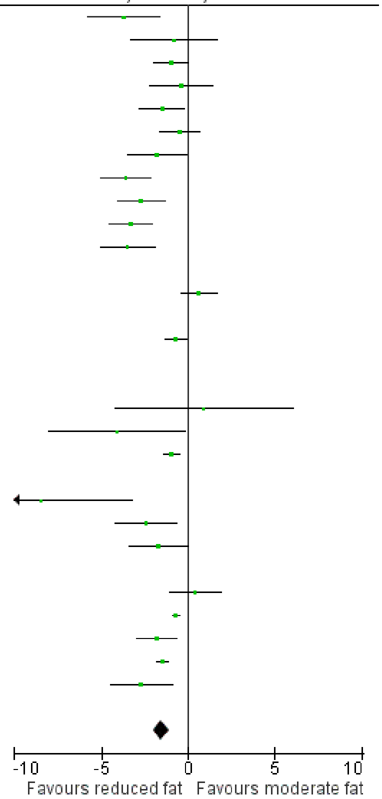
Weight

Eating a lower proportion of energy as fat results in lower weight (or lower weight gain, or greater weight reductions) than eating the usual proportion of fat (-1.5 kg, 95% confidence interval (CI) -2.0 to -1.1, 53,647 participants, 24 estimable comparisons, I^2 = 77%, Analysis 1.1; Figure 3). The effect was small but statistically significant, and the best estimate of effect being a reduction in weight was consistent across 21 of the 24 comparisons with numerical data. Additionally, all of the six comparisons that did not have an estimable effect size, due to lack of variance data or large baseline differences, were consistent with greater weight reduction in the reduced fat arms (Figure 3). The same effect was reported in two of the three comparisons that were not included in the forest plot (as they provided insufficient information). The exception was Sondergaard 2003, which reported "in both groups, body weight remained unchanged after 12 months".

Figure 3. Forest plot of comparison: 1 Fat reduction versus usual fat diet, adult RCTs, outcome: 1.1 Weight, kg.

Study or Subgroup	Reduced fat Mean	Reduced fat SD	Reduced fat Total	Usual or modified fat Mean	Usual or modified fat SD	Usual or modified fat Total	Weight	Mean Difference IV, Random, 95% CI
Auckland reduced fat 1999	-1.6	5.4	48	2.13	5	51	2.8%	-3.73 [-5.78, -1.68]
BDIT Pilot Studies 1996	59.6	7.3	76	60.4	8.4	78	2.1%	-0.80 [-3.28, 1.68]
Bloemberg 1991	-0.94	2.68	39	0.06	1.86	40	5.5%	-1.00 [-2.02, 0.02]
BRIDGES 2001	0.1	4.85	48	0.5	4.07	46	3.3%	-0.40 [-2.21, 1.41]
Canadian DBCP 1997	62	9.1	388	63.5	9.4	401	4.6%	-1.50 [-2.79, -0.21]
de Bont 1981 non-obese	-0.4	2.8	36	0.1	2	29	5.0%	-0.50 [-1.67, 0.67]
de Bont 1981 obese	-2.7	3.6	34	-0.9	3.5	35	3.5%	-1.80 [-3.48, -0.12]
DEER 1998 exercise men	-4.2	4.2	48	-0.6	3.1	47	4.0%	-3.60 [-5.08, -2.12]
DEER 1998 exercise women	-3.1	3.7	43	-0.4	2.5	43	4.5%	-2.70 [-4.03, -1.37]
DEER 1998 no exercise men	-2.8	3.5	49	0.5	2.7	46	4.7%	-3.30 [-4.55, -2.05]
DEER 1998 no exercise wom	-2.7	3.5	46	0.8	4.2	45	3.8%	-3.50 [-5.09, -1.91]
Diet and Hormone Study 2003	-0.68	0	81	-0.14	0	96		Not estimable
Kentucky Low Fat 1990	1.06	2.49	47	0.44	2.68	51	5.4%	0.62 [-0.40, 1.64]
MeDiet 2006	-1.3	0	51	-0.6	0	55		Not estimable
MSFAT 1995	0.4	2.36	117	1.12	2.36	103	6.8%	-0.72 [-1.34, -0.10]
NDHS Open 1st L&M 1968	-2.45	0	332	-1.91	0	348		Not estimable
NDHS Open 2nd L&M 1968	-1.8	0	179	-1.2	0	215		Not estimable
Nutrition & Breast Health	67.3	13.8	47	66.4	12	50	0.6%	0.90 [-4.26, 6.06]
Pilkington 1960	66.7	5.9	12	70.8	5.2	23	1.0%	-4.10 [-8.06, -0.14]
Polyp Prevention 1996	-0.65	5.22	943	0.31	5.22	943	7.3%	-0.96 [-1.43, -0.49]
Rivellese 1994	-1.8	0	27	-1.6	0	17		Not estimable
Simon Low Fat Breast CA	63.4	11.1	34	71.9	11.7	38	0.6%	-8.50 [-13.77, -3.23]
Strychar 2009	-0.83	3	15	1.6	1.8	15	3.3%	-2.43 [-4.20, -0.66]
Swedish Breast CA 1990	-0.4	5.5	63	1.3	5.5	106	3.5%	-1.70 [-3.41, 0.01]
Veterans Dermatology 1994	-2	0	38	0.5	0	58		Not estimable
WHEL 2007	74.1	19.53	1308	73.7	19.2	1313	4.0%	0.40 [-1.08, 1.88]
WHI 2006	-0.8	10.1	16297	-0.1	10.1	25056	7.9%	-0.70 [-0.90, -0.50]
WHT Feasibility 1990	-1.91	4.9	159	-0.08	4.3	102	5.1%	-1.83 [-2.96, -0.70]
WHT:FSMP 2003	-1.8	4	1325	-0.3	4.2	883	7.6%	-1.50 [-1.85, -1.15]
WINS 1993	-2.7	15.3	386	0	15.3	998	3.3%	-2.70 [-4.50, -0.90]
Total (95% CI)			**22316**			**31331**	**100.0%**	**-1.54 [-1.97, -1.12]**

Heterogeneity: Tau² = 0.58; Chi² = 99.49, df = 23 (P < 0.00001); I² = 77%
Test for overall effect: Z = 7.14 (P < 0.00001)



The statistical significance of this relative weight reduction was not lost when we removed studies providing greater time or resources to the reduced fat group (-1.3 kg, 95% CI -2.1 to -0.4), when we removed studies with additional dietary interventions (-1.9 kg, 95% CI -2.6 to -1.3), when we used fixed-effect meta-analysis (rather than random-effects analysis) (-1.0 kg, 95% CI -1.2 to -0.9), when we removed the largest RCT (WHI 2006) (-1.6 kg, 95% CI -2.1 to -1.2), or when we removed studies with high or unclear risk of selection bias (-1.0 kg, 95% CI -1.4 to -0.5).

We examined the influence of potential effect modifiers through subgrouping (Table 8). There was a suggestion of a dose effect, with studies that reduced total fat in the intervention group by a greater amount compared with the control group showing greater reductions in weight (test for subgroup differences: P value = 0.003). Where the reduction in total fat was less than 5%E compared with control, weight loss was not statistically significant (mean difference (MD) -0.2 kg, 95% CI -0.9 to 0.6), but as the difference in total fat increased, weight reductions were seen (5%E to < 10%E from fat difference between intervention and control groups, MD -2.1 kg, 95% CI -2.9 to -1.4, and 10%E to < 15%E from fat difference, MD -1.3 kg, 95% CI -1.7 to -1.0). As few studies altered the %E from fat by 15% or more, power was limited so the suggested effect size was large but non-significant (MD -3.9 kg, 95% CI -8.8 to 1.0). Similarly there was a suggestion that in low fat arms with greater reductions in energy intake there were greater relative falls in weight (test for subgroup differences: P value = 0.04).

The time point at which weight is assessed following the onset of a reduced compared with a moderate fat diet may be important. The effect in studies that assessed weight from six to up to 12 months, 12 to up to 24 months and 24 to up to 60 months was statistically significant, but at 60+ months (MD -0.7 kg, 95% CI -1.7 to 0.3) statistical significance was lost (test for subgroup differences: P value = 0.04).

The level of fat in the control group may also be important. Weight loss was statistically significant where the control group intake was over 35% of energy from fat, over 30% to 35% of energy or over 25% to 30% of energy, with a suggestion of greater weight loss in groups with lower baseline fat intake (test for subgroup differences: P value < 0.00001) (see Table 8).

There was a suggestion that dietary advice was more effective in weight reduction with low fat eating than provision of low fat foods, however the power of the analysis was limited (only one study that provided foods also supplied numerical data for meta-analysis (test for subgroup differences: P value = 0.04).

There were no clear effects of: sex on weight (studies in men, in women and in mixed sexes all showed significant weight loss; test for subgroup differences: P value = 0.20), year of first publication (studies published in the 1960s, 1980s, 1990s and 2000s were all statistically significant; test for subgroup differences: P value = 0.07), the total fat intake goal in the intervention group (test for subgroup differences: P value = 0.34), whether the low fat arm achieved a fat intake of ≤ 30%E or not (test for subgroup differences: P value = 0.42), body mass index at baseline (test for subgroup differences: P value = 0.17), or whether participants were recruited as healthy, with risk factors (such as lipids, hormone levels or breast cancer risk factors), or with existing disease (such as diabetes, previous myocardial infarction or polyps) (test for subgroup differences: P value = 0.12). For all of these subgroupings all of the subgroups examined showed statistically significant weight loss in the low fat arms compared with the control arms.

Meta-regression (multiple regression model on dose, duration and control group fat intake, all at once) suggested that the degree of fat reduction was significantly associated with the degree of weight loss in the intervention arm compared with the control arm (coefficient -0.20 kg/1% energy from total fat reduction, 95% CI -0.34 to -0.05, P value = 0.010), suggesting that greater reduction in fat intake was associated with greater weight loss. Fat intake in the control group (equivalent to baseline fat intake) was also significantly associated with the degree of weight loss in the intervention group (coefficient 0.17 kg/1% energy from fat in the control group, 95% CI 0.04 to 0.29, P value = 0.010), suggesting that a reduction in fat intake was more effective at reducing weight in those with a lower baseline fat intake. There was no clear association between trial duration and degree of weight loss (coefficient 0.01 kg/month, 95% CI -0.006 to 0.030, P value = 0.19). Together these factors explained 56% of variance between studies, using the equation: weight change (kg) = -5.97 kg + 0.17 kg/1% energy from total fat in control group -0.20 kg/1% decrease in energy from total fat in intervention group + 0.01 kg/months' duration.

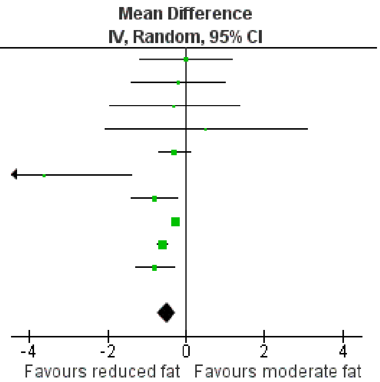
Body mass index (BMI), waist circumference and other measures of body fatness

Fewer studies reported BMI than weight, but the effect of a lower proportion of energy from fat on BMI appeared similar to that on weight (-0.5 kg, 95% CI -0.7 to -0.3, 45,703 participants, 10 comparisons, I^2 = 74%) (Analysis 1.2; Figure 4). As there were fewer studies than for weight, we did not attempt sensitivity analyses and subgrouping for BMI.

Figure 4. Forest plot of comparison: 1 Fat reduction versus usual fat diet, adult RCTs, outcome: 1.2 BMI, kg/m2.

	Reduced fat			Usual or modified fat				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
BDIT Pilot Studies 1996	24.3	3.8	76	24.3	3.6	81	3.7%	0.00 [-1.16, 1.16]
Diet and Hormone Study 2003	23.5	4.4	81	23.7	3.5	96	3.5%	-0.20 [-1.39, 0.99]
Kuopio Reduced & Mod 1993	26	4	41	26.3	3.6	41	2.0%	-0.30 [-1.95, 1.35]
Kuopio Reduced Fat 1993	26.2	3.2	40	25.7	4.2	12	0.8%	0.50 [-2.07, 3.07]
Moy 2001	-0.1	1	117	0.21	2	118	15.2%	-0.31 [-0.71, 0.09]
Simon Low Fat Breast CA	23.8	4.7	34	27.4	4.9	38	1.1%	-3.60 [-5.82, -1.38]
Strychar 2009	-0.24	1	15	0.56	0.6	15	10.2%	-0.80 [-1.39, -0.21]
WHI 2006	0.03	3.2	16230	0.3	3.1	24943	26.3%	-0.27 [-0.33, -0.21]
WHT:FSMP 2003	-0.7	1.2	1094	-0.1	1.4	646	24.9%	-0.60 [-0.73, -0.47]
WINS 1993	26.8	5.608	755	27.6	5.368	1230	12.3%	-0.80 [-1.30, -0.30]
Total (95% CI)			**18483**			**27220**	**100.0%**	**-0.50 [-0.74, -0.26]**

Heterogeneity: Tau² = 0.06; Chi² = 35.05, df = 9 (P < 0.0001); I² = 74%
Test for overall effect: Z = 4.07 (P < 0.0001)



Only one RCT reported waist circumference, finding that waist circumference in those on low fat diets was significantly lower than in those on usual fat diets at five and seven years (by 0.3 cm, 95% CI -0.6 to -0.02, 15,671 women) (WHI 2006). No adult RCTs reported other measures of body fatness.

Secondary outcomes - lipids and blood pressure

There was no suggestion of harms associated with low fat diets that might mitigate any benefits on weight.

Effects of reduced fat compared with usual or modified fat diets suggested that the lower fat diets were associated with lower total and low-density lipoprotein (LDL) cholesterol, without important effects on high-density lipoprotein (HDL) or triglycerides. Effects on LDL (-0.1 mmol/L, 95% CI -0.2 to -0.03, 7285 participants, 18 comparisons, I^2 = 65%) were similar to those on total cholesterol (-0.2 mmol/L, 95% CI -0.3 to -0.1, 7715 participants, 20 comparisons, I^2 = 54%). The effect on HDL suggested slight harm from lower fat diets (-0.01 mmol/L, 95% CI -0.03 to 0.00, P value = 0.11, 7166 participants, 19 comparisons, I^2 = 0%). Given the weight loss, there was little evidence of a benefit on triglycerides (-0.02 mmol/L, 95% CI -0.12 to 0.08, 6976 participants, 17 comparisons, I^2 = 56%). There was a reduction in total cholesterol/HDL ratio over the seven comparisons that reported it (-0.10, 95% CI -0.16 to -0.04, 3332 participants, I^2 = 0%).

There were small and statistically significant beneficial effects of a lower fat diet on systolic and diastolic blood pressure (although these were reported in relatively few studies). The effect on systolic blood pressure (-1.2 mmHg, 95% CI -2.0 to -0.4, 5159 participants, nine comparisons, I^2 = 0%) was greater than that on diastolic blood pressure (-0.7 mmHg, 95% CI -1.4 to -0.1, 5159 participants, nine comparisons, I^2 = 23%).

Secondary outcomes - effects of reducing fat intake on intakes of energy, protein, carbohydrate, sugars and alcohol

Indications were that during the studies energy intake was usually lower in the low fat group than in the control or usual fat groups. Sugar intake was not measured often but where reported sugar intake appeared higher in low fat arms (except in MeDiet 2006, see Table 9). Carbohydrate intakes appeared almost universally higher in low fat arms than in usual fat arms, and protein intakes were sometimes higher and sometimes similar. There was no consistent pattern in alcohol intake.

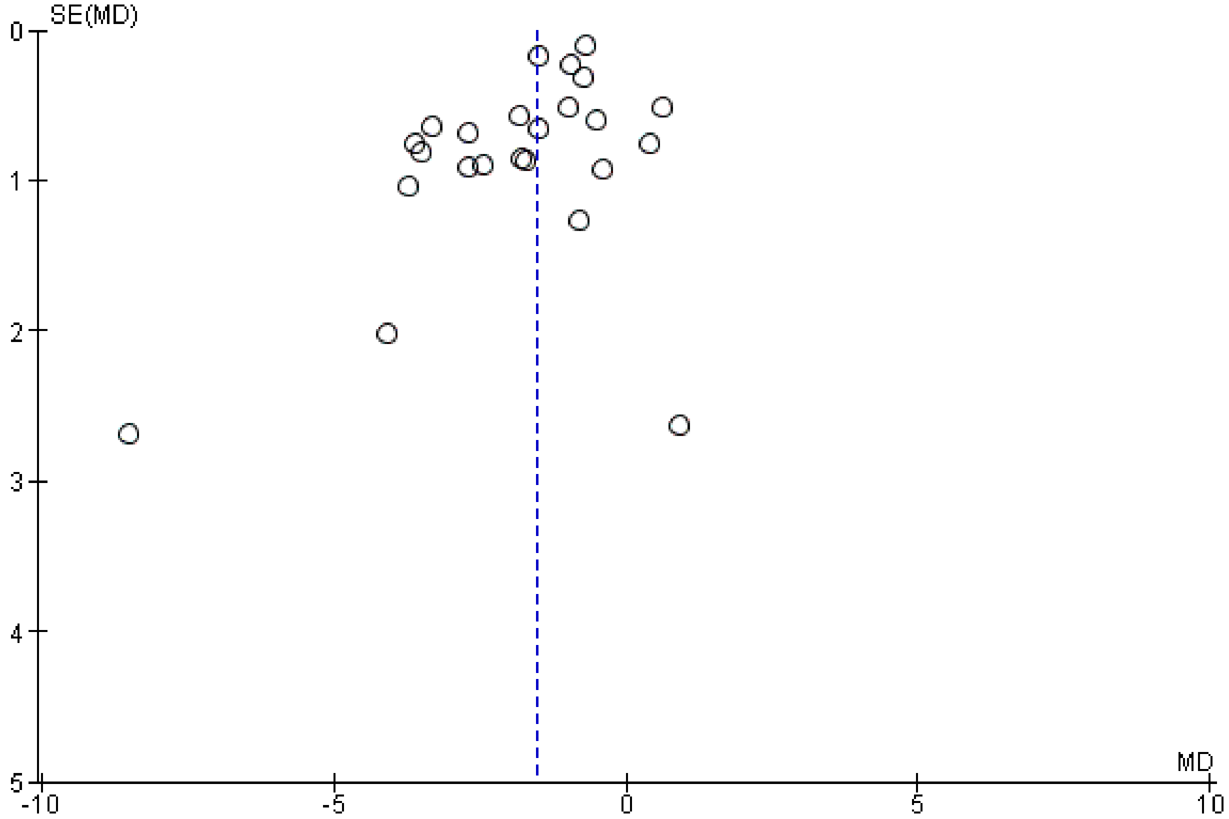
Secondary outcomes - effects of reducing fat intake on quality of life measures

Quality of life outcomes were rarely measured or reported. It appears that quality of life was assessed in WHI 2006 but we were unable to find any reference to this outcome by dietary intervention group. No other relevant data were located.

Publication bias

The funnel plot of studies assessing effects on weight did not suggest any serious publication bias (Figure 5), and neither did the funnel plot of effects on BMI (not shown). The studies that assessed weight, but where we could not include the data provided in meta-analysis, did not appear to differ importantly in their results from the studies that provided variance data and were included in the analyses.

Figure 5. Funnel plot of comparison: 1 Fat reduction versus usual fat diet, outcome: 1.1 Weight, kg.



Effects of reducing dietary fat on weight and body fatness in children (as seen in RCTs)

As part of the single RCT in children, VYRONAS 2009 randomised 213 students aged 12 to 13 years at baseline to intervention or usual diet, of whom 191 were analysed at 17 months. The validity of this RCT was discussed with the adult RCTs and is shown in Figure 2). The intervention group (n = 98) had a 12-week school-based health and nutrition interventional programme with a 17-month follow-up period. After 17 months, total fat intake (as %E) showed a significant reduction 31.3% (standard deviation (SD) 4.4) compared with baseline intake of 35.4% (SD 4.7) in the intervention group (P value < 0.001). In the control group fat intake at 17 months was 36.2% (SD 5.2) compared with 36.9% (SD 4.8) at baseline (P value = 0.343). Mean BMI (kg/m^2) also decreased significantly (adjusting for age and sex) to 23.3 kg/m^2 (SD 2.8) compared with 24.0 kg/m^2 (SD 3.1) at baseline in the intervention group (P value < 0.001), but was more similar in the control group (24.8 (SD 3.8) versus 24.3 (SD 3.3), P value = 0.355). The difference in weight between intervention and control arms was not reported, and as the difference between intervention and control groups for baseline BMI was greater than the changes in BMI in either arm a direct comparison of BMI is probably inappropriate statistically. Mean change in BMI was a fall of 0.7 kg/m^2 in the intervention group and an increase of 0.5 kg/m^2 in the control group, a difference of 1.2 kg/m^2 (but we do not have variance data for these changes, so cannot comment on statistical significance). Analysis of 17-month BMI data by the review authors in RevMan (RevMan 2014) suggested that the effect of a low fat diet compared with a usual fat diet in children was -1.50 kg/m^2 (95% CI -2.45 to -0.55), however this was assessed on adjusted data, with a large baseline difference in BMI between groups. Without analysis of the original data set this should therefore be considered with caution.

Associations between total dietary fat and measures of body fatness in adults (as seen in cohorts)

We included 14 adult cohorts (20 published papers, cohorts presented their results in from one to eight main analyses, 39 analyses in total) which reported on baseline total fat intake and reported on a measure of body fatness at least one year later. Eleven cohorts reported change in weight, BMI and/or waist circumference over the course of the follow-up, while three cohorts reported absolute weight or BMI at follow-up (for characteristics of these studies see Table 1). We considered meta-analysis of beta values, but the different methodologies, methods of modelling, numbers of baseline dietary assessments, numbers of relevant statistical analyses per single cohort, time periods between dietary assessment and body fatness assessment, ages at baseline and outcome measures (weight, change in weight, BMI, change in BMI, change in waist circumference) were so varied that we felt combining studies in meta-analysis was inappropriate.

The single study at moderate risk of bias (Danish MONICA, Iqbal 2006, Table 1) found no relationship between fat intake and change in weight five years later. Four further cohorts reported no relationship between fat intake and measures of body fatness in the whole cohort or in any reported subgroup (Cundiff 2012; Ma 2005; Parker 1997; Halkjaer 2009). Eight cohorts reported relationships in some subgroups but not others (CARDIA found a relationship for black men and women, but not white men and women; EPIC negative relationships when replacing fat with protein, and when replacing carbohydrates with total fat, but not when replacing fat with carbohydrates; Coakley 1998 a relationship between total fat and change in weight in 45 to 54 year old men and 55 to 64 year old men, but not in men aged 65 or more; MacInnis 2013 found associations between baseline fat intake with final weight and waist circumference overall, but this was only significant in some age subgroupings; Klesges 1992 found a positive relationship with change in weight in women, but not in men, and a negative relationship with change in waist circumference in men, but not in women; Kant 1995 found a relationship with change in weight in younger women, but not in older women or men of either age group; Nurses Health Study found no relationship with change in weight in one paper, and the relationship was unclear in another paper; Lissner 1997 found a relationship between fat intake and change in weight in sedentary participants, but not in moderate or active participants). One cohort reported a positive association between total fat intake and change in weight in a mixed group of Hispanic and non-Hispanic men and women (Mosca 2004).

Overall, of the 39 reported analyses of the relationship between total fat intake and measures of body fatness in adults, 12 suggested a positive relationship, three a negative relationship and one was unclear. The remainder (23 analyses) were neutral (no statistically significant relationship).

Associations between total dietary fat in youth and measures of body fatness in children, young people and adults (as seen in cohorts)

The 11 included cohorts that recruited children and young people were reported in 13 published papers, and provided 101 separate analyses. Two cohorts assessed outcomes in adulthood, the remainder later in childhood.

Of the nine child or young person cohorts that assessed effects on body fatness in childhood or adolescence, three cohorts, including the study at moderate risk of bias, Davison 2001) suggested that higher dietary fat intakes predicted greater body fatness (assessed as % body fat and BMI in Carruth & Skinner 2001, change in BMI in Davison 2001, and change in weight in Viva la Familia). Four cohorts suggested no clear relationship between fat intake and fatness (assessed as BMI, triceps skinfold and subscapular skinfold in the Adelaide Nutrition Study, change in BMI in Bogaert 2003 and Obesity and Metabolic Disorders Cohort in Children, and change in BMI z-score in the European Youth Heart Study). Two cohorts reported effects in some measures of body fatness or some analysed age groups but not others (Trial of Activity for Adolescent Girls found no relationship of fat with BMI percentile, but a negative relationship with % body fat, while Klesges 1995 found no relationship in 3 of four assessments of change in BMI). For details of these cohort studies see Table 2.

We considered meta-analysis, but the different methodologies, methods of modelling, numbers of baseline dietary assessments, numbers of relevant statistical analyses per single cohort (from 1 to 63), time periods between dietary assessment and body fatness assessment, ages at baseline and outcome measures (weight, change in weight, BMI, change in BMI z-score, change in BMI, body fat percentage, various skinfold measures) were so varied that we felt combining studies in meta-analysis was inappropriate.

The two cohorts (two analyses of the Amsterdam Growth and Health Longitudinal Study, and one of ELANCE, Table 2), which assessed the relationship between fat intake in childhood and body fatness in early adulthood (ages 20, 27 and 36), found no clear relationships between baseline fat intake and BMI, percentage body fat, sum of skinfolds or % triceps skinfold. The exception was ELANCE, which found that greater total fat intake in youth was related to lower percentage sub-scapular skinfold and fat mass (though not to BMI or % triceps skinfold).

Overall, the included cohorts reported a total of 101 analyses of the relationship between total fat intake and body fatness in cohorts recruiting children and young people. Nine suggested positive relationships and three suggested negative relationships. The vast majority were neutral.

DISCUSSION

Summary of main results

Randomised controlled trials (RCTs) of the effects on body fatness of reducing total fat intake (without any intention to reduce body weight) show a small but consistent reduction in weight in the low fat arm compared with the usual fat arm. There is some heterogeneity between studies in the size of this effect, but not in its presence, and the effect was highly resistant to sensitivity analyses. The heterogeneity was explained by the degree of total fat reduction and baseline total fat intake (in meta-regression and in subgrouping). The small reduction in weight (1.5 kg, 95% confidence interval (CI) -2.0 to -1.1 kg) was also reflected in a reduction in body mass index (BMI) (-0.50 kg/m^2, 95% CI -0.74 to -0.26) and waist circumference (0.3 cm, 95% CI -0.6 to -0.02) in the adult studies that reported these data, and in a suggested reduction in BMI in the one child study (VYRONAS 2009): a fall of 0.7 kg/m^2 in the intervention arm and a rise of 0.5 kg/m^2 in the control arm). Additionally, there was no suggestion of harms that might mitigate any benefits on weight, and some suggestion of benefit to serum lipids and blood pressure resulting from low fat diets.

Cohort studies in adults and children generally found no clear relationship between total fat intake and measures of body fatness later in life, but a few did see positive relationships (higher total fat intake was associated with higher later body fatness), and fewer suggested negative relationships.

Overall completeness and applicability of evidence

We have searched very carefully and used a set of comprehensive search strategies to find the full set of RCTs and cohort studies assessing the relationship between total fat intake and measures of body fatness. We did this by searching for trials that reduced total fat in one arm and not in the other, regardless of the primary aims or outcomes mentioned in the title or abstracts. Indeed, the included RCTs rarely had weight as a key outcome. Reflecting this, there was little suggestion (from the funnel plot of adult RCTs assessing effects on weight and BMI) that we have missed a sample of RCTs. However, we are limited in how well we are able to assess this for cohort studies, where the risk of missing studies is keener (where sometimes the relevant analysis is added into the text as an afterthought (e.g. Working Well 1996) and does not appear in the title or abstract).

The studies are highly applicable to the question, allowing us to draw conclusions on the effect of altering the percentage of energy from total fat on body fatness.

Quality of the evidence

The included RCTs were often at unclear risk of selection bias due to unclear allocation concealment, but this did not appear to affect the results of the review as omitting all RCTs with unclear or poor allocation concealment still resulted in a statistically significant weight reduction in the intervention arms. Lack of blinding was a validity issue in most included RCTs, reflecting the difficulties of blinding dietary intervention studies. We assessed the effects of attention bias in sensitivity analyses, removing studies that provided more time or review or education to the intervention group compared with the control group, and also the effect of removing studies that provided dietary advice other than on dietary fat (in case effects were being driven by other dietary interventions) and in neither case did we lose the significant weight reduction seen in the low fat arms. In each case the higher validity trials reflect the main message, that eating a lower proportion of energy from fat results in slightly lower body fatness.

The included cohort studies were generally at high risk of bias due to the high proportion of participants lost to follow-up or lack of adjustment for potential confounders. Although the included cohorts reported on a large number of participants, they did not add significantly to the conclusions of the review as their findings were not conclusive.

Potential biases in the review process

When compiling the included studies we tried to locate RCTs that investigated the effects of reducing total dietary fat for at least six months. There was a high degree of heterogeneity among trials from different sources, including the type and number of participants, the duration and nature of interventions, control methods and follow-up. However, our sensitivity analyses and subgrouping to examine the effect of the potential effect modifiers mentioned above did not affect the statistical significance of the suggested effect, finding it remarkably robust to subgroup and sensitivity analyses.

Our review included only published studies (we did not seek unpublished data), which could bias the results due to the lack of publication of negative or inconclusive studies. However, our funnel plots did not suggest serious publication bias (Figure 5).

Our decision to exclude trials that explicitly or implicitly aimed to reduce weight may have led to missing some trials or restricting the number of included studies, especially excluding studies where there was no energy restriction, no explicit aim of weight loss, or encouraging of weight loss for some and not all participants. However, this decision makes the effect we found on weight and other measures of body fatness more reliable and avoids the potential confounding effects of dieting and unconscious energy restriction or other diet changes.

The restriction of inclusion to studies with a minimum of six months duration for RCTs or one year for cohorts led to missing some potentially relevant studies (for example, studies of 24 weeks duration, which just missed the 26-week limit). However, it is essential to draw the line at some point, and longer trials and follow-up ensure that the data are relevant to long-term fatness, which affects long-term health.

A limitation of the review was that we did not assess the causal pathway between restriction of energy from fat and weight and so the mechanism of the effect is not clear. It is likely that restricting energy from fat also reduces energy intake (see Table 9), which leads to lower body weight. Further evidence that energy intake is important in mediating the effect of lowering fat intake on body weight is suggested by a higher relative weight loss in the low fat arms with greater energy reduction.

Most (22 of 32) included RCTs were published before the year 2000 - this is primarily because most recent studies have focused on weight reduction so were ineligible for this review. However, there was no suggestion when subgrouping by decade of publication that effects have altered over time.

Agreements and disagreements with other studies or reviews

The conclusions of this updated review have not altered in overall import from the original review (Hooper 2012b). Yu-Poth 1999 found that dietary trials (excluding trials that also assessed exercise interventions) of the National Cholesterol Education Program's Step I and Step II dietary intervention programmes resulted in weight reductions (compared with control groups) of just under 3 kg, and that this was related to the degree of total fat reduction. Their regression suggested that for every 1% decrease in energy as total fat, there was a 0.28 kg decrease in body weight, while our meta-regression found that for every 1% decrease in energy as total fat there was a slightly smaller 0.20 kg decrease in weight (95% CI -0.34 to -0.05, P value = 0.010). The slightly smaller effect size in this review may be due to our excluding shorter duration studies and studies that aimed to reduce weight in the intervention arm.

However, some recent cardiovascular disease prevention guidelines have not mentioned total fat intake as regards to either weight control or prevention of cardiovascular disease (Joint ESC guidelines 2012).

AUTHORS' CONCLUSIONS

Implications for practice

Attempts should be made to reduce total fat intake in populations where mean total fat intake is 30% or more of energy, in order to support maintenance of healthy weights. For populations where the mean total fat intake is below 30% of energy, then interventions to restrict increases in total fat intake to over 30% of energy may help to avoid obesity.

Implications for research

High quality trials are needed to investigate the effect on body weight of reducing fat intake in developing or transitional countries with total fat intakes greater than 30% of energy, and of preventing total fat intake rising above 30% of energy in countries with total fat intakes of 25% to 30% of energy. High quality trials are also required in children.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Auckland reduced fat 1999

Methods	RCT
Participants	People with impaired glucose intolerance or high normal blood glucose (New Zealand) CVD risk: moderate Control: unclear how many randomised (176 between both groups), 51 analysed Intervention: unclear how many randomised (176 between both groups), 48 analysed Mean years in trial: 4.1 over whole trial % male: control 80%, intervention 68% Age: mean control 52.0 (SE 0.8), intervention 52.5 (SE 0.8) Baseline BMI: mean control 29.1 (SE 0.6), intervention 29.3 (SE 0.6)
Interventions	Reduced fat vs usual diet Control aims: usual diet Intervention aims: reduced fat diet (no specific goal stated) Control methods: usual intake Intervention methods: monthly meetings to follow a 1-year structured programme aimed at reducing fat in the diet; includes education, personal goal setting, self monitoring Weight goals: weight and calories not mentioned, diet was "aimed solely at reducing the total amount of fat in their diet" Total fat intake (at 1 year): low fat 26.1 (SD 7.7), cont 33.6 (SD 7.8) %E Saturated fat intake (at 1 year): low fat 10.0 (SD 4.2), cont 13.4 (SD 4.7) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: lipids, glucose, blood pressure Available outcomes: weight, total, LDL and HDL cholesterol, TG, BP

Auckland reduced fat 1999 *(Continued)*

Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Unmarked opaque envelopes were opened by the person recruiting, unable to alter allocation later
Allocation concealment (selection bias)	Low risk	Unmarked opaque envelopes were opened by the person recruiting, unable to alter allocation later
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were not blinded, outcome assessors were
Incomplete outcome data (attrition bias) All outcomes	High risk	77 of 176 recruited lost to follow-up, 44% over 5 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

BDIT Pilot Studies 1996

Methods	RCT
Participants	Women with mammographic dysplasia (Canada) CVD risk: low Control: 147 randomised, 78 analysed Intervention: 148 randomised, 76 analysed Mean years in trial: control 7.5, intervention 6.8 % male: 0 Age: mean control 45, intervention 44 (all > 30) Baseline BMI: mean intervention 24.3 (SD 3.8), control 24.3 (SD 3.6)
Interventions	Reduced fat intake vs usual diet Control aims: healthy diet advice, no alteration in dietary fat advised, aim to maintain weight Intervention aims: total fat 15%E, replace fat by complex CHO, aim to maintain weight Control methods: seen for advice once every 4 months for 12 months Intervention methods: seen for advice once a month for 12 months Weight goal: low fat group - "isocaloric exchange of complex carbohydrate for fat. We tried to maintain an isocaloric diet to avoid weight loss...". Not discussed for control group

BDIT Pilot Studies 1996 *(Continued)*

	Total fat intake (at 9.2 years): low fat 31.7 (SD 7.3) %E, control 35.3 (SD 5.6) %E Saturated fat intake (at 9.2 years): low fat 10.6 (SD 4.6) %E, control 12.3 (SD 4.6) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary fat, serum cholesterol Available outcomes: weight, BMI, total and HDL cholesterol
Notes	Weight data available for 1 year, 2 years and 9 years. Unclear whether participants were still in the trial by 9 years, so 2-year data used in main analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	Randomisation not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants not blinded, but outcome assessors blinded to intervention
Incomplete outcome data (attrition bias) All outcomes	High risk	141 of 295 (48%) lost over 8 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Minor: women in intervention group seen more frequently. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

beFIT 1997

Methods	RCT
Participants	Women and men with mild hypercholesterolaemia (USA) CVD risk: moderate Control: unclear how many randomised, 192 analysed Intervention: unclear how many randomised, 217 analysed Mean years in trial: unclear (max duration 0.5 years) % male: 52 (not divided by intervention group) Age: mean 43.2 (not divided by intervention group) (all > 30)

beFIT 1997 *(Continued)*

	Baseline BMI (not reported by intervention): women with hypercholesterolaemia (n = 84) mean 25.9 (SD 4.9), women with combined hyperlipidaemia (n = 94) mean 29.2 (SD 6.1), men with hypercholesterolaemia (n = 123) mean 26.6 (SD 3.3), men with combined hyperlipidaemia (n = 108) mean 27.5 (SD 3.2)
Interventions	Reduced and modified fat vs usual diet Control aims: asked to delay dietary changes (provided intervention after the randomised trial) Intervention aims: total fat < 30%E, SFA < 7%E, dietary cholesterol < 200 mg/d Control methods: usual intake Intervention methods: 8 weekly classes with nutrition info and behaviour modification with spouses, plus individual appointments at 3 and 6 months Weight goals: intervention group "assigned food group pattern for their calorie needs", no information for control group. Total fat intake (at 6 months): intervention 25.2 (SD unclear) %E, control unclear - no significant difference from baseline 34 (SD unclear) %E Saturated fat intake (at 6 months): intervention 7.6% (SD unclear) %E, control unclear - no significant difference from baseline 12 (SD unclear)%E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: lipids Available outcomes: weight, total, LDL and HDL cholesterol, TG (but variance data only provided for the randomised comparison for LDL cholesterol)
Notes	Weight: control 'no change', intervention -2.7 kg at 6 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified random sampling scheme
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants knew their allocation, unclear for outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear what proportion lost over trial as unclear how many recruited
Selective reporting (reporting bias)	High risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Intensive intervention for intervention group, but no intervention during the 6 months of the randomised part of the study for the control group. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above

beFIT 1997 *(Continued)*

Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Bloemberg 1991

Methods	RCT
Participants	Men with untreated raised total cholesterol (the Netherlands) CVD risk: moderate Control: randomised 41, analysed 40 Intervention: randomised 39, analysed 39 Mean years in trial: control 0.5, randomised 0.5 % male: 100% Age: mean control 47.5 (SD 8.0), intervention 47.2 (SD 8.3) Baseline BMI: mean control 26.3 (SD 2.3), intervention 26.0 (SD 2.6)
Interventions	Reduced and modified fat vs usual diet Control aims: usual diet Intervention aims: 30%E from fat, PUFA/SFA 1.0, dietary cholesterol 20 mg Control methods: no advice provided Intervention methods: individual advice provided face to face, followed by 2 phone calls and 5 mailings of information on healthy foods Weight goals: weight and calories not mentioned Total fat intake (change to 6 months): intervention -5.0 (SD 6.5) (33.5 overall), control -1.5 (SD 5.9) (36.8 overall) %E Saturated fat intake (change to 6 months): intervention-4.3 (SD 3.9), control -0.7 (SD 2.9) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: lipids Available outcomes: weight, total and HDL cholesterol
Notes	—

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"randomised" and stratified by age and BMI (each dichotomised)
Allocation concealment (selection bias)	Unclear risk	No method stated (as above)
Blinding (performance bias and detection bias) All outcomes	High risk	No for participants, yes for laboratory staff

Bloemberg 1991 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	1 of 80 (< 1%) lost over 0.5 years (< 5% per year)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Much more time spent on those in the intervention group
Free of dietary differences other than fat?	Low risk	Dietary focus on fats alone

BRIDGES 2001

Methods	RCT
Participants	Women diagnosed with stage I or II breast cancer over the past 2 years (USA) CVD risk: low Control: randomised unclear (at least 56), analysed 46 Intervention: randomised unclear (at least 50), analysed 48 Mean years in trial: unclear (1 year max follow-up) % male: 0 Age: mean control unclear (71% postmenopausal), intervention unclear (56% postmenopausal) (all 20 to 65) Baseline BMI: not reported
Interventions	Reduced fat vs usual diet Control aims: no formal intervention Intervention diet aims: total fat 20%E, high fibre, plant-based micronutrients Intervention stress: separate parallel arm, stress reduction programme (data not used here) Control methods: no formal intervention Intervention methods: nutrition intervention programme, 15 sessions (42 hours) over 15 weeks, group-based, dietitian led, 2 individual sessions using social cognitive theory and patient centred counselling to increase self efficacy and confidence Weight goals: "reduction in body mass was not a primary goal of NEP. (NEP was neither designed nor presented to participants as a weight loss or weight control program)." The control group was presented as "individual choice". Total fat intake (at 12 months): low fat 29.9 (SD unclear), control 33.6 (SD unclear) %E Saturated fat intake: unclear Style: diet advice Setting: community
Outcomes	Stated trial outcomes: diet and BMI Available outcomes: weight

BRIDGES 2001 *(Continued)*

Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomised", stratified by medical centre, cancer stage and age, randomised number/envelope method by project co-ordinator
Allocation concealment (selection bias)	Low risk	The project co-ordinator had contact with those from the University of Massachusetts, but not those from the other 3 centres, and allocation could not be altered later
Blinding (performance bias and detection bias) All outcomes	High risk	Participants not blinded, unclear about researchers
Incomplete outcome data (attrition bias) All outcomes	High risk	Unclear how many recruited, so unclear how many were lost to follow-up (at least 12 of 106 (11%) over 1 year, so > 5%/year
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	High-intensity programme for intervention group, nothing for control group. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	High risk	Intervention also focused on fibre and plant based micronutrients. See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Canadian DBCP 1997

Methods	RCT
Participants	Women with mammographic densities > 50% breast area (Canada) CVD risk: low Control: randomised 448+, analysed 401 Intervention: randomised 448+, analysed 388 Mean years in trial: control 2.0, randomised 2.0 (note, papers suggest a 10-year follow-up overall) % male: 0% Age: mean control 45.9 (SD unclear), intervention 46.5 (SD unclear) Baseline BMI: mean control 23.6, intervention 23.4, no variance reported
Interventions	Reduced fat vs usual diet Control aims: usual diet Intervention aims: total fat 15%E, protein 20%E, CHO 65%E, isocaloric diet Control methods: encouraged to continue usual diet, interviewed by dietitian every 4 months during first year, then every 3 months in the second year Intervention methods: dietary prescription using food exchange (fat calories replaced by CHO), met with dietitian monthly during first year, then every 3 months. Scales, recipes, shopping guide provided

Canadian DBCP 1997 *(Continued)*

	Weight goals: "calories derived from fat were replaced by isocaloric exchange with carbohydrate" Total fat intake (at 2 years): intervention 21.3 (SD 6.2), control 31.8 (SD 6.7) %E Saturated fat intake (at 2 years): intervention 7.1 (SD 2.5), control 11.5 (SD 3.3) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: incidence of breast cancer Available outcomes: weight
Notes	Weight data available for 1 and 2 years, 2-year data used in main analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly allocated by telephone to Dept. of Biostatistics at Ontario Cancer Institute, stratified by centre
Allocation concealment (selection bias)	Low risk	As above
Blinding (performance bias and detection bias) All outcomes	High risk	Participants knew what arm they were in
Incomplete outcome data (attrition bias) All outcomes	High risk	At least 107 of at least 896 (12%) lost over 2 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Minor difference in attention for participants in intervention and control in first year
Free of dietary differences other than fat?	Low risk	Focus on dietary fat

de Bont 1981 non-obese

Methods	RCT
Participants	Women with type 2 diabetes (UK) CVD risk: moderate Control: randomised unclear (total in control and intervention 148), analysed 65 (for obese and non-obese) Intervention: randomised unclear, analysed 71 (for obese and non-obese) Mean years in trial: control 0.5, randomised 0.5 % male: 0% Age: mean control 54 (SD 8), intervention 56 (SD 7), (all 35 to 64) (for obese and non-obese)

de Bont 1981 non-obese *(Continued)*

	Baseline BMI: chosen for BMI < 28, mean not reported
Interventions	Reduced and modified fat vs usual diet Control aims: usual diet but with CHO ≤ 40%E Intervention aims: 30%E from fat, focus on reducing meat fat, dairy foods and substituting margarines to improve the SFA/PUFA ratio, CHO increased to maintain energy intake Control methods: 3 home visits from a nutritionist over the 6 months of the trial Intervention methods: 3 home visits from a nutritionist over the 6 months of the trial Weight goals: to maintain the required total energy intake the proportion of carbohydrates in these diets was increased. Total fat intake (change to 6 months): intervention-10.1 (SD 10.8) (overall 31.1), control -1.0 (SD 10.5) (overall 41.8) %E (for obese and non-obese) Saturated fat intake (change to 6 months): intervention-8.1 (SD 5.8), control -1.1 (SD 5.7) %E (for obese and non-obese) Style: diet advice Setting: community
Outcomes	Stated trial outcomes: diet, weight, lipids Available outcomes: weight, total and HDL cholesterol, triglycerides
Notes	Outcome data separated by those obese (BMI ≥ 28) or not obese at baseline

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding (performance bias and detection bias) All outcomes	High risk	No for participants, unclear for outcome assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	12 of 148 (8%) lost over 0.5 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Follow-up similar
Free of dietary differences other than fat?	Low risk	Diet focusses on fat

de Bont 1981 obese

Methods	RCT
Participants	Women with type 2 diabetes (UK) CVD risk: moderate Control: randomised unclear (total in control and intervention 148), analysed 71 (for obese and non-obese) Intervention: randomised unclear, analysed 65 (for obese and non-obese) Mean years in trial: control 0.5, randomised 0.5 % male: 0% Age: mean control 54 (SD 8), intervention 56 (SD 7), (all 35 to 64) (for obese and non-obese) Baseline BMI: chosen for BMI ≥ 28, mean not reported
Interventions	Reduced and modified fat vs usual diet Control aims: usual diet but with CHO ≤ 40%E Intervention aims: 30%E from fat, focus on reducing meat fat, dairy foods and substituting margarines to improve the SFA/PUFA ratio, CHO increased to maintain energy intake Control methods: 3 home visits from a nutritionist over the 6 months of the trial Intervention methods: 3 home visits from a nutritionist over the 6 months of the trial Weight goals: to maintain the required total energy intake the proportion of carbohydrates in these diets was increased Total fat intake (change to 6 months): intervention-10.1 (SD 10.8) (overall 31.1), control -1.0 (SD 10.5) (overall 41.8) %E (for obese and non-obese) Saturated fat intake (change to 6 months): intervention-8.1 (SD 5.8), control -1.1 (SD 5.7) %E (for obese and non-obese) Style: diet advice Setting: community
Outcomes	Stated trial outcomes: diet, weight, lipids Available outcomes: weight, total and HDL cholesterol, triglycerides
Notes	Outcome data separated by those obese (BMI ≥ 28) or not obese at baseline

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding (performance bias and detection bias) All outcomes	High risk	No for participants, unclear for outcome assessors
Incomplete outcome data (attrition bias)	High risk	12 of 148 (8%) lost over 0.5 years (> 5% per year)

de Bont 1981 obese *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Similar follow-up
Free of dietary differences other than fat?	Low risk	Focus on fat

DEER 1998 exercise men

Methods	RCT
Participants	Men with raised LDL and low HDL cholesterol (USA) CVD risk: moderate Control: randomised 50, analysed 47 Intervention: randomised 51, analysed 48 Mean years in trial: control 1.0, intervention 1.0 % male: 100% Age: mean 47.8 (SD 8.9) for all men (including the non-exercise part of this trial) Baseline BMI: intervention 26.6 (SD 2.6), control 26.9 (SD 2.6)
Interventions	Reduced fat vs usual diet Control aims: usual diet (and exercise intervention) Intervention aims: NCEP step 2 diet: < 30%E from fat, < 7%E from SFA, < 200 mg/d cholesterol (and exercise intervention) Control methods: no advice provided Intervention methods: individual advice provided face to face, followed by 8 1-hour group sessions during first 12 weeks, then monthly contact with dietitians by mail, phone, individual or group appointment Weight goals: "weight loss was not emphasised" Total fat intake (change to 12 months): intervention-8.2 (SD 5.9) (22.2 overall), control -0.5 (SD 5.7) (29.9 overall) %E Saturated fat intake (change to 12 months): intervention-3.9 (SD 2.6), control -0.1 (SD 2.6) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake and lipids Available outcomes: weight, total, LDL and HDL cholesterol, triglycerides, systolic and diastolic BP
Notes	Factorial trial re. exercise and reported by sex
Risk of bias	

DEER 1998 exercise men *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Assignments by computer, modified Efron procedure, balanced by HDL and LDL
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of randomisation group
Incomplete outcome data (attrition bias) All outcomes	High risk	6 of 101 (6%) lost over 1 year (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Very different levels of attention and review
Free of dietary differences other than fat?	Low risk	Dietary focus on fat

DEER 1998 exercise women

Methods	RCT
Participants	Postmenopausal women with raised LDL and low HDL cholesterol (USA) CVD risk: moderate Control: randomised 44, analysed 43 Intervention: randomised 43, analysed 43 Mean years in trial: control 1.0, intervention 1.0 % male: 0% Age: mean 56.9 (SD 5.1) for all women (including the non-exercise part of this trial) Baseline BMI: intervention 26.4 (SD 3.5), control 25.9 (SD 2.4)
Interventions	Reduced fat vs usual diet Control aims: usual diet (and exercise intervention) Intervention aims: NCEP step 2 diet: < 30%E from fat, < 7%E from SFA, < 200 mg/d cholesterol (and exercise intervention) Control methods: no advice provided Intervention methods: individual advice provided face to face, followed by 8 1-hour group sessions during first 12 weeks, then monthly contact with dietitians by mail, phone, individual or group appointment Weight goals: "weight loss was not emphasised" Total fat intake (change to 12 months): intervention-8.0 (SD 5.8) (20.4 overall), control 0.3 (SD 6.9) (28.7 overall) %E

DEER 1998 exercise women *(Continued)*

	Saturated fat intake (change to 12 months): intervention-3.0 (SD 2.3), control 0.2 (SD 3.1) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake and lipids Available outcomes: weight, total, LDL and HDL cholesterol, triglycerides, systolic and diastolic BP
Notes	Factorial trial re. exercise and reported by sex

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Assignments by computer, modified Efron procedure, balanced by HDL and LDL
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of randomisation group
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 of 87 (1%) lost over 1 year (< 5% per year)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Very different levels of attention and review
Free of dietary differences other than fat?	Low risk	Focus on dietary fat

DEER 1998 no exercise men

Methods	RCT
Participants	Men with raised LDL and low HDL cholesterol (USA) CVD risk: moderate Control: randomised 47, analysed 46 Intervention: randomised 49, analysed 49 Mean years in trial: control 1.0, intervention 1.0 % male: 100% Age: mean 47.8 (SD 8.9) for all men (including the exercise part of this trial) Baseline BMI: intervention 26.9 (SD 3.1), control 26.7 (SD 3.2)
Interventions	Reduced fat vs usual diet

DEER 1998 no exercise men *(Continued)*

	Control aims: usual diet (and usual exercise) Intervention aims: NCEP step 2 diet: < 30%E from fat, < 7%E from SFA, < 200 mg/d cholesterol (and usual exercise) Control methods: no advice provided Intervention methods: individual advice provided face to face, followed by 8 1-hour group sessions during first 12 weeks, then monthly contact with dietitians by mail, phone, individual or group appointment Weight goals: "weight loss was not emphasised" Total fat intake (change to 12 months): intervention-8.0 (SD 8.1) (22.4 overall), control -0.7 (SD 5.9) (29.7 overall) %E Saturated fat intake (change to 12 months): intervention-3.4 (SD 3.2), control 0.0 (SD 2.4) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake and lipids Available outcomes: weight, total, LDL and HDL cholesterol, triglycerides, systolic and diastolic BP
Notes	Factorial trial re. exercise and reported by sex

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Assignments by computer, modified Efron procedure, balanced by HDL and LDL
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of randomisation group
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 of 96 (1%) lost over 1 year (< 5% per year)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Very different levels of attention and review
Free of dietary differences other than fat?	Low risk	Focus on dietary fat

DEER 1998 no exercise wom

Methods	RCT
Participants	Postmenopausal women with raised LDL and low HDL cholesterol (USA) CVD risk: moderate Control: randomised 47, analysed 46 Intervention: randomised 46, analysed 45 Mean years in trial: control 1.0, intervention 1.0 % male: 0% Age: mean 56.9 (SD 5.1) for all women (including the exercise part of this trial) Baseline BMI: intervention 26.6 (SD 2.8), control 26.0 (SD 3.9)
Interventions	Reduced fat vs usual diet Control aims: usual diet (and usual exercise) Intervention aims: NCEP step 2 diet: < 30%E from fat, < 7%E from SFA, < 200 mg/d cholesterol (and usual exercise) Control methods: no advice provided Intervention methods: individual advice provided face to face, followed by 8 1-hour group sessions during first 12 weeks, then monthly contact with dietitians by mail, phone, individual or group appointment Weight goals: "weight loss was not emphasised" Total fat intake (change to 12 months): intervention-5.7 (SD 7.4) (overall 22.7), control -0.2 (SD 6.7) (overall 28.2) %E Saturated fat intake (change to 12 months): intervention-2.4 (SD 2.8), control 0.2 (SD 2.8) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake and lipids Available outcomes: weight, total, LDL and HDL cholesterol, triglycerides, systolic and diastolic BP
Notes	Factorial trial re. exercise and reported by sex

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Assignments by computer, modified Efron procedure, balanced by HDL and LDL
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of randomisation group
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 of 93 (2%) lost over 1 year (< 5% per year)

DEER 1998 no exercise wom *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Very different levels of attention and review
Free of dietary differences other than fat?	Low risk	Focus on dietary fat

Diet and Hormone Study 2003

Methods	RCT
Participants	Healthy premenopausal women aged 20 to 40 years (USA) CVD risk: low Control: randomised 107, analysed 96 Intervention: randomised 106, analysed 81 Mean years in trial: control 0.95, intervention 0.88 % male: 0% Age: control mean 33.3, intervention 33.5 (SDs not given) Baseline BMI: mean control 23.8 (SD 3.5), intervention 23.7 (SD 4.2)
Interventions	Reduced fat vs usual diet Control aims: usual diet Intervention aims: < 20%E from fat, 25 to 30 g/d fibre, > 8 servings/d fruit and vegetables, CHO 60% to 65%E, protein 15% to 20%E Control methods: received a pamphlet on healthy eating (minimal intervention) Intervention methods: classroom nutrition education (18 group classes) plus 2 individual counselling sessions over 12 months covering knowledge and behavioural skills, appropriate foods served at intervention sessions Weight goals: "not encouraged to reduce total caloric intake and weight was monitored to maintain within 2 kg of baseline weight" Total fat intake (at 12 cycles/months): intervention 22.2 (SD 7.2), control 30.7 (SD 7.5) %E Saturated fat intake (at 12 cycles/months): intervention 14.9 (SD 6.7), control 23.9 (SD 13.2) g/d Style: diet advice Setting: community
Outcomes	Stated trial outcomes: hormonal responses Available outcomes: weight, BMI, dietary intake, hormones, menstrual cycle length
Notes	No answer to requests for data on deaths or health events. Weight and BMI data provided at 4 and 12 cycles
Risk of bias	

Diet and Hormone Study 2003 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomly assigned by reference to a random number table"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of randomisation group, unclear for assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	36 of 213 (17%) lost over 1 year (> 5% per year). Reasons not stated, greater losses in intervention group
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Very different levels of attention and review
Free of dietary differences other than fat?	High risk	Intervention group also asked to increase fibre, fruit and vegetables substantially

Kentucky Low Fat 1990

Methods	RCT
Participants	Moderately hypercholesterolaemic, non-obese Caucasian men and women aged 30 to 50 (USA) CVD risk: moderate Control: randomised 62, analysed 51 Intervention: randomised 56, analysed 47 Mean years in trial: control 0.91, intervention 0.92 % male: control 61, intervention 66 Age: mean control 40.3 (SD 5.4), intervention 40.7 (SD 5.2) (all 30 to 50) Baseline BMI: not reported
Interventions	Reduced fat diet vs usual diet Control aims: no diet intervention Intervention aims: 25%E from fats, 20%E from protein, 55%E from CHO, < 200 mg cholesterol/day (Also an intervention arm with similar aims plus increased fibre intake) Control methods: no intervention Intervention methods: seminars and individual eating patterns taught, 10 weeks teaching and 40 weeks maintenance Weight goals: participants were directed to maintain initial body weight throughout the study Total fat intake (at 1 year): low fat 30 (SD 7.5), control 31 (SD 5.7) %E Saturated fat intake (at 1 year): low fat 9 (SD 2.7), control 10 (SD 2.9) %E

Kentucky Low Fat 1990 *(Continued)*

	Style: diet advice Setting: community
Outcomes	Stated trial outcomes: diet composition, lipids Available outcomes: weight, total, LDL and HDL cholesterol
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"matched on age, gender & cholesterol level, randomly assigned to intervention group using systematic random procedure"
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were aware of their dietary advice, researchers were not
Incomplete outcome data (attrition bias) All outcomes	High risk	20 of 118 (17%) lost over 1 year (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	(As the high fibre arm has not been used in the data set). See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Kuopio Reduced & Mod 1993

Methods	RCT (4 arms have been used here as 2 RCTs)
Participants	Free-living people aged 30 to 60 with serum total cholesterol levels 6.5 to 8.0 mmol/L (Finland) CVD risk: moderate Control (monoene enriched): randomised 41, analysed 41 Intervention AHA: randomised 41, analysed 41 Mean years in trial: for all 4 groups 0.5 % male: control 46, AHA 46 Age: mean control 46.4, AHA 47.3 (all 30 to 60) Baseline BMI: mean control 26.6 (SD 3.8), intervention 26.2 (SD 4.0)
Interventions	Reduced and modified fat vs modified fat diet Control aims mono: total fat 38%E, SFA < 14%E, MUFA 18%E, PUFA < 6%E, rapeseed oil, rapeseed spread and skimmed milk provided

Kuopio Reduced & Mod 1993 *(Continued)*

	Intervention aims AHA: total fat 30%E, SFA < 10%E, MUFA 10%E, PUFA 10%E, sunflower oil, sunflower spread and skimmed milk provided Control and intervention methods: given written dietary instructions and a diet plan with checking and reinforcement for 3 visits, then at 2, 6, 12, 18 and 26 weeks Weight goals: dietary written instructions were designed for 5 energy levels (1800, 2000, 2400, 2800 and 3200) based on individual diet and activity assessment Total fat intake (weeks 14 to 28): low and mod fat 34 (SD 4), control 35 (SD 5) %E Saturated fat intake (weeks 14 to 28): low and mod fat 11 (SD 2), control 11 (SD 2) %E Style: dietary advice and supplement (food) Setting: community
Outcomes	Stated trial outcomes: lipids and blood pressure Available outcomes: BMI, total, LDL and HDL cholesterol, TG, BP
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomisation stratified for men and women, singles and couples, random number tables"
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants and researchers knew allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	0 of 82 (0%) lost over 0.5 years (< 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Similar intensity and duration in both groups. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Kuopio Reduced Fat 1993

Methods	RCT (4 arms have been used here as 2 RCTs)
Participants	Free-living people aged 30 to 60 with serum total cholesterol levels 6.5 to 8.0 mmol/L (Finland) CVD risk: moderate

Kuopio Reduced Fat 1993 *(Continued)*

	Control (high saturated fat): randomised 37, analysed 12 Intervention low fat: randomised 40, analysed 40 Mean years in trial: for both groups 0.5 % male: control 46, low fat 48 Age: mean control 43.2, low fat 45.8 (all 30 to 60) Baseline BMI: mean control 25.6 (SD 4.2), intervention 26.5 (SD 3.4)
Interventions	Reduced fat vs usual diet (low fat vs control) Control aims: advised total fat 38%E, SFA < 18%E, MUFA 15%E, PUFA < 5%E, rapeseed oil, butter and semi-skimmed milk provided Intervention aims low fat: total fat 28%E to 30%E, SFA < 14%E, MUFA 10%E, PUFA 4%E, butter and rapeseed spread and skimmed milk provided Control and intervention methods: given written dietary instructions and a diet plan with checking and reinforcement for 3 visits, then at 2, 6, 12, 18 and 26 weeks Weight goals: dietary written instructions were designed for 5 energy levels (1800, 2000, 2400, 2800 and 3200) based on individual diet and activity assessment Total fat intake (weeks 14 to 28): low fat 31 (SD 5), control 36 (SD 5) %E Saturated fat intake (weeks 14 to 28): low fat 12 (SD 2), control 15 (SD 2) %E Style: dietary advice and supplement (food) Setting: community
Outcomes	Stated trial outcomes: lipids and blood pressure Available outcomes: BMI, total, LDL and HDL cholesterol, TG, BP
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomisation stratified for men and women, singles and couples, random number tables"
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants and researchers knew allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	25 of 77 (32%) lost over 0.5 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Similar intensity and duration in both groups. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above

Kuopio Reduced Fat 1993 *(Continued)*

Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Mastopathy Diet 1988

Methods	RCT
Participants	Women with severe cyclical mastopathy for at least 5 years (Canada) CVD risk: low Control: randomised 10, analysed 9 Intervention: randomised 11, analysed 10 Mean years in trial: control 0.45, intervention 0.45 % male: 0% Age: mean control 36, intervention 38 (variances unclear) Baseline BMI: no data provided
Interventions	Reduced fat vs usual diet Control aims: given principles of healthy diet, not counselled to alter fat content Intervention aims: total fat 15%E, CHO 65%E Control methods: seen every 2 months to monitor symptoms, nutrition and biochemistry Intervention methods: seen monthly to monitor symptoms, nutrition and biochemistry, teaching materials included food guide, recipes, product information and advice on eating out Weight goals: the intervention goals included the isocaloric replacement of complex carbohydrate for fat (no mention for control group) Total fat intake (at 6 months): low fat 22.8 (SD unclear), control 33.4 (SD unclear) %E Saturated fat intake (at 6 months): low fat 8.8 (SD unclear), control 12.3 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: mastopathy symptoms, plasma hormone and lipids Available outcomes: weight, total cholesterol (but variance data not provided)
Notes	Total cholesterol rose by 0.09 mmol/L in control group (from 4.5 to 4.59) and fell by 0.15 mmol/L in intervention group (4.84 to 4.69). Weight changed in the intervention group (mean fall of 2.1 kg over 6 months, no variance provided), but change, or otherwise, in control group not mentioned

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias)	High risk	Participants were not blinded, those assessing physical outcomes were blinded, those assessing symptoms were not

Mastopathy Diet 1988 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	High risk	2 of 21 (10%) lost over 0.5 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Minor differences in follow-up frequency. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

MeDiet 2006

Methods	RCT
Participants	Healthy postmenopausal women with above median serum testosterone (Italy) CVD risk: low Control: randomised 57, analysed at 6 months 55 Intervention: randomised 58, analysed at 6 months 51 Mean years in trial: control 4.38, intervention 4.28 % male: 0 Age: mean unclear (age range 48 to 69) Baseline BMI: not reported
Interventions	Reduced and modified fat vs usual diet Control aims: advised to increase fruit and vegetable intake Intervention aims: taught Sicilian diet including reduced total, saturated and omega-6 fats, increased blue fish (high in omega 3), increased whole cereals, legumes, seeds, fruit and vegetables Control methods: advice Intervention methods: taught Sicilian diet and cooking by professional chefs, with a weekly cooking course including social dinners Weight goals: not mentioned Total fat intake (at 6 months): low and mod fat 30.9 (SD 11.4), control 34.0 (SD 11.8) %E Saturated fat intake (at 6 months): low and mod fat 8.4 (SD 3.0), control 11.2 (SD 5.0) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: breast cancer, weight, lipids, well being Available outcomes: weight
Notes	Weight data provided at 6 months (fall of 0.6 kg in control group, fall of 1.3 kg in intervention group), but without variance information

MeDiet 2006 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"individually randomised"
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were aware of assignment, researchers unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	9 of 115 (8%) lost over 4 years (< 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Intensive cookery course with social element compared with brief advice. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	High risk	Both groups encouraged to increase fruit and vegetables, but intervention group also encouraged to increase fish, pulses, seeds and whole grains

Moy 2001

Methods	RCT
Participants	Middle-aged siblings of people with early CHD, with at least one CVD risk factor (USA) CVD risk: moderate Control: randomised 132, analysed 118 Intervention: randomised 135, analysed 117 Mean years in trial: 1.9 % male: control 49%, intervention 55% Age: control mean 45.7 (SD 7), intervention 46.2 (SD 7) Baseline BMI: control mean 29.5 (SD 7), intervention 28.5 (SD 5)
Interventions	Reduced fat intake vs usual diet Control: physician management (physicians informed on risk factor management) Intervention: nurse management, aim total fat 40 g/d or less Control methods: physician management with risk factor management at 0, 1 and 2 years Intervention methods: nurse management, appointments 6- to 8-weekly for 2 years Weight goals: not mentioned Total fat intake (at 2 years): low fat 34.1 (SD unclear), control 38.0 (SD unclear) %E

Moy 2001 *(Continued)*

	Saturated fat intake (at 2 years): low fat 11.5 (SD unclear), control 14.4 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake Available outcomes: BMI, HDL and LDL cholesterol, TG
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned via computerised schema after all eligible siblings from a family had been screened
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants and trialists clear about their allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	32 of 267 (12%) lost over 2 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Differences in frequency of follow-up, but unclear what differences in care occurred between the physician and nurse-led care. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Unclear risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

MSFAT 1995

Methods	RCT
Participants	Healthy people aged 20 to 55 (Netherlands) CVD risk: low Control: randomised unclear (120?), analysed 103 Intervention: randomised unclear (120?), analysed 117 Mean years in trial: control 0.46, intervention 0.49 % male: control 50%, intervention 50% Age: mean control men 35.6 (SD 10), control women 36.0 (SD 11), intervention men 35.5 (SD 11), intervention women 36.0 (SD 12) (all 19 to 55) Baseline BMI: mean control men 24.9 (SD 2.2), control women 25 (SD 2), intervention men 24.9 (SD 2.3), intervention women 24.7 (SD 2)

MSFAT 1995 *(Continued)*

Interventions	Reduced fat vs usual diet Control aims: advised to use products from trial shop ad lib. (usual fat products provided) Intervention aims: advised to use products from trial shop ad lib. (low fat products provided) Control methods: participants obtained foods in a study shop at least once a week Intervention methods: participants obtained foods in a study shop at least once a week Weight goals: ad libitum diet Total fat intake (at 6 months): low fat 34.7 (SD unclear), control 42.7 (SD unclear) %E Saturated fat intake (at 6 months): low fat 14.2 (SD unclear), control 18.2 (SD unclear) %E Style: food provided Setting: community
Outcomes	Stated trial outcomes: weight, vitamin and fatty acid intake, anti-oxidative capacity Available outcomes: weight (for subgroup), weight and lipids provided for larger group, but without variance data
Notes	Change from baseline to 6 months for whole group (control 103, intervention 117): Weight, kg: 1.1, 0.4 Total cholesterol, mmol/L: 0.07, -0.09 HDL cholesterol, mmol/L: -0.03, -0.06 LDL cholesterol, mmol/L: 0.15, 0.16 TG, mmol/L: 0.04, -0.04

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"stratified randomisation (according to sex, age, QI index and eating behaviour) by co-ordinating centre", a statistician at Unilever Research, SAS software, and allocation could not be altered later
Allocation concealment (selection bias)	Low risk	"stratified randomisation (according to sex, age, QI index and eating behaviour) by co-ordinating centre", a statistician at Unilever Research, SAS software, and allocation could not be altered later
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of allocation, those analysing biochemistry were not
Incomplete outcome data (attrition bias) All outcomes	High risk	20 of 240 (8%) lost over 0.5 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	

MSFAT 1995 *(Continued)*

Free of systematic difference in care?	Low risk	Both groups used study shop. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

NDHS Open 1st L&M 1968

Methods	RCT
Participants	Free-living men (USA) CVD risk: low Control: randomised 382, analysed 348 Intervention B: randomised 385, analysed 332 Intervention X: randomised 54, analysed 46 Mean years in trial: control 1.0, B 0.9, C 0.9, X 0.9 % male: 100 Age: unclear (all 45 to 54) Baseline BMI: not reported
Interventions	Reduced and modified fat diet vs usual diet Control aims: total fat 40%E, SFA 16%E to 18%E, dietary cholesterol 650 to 750 mg/d, P/S 0.4 Intervention B: total fat 30%E, SFA < 9%E, dietary cholesterol 350 to 450 mg/d, PUFA 15%E, P/S 1.5 Intervention X: total fat 30%E, SFA < 9%E, dietary cholesterol 350 to 450 mg/d, PUFA 15%E, P/S 1.5 Control methods: dietary advice to reduce saturated fat and cholesterol (plus 10 follow-up visits with nutritionist), purchase of 'usual fat' items from a trial shop Intervention B methods: dietary advice to reduce saturated fat and cholesterol (plus 10 follow-up visits with nutritionist), plus purchase of appropriately reduced and modified fat items from a trial shop Intervention X methods: dietary advice but no trial shop Weight goals: weight and calories not mentioned Total fat intake (through study): B 29.7 (SD unclear) %E, X 31.7 (SD unclear), control 34.9 (SD unclear) %E Saturated fat intake (through study): B 7.1 (SD unclear) %E, X 8.9 (SD unclear), control 11.6 (SD unclear) %E Style: B diet provided, X - diet advice Setting: community
Outcomes	Stated trial outcomes: lipid levels and dietary assessment Available outcomes: total cholesterol (some weight and BP data presented but no variance info)
Notes	At 52 weeks weight change in the control was not presented, weight change in B was -2.4 kg. Average weight change over the first year (mean of weights at weeks 6, 12, 20, 28, 36 and 44 weeks) was -2.45 kg (-5.4lb) for the low fat group (B) and -1.91 kg (-4.2lb) for the modified fat group (C) and -1.95 kg (-4.3lb) for the control group (D) At 52 weeks diastolic BP change from baseline was -2.2 kg in control, -1.9 in B and -5.8 in X

NDHS Open 1st L&M 1968 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified randomisation by the statistical centre
Allocation concealment (selection bias)	Low risk	Stratified randomisation by the statistical centre
Blinding (performance bias and detection bias) All outcomes	Low risk	Intervention B: all reduced saturated fat and purchased blinded foods from a trial shop, double-blind Intervention X: no trial shop, so participants not blinded, though those analysing blood samples etc. were
Incomplete outcome data (attrition bias) All outcomes	High risk	87 of 821 (11%) lost over 1 year (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Yes for intervention B (as both intervention and control received dietary advice and purchased food from trial shop). No for intervention X (as it did not include a trial shop as in the control group). See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

NDHS Open 2nd L&M 1968

Methods	RCT
Participants	Free-living men who had participated in NDHS 1st studies (USA) CVD risk: low Control: randomised 304, analysed 215 Intervention BC (this study had a range of interventions, we were interested in BC for the systematic review): randomised 194, analysed 179 Mean years in trial: control 0.6, intervention BC 0.6 % male: 100 Age: unclear (all 45 to 54) Baseline BMI: not reported
Interventions	Reduced and modified fat vs usual diet Control aims: total fat 40%E, SFA 16%E to 18%E, dietary cholesterol 650 to 750 mg/d, P/S 0.4, X - advice to continue usual diet Intervention aims: BC total fat 30%E to 40%E, SFA reduced, dietary cholesterol 350 to 450 mg/d, increased PUFA, P/S 1.5 to 2.0 Control methods: dietary advice to reduce saturated fat and cholesterol (plus 10 follow-up visits with nutritionist), purchase of 'usual fat' items from a trial shop

NDHS Open 2nd L&M 1968 *(Continued)*

	Intervention BC methods: dietary advice to reduce saturated fat and cholesterol (plus 10 follow-up visits with nutritionist), plus purchase of appropriately reduced and modified fat items from a trial shop Weight goals: weight and calories not mentioned Total fat intake (through study): BC 32.5 (SD unclear) %E, control 35.5 (SD unclear) %E Saturated fat intake (through study): BC 7.4 (SD unclear) %E, control 12.0 (SD unclear) %E Style: food provided Setting: community
Outcomes	Stated trial outcomes: lipid levels and dietary assessment Available outcomes: weight
Notes	Weight data provided for the BC intervention group -1.8 kg (-4 lb over 6 months), and -0.9 kg (-2 lb) for modified fat diet G, -1.4 kg (-3 lb) for modified fat diet F. No info provided for the control group (D)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified randomisation by the statistical centre
Allocation concealment (selection bias)	Low risk	Stratified randomisation by the statistical centre
Blinding (performance bias and detection bias) All outcomes	Low risk	Some participants continued with advice to reduce saturated fat and purchased blinded foods from a trial shop, but half of the participants were instructed in their own purchase of appropriate foods from normal shops to compile their own dietary regimen
Incomplete outcome data (attrition bias) All outcomes	High risk	104 of 498 (21%) lost over 0.6 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Trial shop used by both groups, plus dietary advice. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Nutrition & Breast Health

Methods	RCT
Participants	Pre-menopausal women at increased risk of breast cancer (USA) CVD risk: low Control: randomised 53, analysed 50 Intervention: randomised 69, analysed 47

Nutrition & Breast Health *(Continued)*

	Mean years in trial: control 1.0, intervention 0.8 % male: control 0%, intervention 0% Age: mean 38 (SD 7) - not provided by study arm (all 21 to 50) Baseline BMI: not reported
Interventions	Reduced fat vs usual diet Control aims: followed usual diet, given daily food guide pyramid (half of this group randomised to 9 portions/d of fruit and vegetables advice) Intervention aims: total fat 15%E (half of this group randomised to 9 portions/d of fruit and vegetables advice) Control methods: no dietary counselling (offered this at the end of study), but those given fruit and vegetables advice had support as below Intervention methods: met dietitian every 2 weeks until compliant, monthly group meetings, counselling on home diets, restaurants, parties, social support, eating at work, exchange booklets, cookbook Weight goals: "goals were derived such that baseline energy intake would be maintained while meeting study goals" Total fat intake (at 12 months): low fat 15.7 (SD 5.1) %E, control 32.7 (SD 6.1) %E Saturated fat intake (at 12 months): low fat 7.2 (SD unclear) %E, control 11.6 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: body weight, dietary compliance Available outcomes: weight, total, LDL and HDL cholesterol, TG, BMI (but variance data not provided for any but weight)
Notes	Change from baseline to 12 months for the control (n = 23), control plus fruit and vegetables (n = 25), low fat (n = 24), low fat plus fruit and vegetables (n = 23): Total cholesterol mg/dl: 9, 2, -8, 0 TG mg/dl: -7, 1, 5, 8 HDL cholesterol mg/dl: 0, 0, -4, 0 LDL cholesterol mg/dl: 11, 2, -6, -2 BMI kg/m^2: 0, 4, -13, 0 For weight end data only are provided (no change data) although the intervention group were considerably heavier at baseline (149 lb and 154 lb) than control groups (both 143 lb)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The statistician made envelopes ahead of time, dietitians handed out envelopes at first visit
Allocation concealment (selection bias)	Low risk	Allocation could not be altered once made

Nutrition & Breast Health *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Participants were aware of allocation, researchers and those assessing lipids were not
Incomplete outcome data (attrition bias) All outcomes	High risk	15 of 122 (12%) lost over 1 year (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	High levels of intervention for those on low fat or high fruit and vegetable diets. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	Randomisation to fruit and vegetable intervention was independent of low fat allocation

Pilkington 1960

Methods	RCT
Participants	Men with angina or who have had a MI (UK) CVD risk: high Reduced fat: randomised unclear, analysed 12 Modified fat: randomised unclear, analysed 23 Mean years in trial:reduced fat 1.1, modified fat 1.1 % male: reduced fat 100%, modified fat 100% Age: not stated Baseline BMI: not reported
Interventions	Reduced fat vs modified fat diet Reduced fat aims: total fat 20 g/d, advice to avoid dairy fats except skimmed milk plus 1 egg or 21 g cheese/d. Lean meat and fish each allowed once/d, other non-fatty foods allowed in unlimited quantities Modified fat aims: fat aims not stated, dairy produce avoided except skimmed milk, 90 ml/d soya oil provided, lean meat originally prohibited but allowed after 6 months along with 113 g/wk of 'relatively unsaturated margarine'. Fish and vegetables allowed freely Reduced fat methods: unclear, "dietary histories taken before and during treatment" Modified fat methods: unclear, "dietary histories taken before and during treatment" Weight goals: non-fatty foods not restricted, no weight goals mentioned Total fat intake (during treatment): low fat 15.8 (SD unclear) %E, mod fat 36 (SD unclear) %E Saturated fat intake: unclear Style: diet advice Setting: community
Outcomes	Stated trial outcomes: lipids

Pilkington 1960 *(Continued)*

	Available outcomes: weight, total and LDL cholesterol
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised"
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding (performance bias and detection bias) All outcomes	High risk	No for participants, unclear for outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear exactly how many were randomised, but paper suggests that all randomised participants were analysed
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Appear to be similar levels of assessment and support in both arms
Free of dietary differences other than fat?	Low risk	Dietary focus entirely on fat

Polyp Prevention 1996

Methods	RCT
Participants	People with at least one adenomatous polyp of the large bowel removed (USA) CVD risk: low Control: 1042 randomised, 943 analysed Intervention: 1037 randomised, 943 analysed Mean years in trial: control 3.05, intervention 3.05 % male: control 64%, intervention 66% Age: mean control 61.5, intervention 61.4 (all at least 35) Baseline BMI: mean control 27.5 (SE 0.12), intervention 27.6 (SE 0.13)
Interventions	Low fat vs usual diet Control: general dietary guidelines Intervention: total fat 20%E, 18 g fibre/1000 kcal, 5 to 8 servings fruit and vegetables daily Control methods: leaflet, no additional information or behaviour modification

Polyp Prevention 1996 *(Continued)*

	Intervention methods: > 50 hours of counselling over 4 years, included skill building, behaviour modification, self monitoring and nutritional materials Weight goals: "weight loss is permitted but not encouraged....counselled to replace fat intake with increased intake of fruit, vegetable and grain products rather than reduce total calorie intake." Total fat intake (at 4 years): low fat 23.8 (SD 6.0), control 33.9 (SD 5.9) %E Saturated fat intake: unclear Style: diet advice Setting: community
Outcomes	Stated trial outcomes: recurrence of polyps, prostate cancer Available outcomes: weight, total cholesterol
Notes	Weight data reported at 1, 2, 3 and 4 years. 3-year data used in main analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomly assigned" by computer randomisation centre, stratified according to centre
Allocation concealment (selection bias)	Low risk	Phone call to computer randomisation centre, stratified according to centre
Blinding (performance bias and detection bias) All outcomes	High risk	Outcome assessors blinded, participants not
Incomplete outcome data (attrition bias) All outcomes	Low risk	193 of 2079 (9%) lost over 3 years (< 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	50 hours behaviour modification in intervention group, not in control. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	High risk	Fibre, fruit and vegetable goals in intervention group

Rivellese 1994

Methods	RCT
Participants	Adults with primary hyperlipoproteinaemia (Italy) CVD risk: moderate Intervention reduced fat: 33 randomised, 27 analysed Intervention modified fat: 30 randomised, 17 analysed

Rivellese 1994 *(Continued)*

	Mean years in trial: reduced fat 0.4, modified fat 0.4 % male: reduced fat 82%, modified fat 63% Age, years: reduced fat 47.4 mean (SD 10.3), modified fat 48.6 (SD 8.1) Baseline BMI: reduced fat 24.4 mean (SD 2.9), modified fat 25.2 (SD 2.7)
Interventions	Reduced fat vs modified fat diet Reduced fat aims: total fat 25%E, SFA 8%E, MUFA 15%, PUFA 2%, dietary cholesterol < 300 mg/d, CHO 58%, protein 17%E, soluble fibre 41 g/d Modified fat aims: total fat 38%E, SFA < 10%E, MUFA 20%E, PUFA 10%E, dietary cholesterol < 300 mg/d, CHO 47%E, protein 15%E, soluble fibre 19 g/d Reduced fat methods: seen monthly by dietitian and doctor, feedback based on 7-day food diary each time Modified fat methods: seen monthly by dietitian and doctor, feedback based on 7-day food diary each time Weight goals: neither weight or energy intake goals mentioned for either group Total fat intake (at 5 to 6 months): low fat 27 (SD unclear) %E, mod fat 36 (SD unclear) %E Saturated fat intake (at 5 to 6 months): low fat 6 (SD unclear) %E, mod fat 7 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: metabolic effects Available outcomes: weight, total, LDL and HDL cholesterol, TG
Notes	Weight data were presented without variance info. Participants in the low fat arm lost 1.8 kg over the 6 months, the modified fat diet arm lost 1.6 kg

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Following 3 or 6 weeks compliance with control diet run-in, stratified block randomisation with tables of random numbers
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	None
Incomplete outcome data (attrition bias) All outcomes	High risk	19 of 63 (30%) lost over 0.4 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Identical follow-up. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above

Rivellese 1994 *(Continued)*

Free of dietary differences other than fat?	High risk	Some differences in soluble fibre intake

Simon Low Fat Breast CA

Methods	RCT
Participants	Women with a high risk of breast cancer (USA) CVD risk: low Control: randomised 96, analysed 38 Intervention: randomised 98, analysed 34 Mean years in trial: control 1.8, intervention 1.7 % male: 0 Age: mean control 46, intervention 46 Baseline BMI: mean intervention 25.2 (SE 0.8), control 28.1 (SE 0.8)
Interventions	Reduced fat vs usual diet Control aims: usual diet Intervention aims: total fat 15%E Control methods: continued usual diet Intervention methods: biweekly individual dietetic appointments over 3 months followed by monthly individual or group appointments, including education, goal setting, evaluation, feedback and self monitoring Weight goals: weight and calorie goals not discussed Total fat intake (at 12 months): low fat 18.0 (SD 5.6), control 33.8 (SD 7.4) %E Saturated fat intake (at 12 months): low fat 6.0 (SD unclear), control 11.3 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: intervention feasibility Available outcomes: weight, total, LDL and HDL cholesterol, TG
Notes	—

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Stratified by age and randomised (block size 2)
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants knew their allocation, unclear whether physicians did

Simon Low Fat Breast CA *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	122 of 194 (63%) lost over 2 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Very different contact time with dietitian, but medical appointments same in both groups. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Sondergaard 2003

Methods	RCT
Participants	People with IHD plus total cholesterol at least 5 mmol/L (Denmark) CVD risk: high Control: 63 randomised, 52 analysed Intervention: 68 randomised, 63 analysed Mean years in trial: 1.0 % male: control 79%, intervention 62% Age: control mean 62.8 (SD 10.5), intervention mean 62.1 (SD 9.3) Baseline BMI: intervention 26.6 (SD 3.9), control 26.7 (SD 4.2)
Interventions	Reduced and modified fat intake vs usual diet Control: aims unclear Intervention: aims reductions in total and saturated fat, replace fats with oils, 600 g fruit and vegetables/d, fatty fish at least once a week, eat plenty of bread and cereals Control methods: booklets plus one dietetic interview, and 3 monthly clinical review Intervention methods: 1-hour nutrition interview every 3 months, plus 3 monthly clinical review Weight goals: weight not mentioned Total fat intake (at 12 months): low and mod fat 26.2 (SD 5.1), control 28.9 (SD 7.9) %E Saturated fat intake (at 12 months): unclear Style: diet advice Setting: community
Outcomes	Stated trial outcomes: endothelial function Available outcomes: weight, total, LDL and HDL cholesterol, TG
Notes	No outcome data provided on weight, except the statement "in both groups, body weight remained unchanged after 12 months".

Sondergaard 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised in unblinded 1:1 fashion"
Allocation concealment (selection bias)	High risk	"randomised in unblinded 1:1 fashion"
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of allocation, unclear about others
Incomplete outcome data (attrition bias) All outcomes	High risk	16 of 131 (12%) lost over 1 year (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Additional dietetic time for intervention group. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	High risk	Additional dietary advice for intervention group (fruit, vegetables, fish, cereals)

Strychar 2009

Methods	RCT
Participants	People with well controlled type I diabetes mellitus (Canada) CVD risk: moderate Intervention reduced fat: 18 randomised, 15 analysed Intervention modified fat: 17 randomised, 15 analysed Mean years in trial: reduced fat 0.46, modified fat 0.47 % male: reduced fat unclear, modified fat unclear Age, years: 37.9 (8.1 SD) (not specified by study arm) Baseline BMI: mean reduced fat 24.3 (SD 2.6), modified fat 24.3 (SD 2.7)
Interventions	Reduced fat vs modified fat diet Reduced fat aims: total fat 27%E to 30%E, SFA ≤ 10%E, MUFA 10%, CHO 54% to 57% Modified fat aims: total fat 37%E to40%E, SFA ≤ 10%E, MUFA 20%E, CHO 43%E to 46%E Reduced fat methods: after initial dietary advice monitored weekly by phone by a dietitian (24-hour food recall). Glycaemia, insulin doses, CHO at meals, hypoglycaemic attacks all self monitored daily and reported weekly Modified fat methods: after initial dietary advice monitored weekly by phone by a dietitian (24-hour food recall). Glycaemia, insulin doses, CHO at meals, hypoglycaemic attacks all self monitored daily and reported weekly Total fat intake (at 6 months): not stated

Strychar 2009 *(Continued)*

	Saturated fat intake (at 6 months): not stated Style: diet advice Setting: community
Outcomes	Stated trial outcomes: triglycerides and other CVD risk factors Available outcomes: weight; BMI; total, LDL and HDL cholesterol; TG; systolic and diastolic blood pressure
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned"
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding (performance bias and detection bias) All outcomes	High risk	No details provided, but participants had to make decisions about what they ate
Incomplete outcome data (attrition bias) All outcomes	High risk	5 of 35 (14%) lost over 0.5 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	Low risk	Similar intervention in both groups
Free of dietary differences other than fat?	Low risk	Focus on fat and CHO intake

Swedish Breast CA 1990

Methods	RCT
Participants	Women who had had surgery for breast cancer (Sweden) CVD risk: low Control: randomised 121, analysed 63 Intervention: randomised 119, analysed 106 Mean years in trial: control 1.9, randomised 1.5 % male: 0% Age: mean 58 (not described by randomisation group) Baseline BMI: intervention 6 BMI < 20, 81 BMI 20 to 24.9, 34 BMI ≥ 25; control 9 BMI < 20, 74 BMI 20 to 24.9, 36 BMI ≥ 25
Interventions	Reduced fat vs usual diet

Swedish Breast CA 1990 *(Continued)*

	Control aims: usual diet Intervention aims: 20%E to 25%E from fat, increase energy from CHO to replace lost energy Control methods: no advice provided, only seen at baseline and 2 years Intervention methods: 4 to 6 sessions during the first 2 months, group meetings every 6 to 8 weeks, evening classes in low fat cooking, 3 monthly counselling during the first year, then at 18 months Weight goals: "The total energy and/or protein intake was to be held constant" Total fat intake (at 2 years): intervention -12.9 (SD unclear) (24 overall), control -3.1 (SD unclear) (34.1 overall) %E Saturated fat intake (change to 2 years): intervention -6.8 (SD unclear), control -1.9 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake Available outcomes: weight, BMI
Notes	No exact variance or P values reported for weight and BMI outcomes, so have estimated variance from P value < 0.05 for the difference between the 2 arms for weight. As P value > 0.05 for BMI no variance could be estimated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned"
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding (performance bias and detection bias) All outcomes	High risk	No for participants, unclear for those assessing outcomes
Incomplete outcome data (attrition bias) All outcomes	High risk	Outcome data ignored for those who dropped out (48% of the intervention group), > 5%/year
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	
Free of systematic difference in care?	High risk	Different levels of time and follow-up in the 2 groups
Free of dietary differences other than fat?	Low risk	Focus on fat

Veterans Dermatology 1994

Methods	RCT
Participants	People with non-melanoma skin cancer (USA) CVD risk: low Control: randomised 67, analysed 58 Intervention: randomised 66, analysed 38 Mean years in trial: 1.9 % male: control 67%, intervention 54% Age: mean control 52.3 (SD 13.2), intervention 50.6 (SD 9.7) Baseline BMI: data not provided
Interventions	Reduced fat vs usual diet Control aims: no dietary advice Intervention aims: total fat 20%E, protein 15%E, CHO 65%E Control methods: no dietary change, 4 monthly clinic visits Intervention methods: 8 weekly classes, with behavioural techniques, plus 4 monthly clinic visits Weight goals: "to maintain body weight .... patients were instructed to increase their intake of carbohydrate, particularly complex carbohydrate" Total fat intake ("during study" months 4 to 24): low fat 20.7 (SD 5.5), control 37.8 (SD 4.1) %E Saturated fat intake ("during study, months 4 to 24): low fat 6.6 (SD 1.8), control 12.8 (SD 2.0) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: incidence of actinic keratosis and non-melanoma skin cancer Available outcomes: none (weight data provided, but no variance info)
Notes	At 2 years control -1.5 kg n = 50?, intervention -1 kg n = 51?

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"list of randomly generated numbers"
Allocation concealment (selection bias)	Unclear risk	Randomisation method not clearly described
Blinding (performance bias and detection bias) All outcomes	High risk	Physician blinding: adequate Participant blinding: inadequate
Incomplete outcome data (attrition bias) All outcomes	High risk	37 of 133 (28%) lost over 2 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	

Veterans Dermatology 1994 *(Continued)*

Free of systematic difference in care?	High risk	Minor: all have 4 monthly clinic visits, the intervention group had 8 behavioural technique classes that the control group did not have
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

VYRONAS 2009

Methods	RCT
Participants	12 to 13-year olds attending schools in Vyronas, Athens (Greece) CVD risk: low Control: randomised n = 105, analysed at 17 months n = 93 Intervention: randomised n = 108, analysed at 17 months n = 98 Mean years in trial: control 1.3, intervention 1.4 % male: control 49.5%, intervention 49.0% Age: control mean 13.3 (SD 0.9), intervention 13.1 (SD 0.8) Baseline BMI: control mean 24.3 (SD 3.3), intervention 24 (SD 3.1)
Interventions	Reduced fat vs usual diet Control aims: not stated, usual intake assumed Intervention aims: unclear, but appears to have been low fat and dental hygiene Control methods: screening results were posted to parents, no other information Intervention methods: 12 hours of classroom materials over 12 weeks, taught by home economics teacher supervised by health visitor or family doctor, including multi-component workbooks, "interactions among environmental, cognitive and behavioural factors", "classroom modules developed behaviour capability, expectations and self-efficacy for healthful eating and healthy foods selection", 2 meetings including presentations were held with parents Weight goals: not mentioned except that note was made of obese children (unclear in what respect) Total fat intake (at 17 months): low fat 31.3 (SD 4.4), control 36.9 (SD 4.8) %E Saturated fat intake (at 17 months): low fat 10.3 (SD 1.9), control 13.4 (SD 2.8) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: diet, nutrition intake and BMI Available outcomes: nutritional intake, BMI
Notes	BMI reported compared with baseline in each group, but change in BMI not directly compared between intervention and control groups (calculated by review authors)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"computerised random number generator"

VYRONAS 2009 *(Continued)*

Allocation concealment (selection bias)	Low risk	Recruitment appeared to have been completed before allocation occurred
Blinding (performance bias and detection bias) All outcomes	High risk	"Because of the nature of the intervention, blinding was not feasible"
Incomplete outcome data (attrition bias) All outcomes	High risk	Similar in both arms, paper mentions loss of 5 participants during trial (due to health problems, lack of interest and move to other schools). Of 109 allocated in each arm 10 were not included in analysis of the intervention group and 12 in the control (reasons unclear). 22 of 213 (10%) lost over 17 months (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	High risk	Unclear how intervention was delivered to some children but not others as randomisation appeared to be individual, not by class. Intervention methods imply an individualised intervention, but unclear what elements were individualised
Free of systematic difference in care?	High risk	No, intervention group appear to have received modules designed to develop behavioural capability, expectations and self efficacy, and included motivational methods and strategies as well as social influence
Free of dietary differences other than fat?	High risk	Exact goals of intervention unclear, but appears to have focused on "mainly dietary issues, but also dental health hygiene and consumption attitudes"

WHEL 2007

Methods	RCT
Participants	Women with previously treated early breast cancer (USA) CVD risk: low Control: randomised 1561, analysed 1313 Intervention: randomised 1546, analysed 1308 Mean years in trial: unclear, 11 years max, around 11 years mean? % male: 0 Age: control mean 53.0 (SD 9.0), intervention mean 53.3 (SD 8.9) Baseline BMI: control mean 27.2 (SD 6.1), intervention mean 27.2 (SD 6.1)
Interventions	Reduced fat intake vs usual diet Control: aim 30%E from fat Intervention: aim 15%E to 20%E from fat, 5 vegetables/d, 3 fruit/d, 16 oz vegetable juice and 30 g/d fibre Control methods: given print materials only Intervention methods: telephone counselling programme (31 calls by study end), cooking classes (12 offered in first year, 4 attended on average) and monthly newsletters (48 by study end), all focused on self efficacy, self monitoring and barriers, retaining motivation Weight goal: intervention goal was to achieve the change in dietary pattern without weight reduction, weight and calories not mentioned in the control group

WHEL 2007 *(Continued)*

	Total fat intake (at 72 months): low fat 28.9 (SD 9.0), control 32.4 (SD 8.0) %E Saturated fat intake (at 72 months): low fat 7.2 (SD unclear), control 8.9 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: mortality, invasive breast cancer Available outcomes: weight, total, LDL and HDL cholesterol, TG
Notes	Weight reported at 1, 2, 3, 4 and 6 years, and 3-year data used in main analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation via computer program
Allocation concealment (selection bias)	Low risk	Randomisation via computer program
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	486 of 3107 (16%) lost over 11 years (< 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	High-intensity intervention compared with leaflets. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	High risk	Fruit and vegetable intervention in low fat arm, not in control

WHI 2006

Methods	RCT
Participants	Postmenopausal women aged 50 to 79 (USA) CVD risk: mixed, mostly low but some participants had CVD at baseline Control: randomised 29,294, analysed 25,056 Intervention: randomised 19,541, analysed 16,297 Mean years in trial: control 8.1, intervention 8.1 % male: 0 Age: mean intervention 62.3 (SD 6.9), control 62.3 (SD 6.9) Baseline BMI: mean intervention 29.1 (SD 5.9), control 29.1 (SD 5.9)

WHI 2006 *(Continued)*

Interventions	Reduced fat vs usual diet Control: diet-related education materials Intervention: low fat diet (20%E from fat) with increased fruit and vegetables Control methods: given copy of 'Dietary Guidelines for Americans' Intervention methods: 18 group sessions with trained and certified nutritionists in the first year, quarterly maintenance sessions thereafter, focusing on diet and behaviour modification Weight goals: "the intervention did not include total energy reduction or weight-loss goals" Total fat intake (at 6 years): intervention 28.8 (SD 8.4) %E, control 37.0 (SD 7.3) %E Saturated fat intake (at 6 years): intervention 9.5 (SD 3.2) %E, control 12.4 (SD 3.1) %E Style: dietary advice Setting: community
Outcomes	Stated trial outcomes: breast cancer, mortality, other cancers, cardiovascular events, diabetes Available outcomes: weight, BMI, total, LDL and HDL cholesterol, TG, systolic and diastolic BP
Notes	Weight data available at 1 year, 3 years, 6 years and 7.5 years. Latest (7.5 year) data used for main analysis for weight, BMI and waist circumference.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer algorithm
Allocation concealment (selection bias)	Low risk	
Blinding (performance bias and detection bias) All outcomes	High risk	Participants aware of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	7482 of 48,835 (15%) lost over 8 years (< 5% per year)
Selective reporting (reporting bias)	Low risk	Weight and secondary outcomes reported as in protocol
Other bias	Low risk	
Free of systematic difference in care?	High risk	Intervention participants received 18 group sessions with behavioural modification plus quarterly maintenance sessions thereafter. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	High risk	Also fruit and vegetable intervention. See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

WHT Feasibility 1990

Methods	RCT
Participants	Women at increased risk of breast cancer (USA) CVD risk: low Control: randomised 184, analysed 159 Intervention: randomised 119, analysed 102 Mean years in trial: control 1.9, randomised 1.9 % male: 0% Age: mean control 55.6 (SD 6.3), intervention 55.6 (SD 6.2) Baseline BMI: mean intervention 26 (SD 4), control 25 (SD 4)
Interventions	Reduced fat vs usual diet Control aims: maintain usual diet Intervention aims: 20%E from fat Control methods: no advice provided, only seen at baseline, then 6, 12 and 24 months for assessment Intervention methods: women were given flexible diet plans and responsible for their own monitoring, they had individual appointments with a nutritionist at 2 and 12 weeks, plus small group meetings (weekly for 8 weeks, then biweekly for 8 weeks, then monthly to 2 years) Weight goals: weight and calories not mentioned Total fat intake (at 2 years): intervention 22.6 (SD 7.1), control 36.8 (SD 8.0) %E Saturated fat intake (at 2 years): intervention 7.2 (SD 2.7), control 12.3 (SD 3.6) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake/feasibility Available outcomes: weight, total cholesterol
Notes	Weight data provided at 6, 12 and 24 months. 2-year data used in main analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	42 of 303 (14%) lost over 2 years (> 5% per year)
Selective reporting (reporting bias)	Low risk	Design paper published, weight and serum total cholesterol reported

WHT Feasibility 1990 *(Continued)*

Other bias	Low risk	
Free of systematic difference in care?	High risk	Different levels of attention and time
Free of dietary differences other than fat?	Low risk	Focus on fat only

WHT:FSMP 2003

Methods	RCT
Participants	Postmenopausal women from diverse ethnic and socioeconomic backgrounds (USA) CVD risk: low Control: randomised 883, analysed 649 at 6 mo, 443 at 12 mo, 194 at 18 mo Intervention: randomised 1325, analysed 1071 at 6 mo, 698 at 12 mo, 285 at 18 mo Mean years in trial: unclear, follow-up from 6 to 18 months % male: 0% Age: mean control 59.8 (SD 6.6), intervention 60.1 (SD 6.6) Baseline BMI: 28.8 (SD 4.7) for all
Interventions	Reduced fat vs usual diet Control aims: maintain usual diet Intervention aims: up to 20%E from fat, reduced saturated fat and dietary cholesterol, increased fruit, vegetables and whole grains Control methods: pamphlet on general dietary guidelines provided, no other follow-up, seen at baseline, then 6, 12 and 18 months for assessment Intervention methods: women allocated to groups of 8 to 15 women with a nutritionist leader, meeting weekly for 6 weeks, bi-weekly for 9 months then quarterly. Women provided with personal fat gram goals Weight goals: weight and calories not mentioned Total fat intake (at 1 year): intervention 25.4 (SD unclear), control 36.0 (SD unclear) %E Saturated fat intake (at 1 year): intervention 8.7 (SD unclear), control 12.1 (SD unclear) %E Style: diet advice Setting: community
Outcomes	Stated trial outcomes: dietary intake/feasibility Available outcomes: weight, BMI, blood pressure
Notes	Weight and BMI data only found for 6 months of intervention

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised"

WHT:FSMP 2003 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not discussed
Blinding (performance bias and detection bias) All outcomes	High risk	No for participants, though outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those randomised were analysed for weight
Selective reporting (reporting bias)	Low risk	For weight
Other bias	Low risk	
Free of systematic difference in care?	High risk	Greater time and support provided to intervention group
Free of dietary differences other than fat?	High risk	Suggestion to intervention group to increase fruit, vegetable and whole grain intakes

WINS 1993

Methods	RCT
Participants	Women with localised resected breast cancer (USA) CVD risk: low Control: 1462 randomised, 998 analysed Intervention: 975 randomised, 386 analysed Mean years in trial: overall 5.0 % men: 0 Age: control mean 58.5 (95% CI 43.6 to 73.4), intervention mean 58.6 (95% CI 44.4 to 72.8) (all post-menopausal) Baseline BMI: mean intervention 27.6 (95% CI 27.2 to 28.0), control 27.5 (95% CI 27.2 to 27.8)
Interventions	Reduced fat intake vs usual diet Control aims: minimal nutritional counselling focused on nutritional adequacy Intervention aims: total fat 15%E to 20%E Control methods: 1 baseline dietetic session plus 3-monthly sessions Intervention methods: 8 bi-weekly individual dietetic sessions, then optional monthly group sessions, incorporating individual fat gram goals, social cognitive theory, self monitoring, goal setting, modelling, social support and relapse prevention and management Weight goals: "fat gram goals were based on energy needed to maintain weight, and no counselling on weight reduction was provided", not mentioned for control Total fat intake (at 1 year): low fat 20.3 (SD 8.1), control 29.2 (SD 7.4) %E Saturated fat intake (at 1 year): low fat 10.4 (SD 6.7), control 16.6 (SD 9.3) %E Style: dietary advice

WINS 1993 *(Continued)*

	Setting: community
Outcomes	Stated trial outcomes: dietary fat intake, total cholesterol, weight and waist Available outcomes: weight, BMI
Notes	Weight data reported at 1, 3 and 5. 3-year data used in main analysis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random stratified permuted block design, carried out at the statistical co-ordinating centre of WINS
Allocation concealment (selection bias)	Low risk	
Blinding (performance bias and detection bias) All outcomes	High risk	Participants not blinded, not relevant for assessment of mortality by researchers
Incomplete outcome data (attrition bias) All outcomes	High risk	1053 of 2437 (43%) lost over 5 years (> 5% per year)
Selective reporting (reporting bias)	Unclear risk	Protocol not seen
Other bias	Low risk	
Free of systematic difference in care?	High risk	Differences in attention - more time for those in intervention group. See 'Control methods' and 'Intervention methods' in the 'Interventions' section above
Free of dietary differences other than fat?	Low risk	See 'Control aims' and 'Intervention aims' in the 'Interventions' section above

Abbreviations:
%E: percentage of total energy intake
AHA: American Heart Association
BC:
BMI: body mass index
BP: blood pressure
CHD: coronary heart disease
CHO: carbohydrates
CI: confidence interval
CVD: cardiovascular disease
HDL: high-density lipoprotein
IHD: ischaemic heart disease
LDL: low-density lipoprotein
MI: myocardial infarction
MUFA: monounsaturated fatty acid
NCEP: National Cholesterol Education Program
NEP: Nutrition Education Program
NDHS: National Diet-Heart Study
P/S: polyunsaturated/saturated fat ratio
PUFA: polyunsaturated fatty acid
RCT: randomised controlled trial

SD: standard deviation
SE: standard error
SFA: saturated fatty acid
TG: triglycerides

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Agewall 2001	Multifactorial intervention
Ammerman 2003	No appropriate control group (and not low fat vs modified fat)
Anti-Coronary C 1966	Not randomised
Aquilani 2000	No appropriate control group (and not low fat vs modified fat)
Arne 2014	Intervention aimed at weight management
Arntzenius 1985	No appropriate control group (and not low fat vs modified fat)
Aro 1990	Intervention and randomised follow-up less than 6 months
ASSIST 2001	Intervention is not dietary fat modification or low fat diet
Australian Polyp Prev	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Baer 1993	Not randomised
Bakx 1997	Multifactorial intervention
Barnard 2009	Weight reduction encouraged in the conventional diet, but not in the vegan diet arm
Barndt 1977	No appropriate control group (and not low fat vs modified fat)
Baron 1990	Multifactorial intervention
Barr 1990	Intervention and randomised follow-up less than 6 months
Baumann 1982	Intervention and randomised follow-up less than 6 months
Bazzano 2012	Participants selected on basis of BMI (30 to 45)
Beckmann 1988	Not randomised
Beckmann 1995	Intervention is not dietary fat modification or low fat diet
Beresford 1992	Intervention and randomised follow-up less than 6 months
Bergstrom 1967	Intervention and randomised follow-up less than 6 months
Bierenbaum 1963	No appropriate control group (and not low fat vs modified fat)
Bloomgarden 1987	Multifactorial intervention
Bonnema 1995	No appropriate control group (and not low fat vs modified fat)

Study	Reason for exclusion
Bosaeus 1992	Intervention and randomised follow-up less than 6 months
Boyar 1988	Not randomised
Brehm 2009	Participants recruited on basis of being overweight or obese
Brensike 1982	No appropriate control group (and not low fat vs modified fat)
Broekmans 2003	Intervention is not dietary fat modification or low fat diet
Brown 1984	No appropriate control group (and not low fat vs modified fat)
Bruce 1994	No appropriate control group (and not low fat vs modified fat)
Bruno 1983	Multifactorial intervention
Butcher 1990	Intervention and randomised follow-up less than 6 months
Butowski 1998	Not randomised
Byers 1995	No appropriate control group (and not low fat vs modified fat)
Caggiula 1996	No appropriate control group (and not low fat vs modified fat)
CARMEN 2000	Participants recruited on basis of BMI (26 to 34)
CARMEN MS sub-study	Substudy of CARMEN 2000, participants recruited on basis of BMI
Cerin 1993	Intervention and randomised follow-up less than 6 months
Chan 1993	Intervention and randomised follow-up less than 6 months
Chapman 1950	Intervention and randomised follow-up less than 6 months
Charbonnier 1975	Intervention and randomised follow-up less than 6 months
Cheng 2004	Intervention and randomised follow-up less than 6 months
Chicago CPEP 1977	Not randomised
Chiostri 1988	Intervention and randomised follow-up less than 6 months
Choudhury 1984	Intervention and randomised follow-up less than 6 months
Clark 1997	Multifactorial intervention
Clifton 1992	Intervention and randomised follow-up less than 6 months
Cobb 1991	Intervention and randomised follow-up less than 6 months
Cohen 1991	Intervention is not dietary fat modification or low fat diet
Cole 1988	Intervention and randomised follow-up less than 6 months
Colquhoun 1990	Intervention and randomised follow-up less than 6 months

Study	Reason for exclusion
Consolazio 1946	Intervention and randomised follow-up less than 6 months
Coppell 2010	Weight loss recommended
Cox 1996	Multifactorial intervention
Croft 1986	Intervention is not dietary fat modification or low fat diet
Crouch 1986	Not randomised
Da Qing IGT 1997	Intervention is not dietary fat modification or low fat diet
Dalgard 2001	No appropriate control group (and not low fat vs modified fat)
DAS 1989	No appropriate control group (and not low fat vs modified fat)
DASH 1997	Intervention and randomised follow-up less than 6 months
Davey Smith 2005	Multifactorial intervention
de Boer 1983	Intervention and randomised follow-up less than 6 months
DeBusk 1994	Multifactorial intervention
Delahanty 2001	No appropriate control group (and not low fat vs modified fat)
Delius 1969	Intervention is not dietary fat modification or low fat diet
Demark 1990	Intervention and randomised follow-up less than 6 months
Dengel 1995	No appropriate control group (and not low fat vs modified fat)
Denke 1994	Intervention and randomised follow-up less than 6 months
Diabetes CCT 1995	Intervention is not dietary fat modification or low fat diet
DIET 1998	Multifactorial intervention
Ding 1992	Intervention and randomised follow-up less than 6 months
DIRECT 2009	Weight reduction aim
DO IT 2004	"Overweight subjects were encouraged to adopt a calorie-restricted diet"
Dobs 1991	No appropriate control group (and not low fat vs modified fat)
Duffield 1982	Multifactorial intervention
Dullaart 1997	Not randomised
Dutch Nutrition Guide	No data on weight or body fatness, or any cardiovascular outcomes
Eating Patterns 1997	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)

Study	Reason for exclusion
Eckard 2013	Energy restricted diet
Ehnholm 1982	Intervention and randomised follow-up less than 6 months
Ehnholm 1984	Intervention and randomised follow-up less than 6 months
Eisenberg 1990	Intervention and randomised follow-up less than 6 months
Elder 2000	No appropriate control group (and not low fat vs modified fat)
Ellegard 1991	Intervention and randomised follow-up less than 6 months
Esposito 2003	No appropriate control group (and not low fat vs modified fat)
Esposito 2004	No appropriate control group (both groups aimed at < 30%E from fat)
Esposito 2014	Energy restricted diet
EUROACTION 2008	Multifactorial intervention
FARIS 1997	Multifactorial intervention
Fasting HGS 1997	No appropriate control group (and not low fat vs modified fat)
Ferrara 2000	No appropriate control group (and not low fat vs modified fat)
Fielding 1995	Intervention and randomised follow-up less than 6 months
Finckenor 2000	Not randomised
Finnish Diabetes 2000	Multifactorial intervention
Finnish Mental 1972	Not randomised (cluster-randomised, but < 6 clusters)
Fisher 1981	Intervention and randomised follow-up less than 6 months
Fleming 2002	No appropriate control group (and not low fat vs modified fat)
Fortmann 1988	Intervention is not dietary fat modification or low fat diet
Foster 2003	Weight reduction in one arm but not the other
FRESH START 2007	Participants were newly diagnosed with cancer
Friedman 2012	Weight loss diets
Gambera 1995	Intervention and randomised follow-up less than 6 months
Gaullier 2007	No appropriate control group (and not low fat vs modified fat)
German Fat Reduced	Participants recruited on basis of their BMI (24 to 29)
Ginsberg 1988	Intervention and randomised follow-up less than 6 months
Gjone 1972	Intervention and randomised follow-up less than 6 months

Study	Reason for exclusion
Glatzel 1966	No appropriate control group (and not low fat vs modified fat)
Goodpaster 1999	No appropriate control group (and not low fat vs modified fat)
Gower 2012	Participants recruited on basis of high BMI
Gregg 2013	Participants recruited on basis of high BMI
Grundy 1986	Intervention and randomised follow-up less than 6 months
Gudlaugsson 2013	Multifactorial intervention
Guelinckx 2010	Participants recruited on basis of high BMI
Guldbrand 2012	Weight loss intended
Hardcastle 2008	Multifactorial intervention
Harris 1990	Intervention and randomised follow-up less than 6 months
Hartman 1993	No appropriate control group (and not low fat vs modified fat)
Hartwell 1986	No appropriate control group (and not low fat vs modified fat)
Hashim 1960	Intervention and randomised follow-up less than 6 months
Haynes 1984	Intervention is not dietary fat modification or low fat diet
Heber 1991	Intervention and randomised follow-up less than 6 months
Heine 1989	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Heller 1993	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Hildreth 1951	No appropriate control group (and not low fat vs modified fat)
Hood 1965	Not randomised
Horlick 1957	Intervention and randomised follow-up less than 6 months
Horlick 1960	Intervention and randomised follow-up less than 6 months
Howard 1977	Intervention and randomised follow-up less than 6 months
Hunninghake 1990	Intervention and randomised follow-up less than 6 months
Hutchison 1983	No appropriate control group (and not low fat vs modified fat)
Hyman 1998	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Iacono 1981	Not randomised; intervention and randomised follow-up less than 6 months

Study	Reason for exclusion
IMPACT 1995A	Multifactorial intervention
Ishikawa 1995	Not randomised
Iso 1991	No appropriate control group (and not low fat vs modified fat)
Ives 1993	Multifactorial intervention
Jalkanen 1991	Multifactorial intervention
Janus 2012	Weight loss intended
Jepson 1969	Not randomised
Jerusalem Nut 1992	Intervention and randomised follow-up less than 6 months
Jonasson 2014	Energy restricted diet
Juanola-Falgarona 2014	Energy restricted diet
Jula 1990	Multifactorial intervention
Junker 2001	Intervention and randomised follow-up less than 6 months
Karmally 1990	Intervention and randomised follow-up less than 6 months
Karvetti 1992	Multifactorial intervention
Kastarinen 2002	Multifactorial intervention
Kather 1985	Intervention and randomised follow-up less than 6 months
Kattelmann 2010	Weight loss intended
Katzel 1995	Not randomised
Katzel 1995A	Intervention is not dietary fat modification or low fat diet
Kawamura 1993	Intervention and randomised follow-up less than 6 months
Keidar 1988	Intervention and randomised follow-up less than 6 months
Kempner 1948	No appropriate control group (and not low fat vs modified fat)
Keys 1952	Not randomised
Keys 1957	Intervention and randomised follow-up less than 6 months
Keys 1957A	Intervention and randomised follow-up less than 6 months
Keys 1957B	Intervention and randomised follow-up less than 6 months
Khan 2003	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)

Study	Reason for exclusion
King 2000	Intervention and randomised follow-up less than 6 months
Kingsbury 1961	Intervention and randomised follow-up less than 6 months
Klemsdal 2010	Participants recruited on basis of high BMI
Kohler 1986	Not randomised
Kontogianni 2012	Not randomised
Koopman 1990	Intervention and randomised follow-up less than 6 months
Koranyi 1963	Unclear whether randomised
Korhonen 2003	Multifactorial intervention
Kriketos 2001	Intervention and randomised follow-up less than 6 months
Kris 1994	Intervention and randomised follow-up less than 6 months
Kristal 1997	Multifactorial intervention
Kromhout 1987	No appropriate control group (and not low fat vs modified fat)
Kummel 2008	Intervention is not dietary fat modification or low fat diet
Laitinen 1993	Multifactorial intervention
Laitinen 1994	Multifactorial intervention
Larsen 2011	Energy restricted diet
Leduc 1994	Multifactorial intervention
Leibbrandt 2010	Participants recruited on basis of high BMI
Lewis 1958	Intervention and randomised follow-up less than 6 months
Lewis 1981	Intervention and randomised follow-up less than 6 months
Lewis 1985	Multifactorial intervention
Lichtenstein 2002	Intervention and randomised follow-up less than 6 months
Linko 1957	Intervention and randomised follow-up less than 6 months
Lipid Res Clinic 1984	No appropriate control group (and not low fat vs modified fat)
Little 1990	Intervention and randomised follow-up less than 6 months
Little 1991	Not randomised
Little 2004	Intervention is not dietary fat modification or low fat diet
Lottenberg 1996	Intervention and randomised follow-up less than 6 months

Study	Reason for exclusion
Luoto 2012	No assessment of total fat intake
Luszczynska 2007	No appropriate control group (and not low fat vs modified fat)
Lyon Diet Heart 1994	Intervention is not dietary fat modification or low fat diet
Lysikova 2003	Intervention and randomised follow-up less than 6 months
Macdonald 1972	Intervention and randomised follow-up less than 6 months
Mansel 1990	Intervention is not dietary fat modification or low fat diet
Marckmann 1993	Not randomised
MARGARIN	No appropriate control group (and not low fat vs modified fat)
Martin 2011	Participants recruited on basis of high BMI
Maruthur 2014	No relevant outcomes available
Mattson 1985	Intervention and randomised follow-up less than 6 months
Mayneris-Perxachs 2014	No assessment of total fat intake
McCarron 1997	Intervention and randomised follow-up less than 6 months
McCarron 2001	Intervention is not dietary fat modification or low fat diet
McManus 2001	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
McNamara 1981	Intervention and randomised follow-up less than 6 months
Medi-RIVAGE 2004	Weight reduction for some low fat diet participants (those with BMI > 25) but not in Mediterranean group
Mensink 1987	Intervention and randomised follow-up less than 6 months
Mensink 1989	Intervention and randomised follow-up less than 6 months
Mensink 1990	Intervention and randomised follow-up less than 6 months
Mensink 1990A	Intervention and randomised follow-up less than 6 months
Merrill 2011	Multifactorial intervention
Metroville Health 2003	No assessment of outcomes further than reduction in fat
Michalsen 2006	Diet plus stress management vs no intervention
Miettinen 1994	Intervention and randomised follow-up less than 6 months
Millar 1973	No appropriate control group (and not low fat vs modified fat)
Miller 1998	Intervention and randomised follow-up less than 6 months

Study	Reason for exclusion
Miller 2001	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Milne 1994	No appropriate control group (and not low fat vs modified fat) - the high CHO diet is neither 'usual' or 'low fat' to compare with the modified fat diet
Minnesota HHP 1990	No appropriate control group (and not low fat vs modified fat)
Mishra 2013	Intervention and randomised follow-up less than 6 months
Mitchell 2011	No relevant outcomes available
Mokuno 1988	Intervention and randomised follow-up less than 6 months
Moreno 1994	Not randomised
Morrison 1950	Not randomised
Morrison 1951	Not randomised
Morrison 1960	Not randomised
Mortensen 1983	Intervention and randomised follow-up less than 6 months
Moses 2014	Intervention and randomised follow-up less than 6 months
MRFIT substudy 1986	Intervention and randomised follow-up less than 6 months
MSDELTA 1995	Intervention and randomised follow-up less than 6 months
MUFObes low fat 2007	Trial aims to assess weight maintenance following major weight loss
MUFObes low vs mod 2007	Trial aims to assess weight maintenance following major weight loss
Mujeres Felices 2003	Diet and breast self examination vs no intervention
Munsters 2010	Weight loss intended
Mutanen 1997	Intervention and randomised follow-up less than 6 months
Muzio 2007	Intervention and randomised follow-up less than 6 months
Naglak 2000	Dietary fat intervention unclear
NAS 1987	Intervention and randomised follow-up less than 6 months
NCEP weight	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Neil 1995	No appropriate control group (and not low fat vs modified fat)
Neverov 1997	Multifactorial intervention
Next Step 1995	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)

Study	Reason for exclusion
Nordoy 1971	Intervention and randomised follow-up less than 6 months
Norway Veg Oil 1968	No appropriate control group (and not low fat vs modified fat)
Novotny 2012	Weight loss intended
Nutrition Ed Study 1980	Those who were overweight were provided with a weight reduction booklet
O'Brien 1976	Intervention and randomised follow-up less than 6 months
ODES 2001	The study aimed for weight loss in some participants
Oldroyd 2001	Multifactorial intervention
Orazio 2011	Weight loss intended
ORIGIN 2008	Intervention is not dietary fat modification or low fat diet
Ornish 1990	Multifactorial intervention (diet, smoking, stress and exercise) compared to no intervention
Oslo Study 1980	Multifactorial intervention
Otago Weight Loss 2005	Although intake was ad libitum the aim was for weight loss to occur - participants presumably joined the study on the basis that it was assessing effects on weight loss, so were keen to lose weight
Pandey 2013	Not randomised
Pascale 1995	Multifactorial intervention
Paz-Tal 2013	No relevant outcomes available
PEP 2001	Multifactorial intervention
PHYLLIS 1993	No appropriate control group (and not low fat vs modified fat)
PREDIMED 2007	Modified fat group is clearly defined, but no fat goals were set for the low fat group. We were unable to verify whether the fat aim was ≤ 30%E
PREMIER 2003	Overweight participants were encouraged to lose weight
Pritchard 2002	The study aimed for weight loss in one arm and not in the comparison arm
Puget Sound EP	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Rabast 1979	Intervention and randomised follow-up less than 6 months
Rabkin 1981	Intervention and randomised follow-up less than 6 months
Radack 1990	Intervention and randomised follow-up less than 6 months
Rasmussen 1995	Intervention and randomised follow-up less than 6 months
Reaven 2001	Intervention and randomised follow-up less than 6 months

Study	Reason for exclusion
Reid 2002	No appropriate control group (and not low fat vs modified fat)
Renaud 1986	Not randomised
Rivellese 2003	Intervention and randomised follow-up less than 6 months
Roderick 1997	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Roman CHD prev 1986	Multifactorial intervention
Rose 1987	No appropriate control group (and not low fat vs modified fat)
Rusu 2013	Energy restricted diet
Sacks 2009	All arms aimed at a 750 kcal/day deficit to ensure weight loss
Salas-Salvado 2014	No assessment of total fat intake
Sandstrom 1992	Not randomised
Sasaki 2000	Not randomised
Schaefer 1995	Intervention and randomised follow-up less than 6 months
Schaefer 1995A	Intervention and randomised follow-up less than 6 months
Schectman 1996	Multifactorial intervention
Schlierf 1995	Multifactorial intervention
Seppanen-Laakso	Intervention and randomised follow-up less than 6 months
Shai 2012	Energy restricted diet
Singh 1990	Not randomised
Singh 1991	Multifactorial intervention
Singh 1992	No appropriate control group (and not low fat vs modified fat)
Siqueira-Catania 2010	Weight loss intended
Sirtori 1992	Intervention and randomised follow-up less than 6 months
SLIM 2008	Multifactorial intervention
Sollentuna Diet	The study aimed for weight loss in one arm and not in the comparison arm
Sollentuna Diet & Ex	The study aimed for weight loss in one arm and not in the comparison arm
Sopotsinskaia 1992	The study aimed for weight loss in one arm and not in the comparison arm
Staff HHP 1994	Not randomised

Study	Reason for exclusion
Stanford NAP 1997	Intervention and randomised follow-up less than 6 months
Stanford Weight	The study aimed for weight loss in one arm and not in the comparison arm
Starmans 1995	Intervention and randomised follow-up less than 6 months
Steinbach 1996	Multifactorial intervention
Steptoe 2001	No appropriate control group (and not low fat vs modified fat)
Stevens 2002	Diet plus breast self examination vs no intervention
Stevenson 1988	No appropriate control group (and not low fat vs modified fat)
Sweeney 2004	Intervention is not dietary fat modification or low fat diet
TAIM 1989	Intervention is not dietary fat modification or low fat diet
Take Heart II 1997	Not randomised
Tapsell 2004	No weight data or cardiovascular outcomes reported
Taylor 1991	Not randomised
THIS DIET 2008	Study states "although this was not a weight loss intervention, participants who were overweight or obese were encouraged to reduce calories to facilitate weight loss".
TOHP I 1992	Multifactorial intervention
TONE 1997	Intervention is not dietary fat modification or low fat diet
Toobert 2003	Multifactorial intervention
Toronto Polyp Prev 1994	No weight or BMI data presented
Towle 1994	Intervention and randomised follow-up less than 6 months
TRANSFACT 2006	Intervention and randomised follow-up less than 6 months
Treatwell 1992	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Tromso Heart 1989	Multifactorial intervention
Turku Weight	Both intervention groups aimed to lose weight, while the control group did not
Turpeinen 1960	Not randomised
UK PDS 1996	No appropriate control group (and not low fat vs modified fat)
Urbach 1952	No appropriate control group (and not low fat vs modified fat)
Uusitupa 1993	Multifactorial intervention
Uusitupa 2013	Intervention and randomised follow-up less than 6 months

Study	Reason for exclusion
Vavrikova 1958	Intervention and randomised follow-up less than 6 months
Wan 2013	Not a RCT
Wass 1981	Intervention and randomised follow-up less than 6 months
Wassertheil 1985	Intervention is not dietary fat modification or low fat diet
WATCH	Neither mortality nor cardiovascular morbidity data available (only decided after contact with at least one author)
Watts 1988	Intervention and randomised follow-up less than 6 months
Weintraub 1992	No appropriate control group (and not low fat vs modified fat)
Westman 2006	Intervention is not dietary fat modification or low fat diet
Weststrate 1998	Intervention and randomised follow-up less than 6 months
WHO primary prev 1979	Multifactorial intervention
WHT	Neither mortality nor cardiovascular morbidity data available as such data were not collected in the study
Wilke 1974	Intervention and randomised follow-up less than 6 months
Williams 1990	Intervention is not dietary fat modification or low fat diet
Williams 1992	Intervention is not dietary fat modification or low fat diet
Williams 1994	Intervention is not dietary fat modification or low fat diet
Wilmot 1952	No appropriate control group (and not low fat vs modified fat)
Wing 1998	No appropriate control group (and not low fat vs modified fat)
Wolever 2008	Weight loss intended in some participants
WOMAN 2007	Lifestyle intervention includes exercise and weight as well as diet
Wood 1988	Intervention is not dietary fat modification or low fat diet
Woollard 2003	Multifactorial intervention including smoking, weight, exercise and alcohol components
Working Well 1996	Multifactorial intervention
Young 2010	Weight loss intended
Zock 1995	Intervention and randomised follow-up less than 6 months

BMI: body mass index
RCT: randomised controlled trial

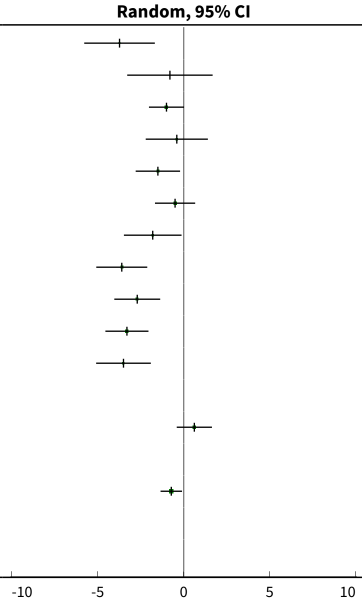
DATA AND ANALYSES

Comparison 1. Fat reduction versus usual fat diet, adult RCTs

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Weight, kg	30	53647	Mean Difference (IV, Random, 95% CI)	-1.54 [-1.97, -1.12]
2 BMI, kg/m2	10	45703	Mean Difference (IV, Random, 95% CI)	-0.50 [-0.74, -0.26]
3 Waist circumference, cm	1	15671	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.58, -0.02]
4 LDL cholesterol, mmol/L	18	7285	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.23, -0.03]
5 HDL cholesterol, mmol/L	19	7166	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.03, 0.00]
6 Total cholesterol, mmol/L	20	7715	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.29, -0.11]
7 Triglycerides, mmol/L	17	6976	Mean Difference (IV, Random, 95% CI)	-0.02 [-0.12, 0.08]
8 Total cholesterol/HDL	7	3332	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.16, -0.04]
9 Systolic blood pressure, mmHg	9	5159	Mean Difference (IV, Random, 95% CI)	-1.16 [-1.95, -0.37]
10 Diastolic blood pressure, mmHg	9	5159	Mean Difference (IV, Random, 95% CI)	-0.74 [-1.40, -0.08]

Analysis 1.1. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 1 Weight, kg.

Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		2.77%	-3.73[-5.78,-1.68]
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		2.13%	-0.8[-3.28,1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		5.46%	-1[-2.02,0.02]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		3.25%	-0.4[-2.21,1.41]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		4.58%	-1.5[-2.79,-0.21]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		4.96%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		3.55%	-1.8[-3.48,-0.12]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		4.03%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		4.45%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		4.7%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		3.75%	-3.5[-5.09,-1.91]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		5.45%	0.62[-0.4,1.64]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		6.81%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable



Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.62%	0.9[-4.26,6.06]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		1%	-4.1[-8.06,-0.14]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		7.27%	-0.96[-1.43,-0.49]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.6%	-8.5[-13.77,-3.23]
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		3.33%	-2.43[-4.2,-0.66]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		3.46%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)			Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		4.03%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		7.85%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		5.09%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		7.58%	-1.5[-1.85,-1.15]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)		3.27%	-2.7[-4.5,-0.9]
Total ***	**22316**		**31331**			**100%**	**-1.54[-1.97,-1.12]**

Heterogeneity: Tau^2=0.58; Chi^2=99.49, df=23(P<0.0001); I^2=76.88%

Test for overall effect: Z=7.14(P<0.0001)

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 1.2. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 2 BMI, kg/m2.

Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
BDIT Pilot Studies 1996	76	24.3 (3.8)	81	24.3 (3.6)		3.67%	0[-1.16,1.16]
Diet and Hormone Study 2003	81	23.5 (4.4)	96	23.7 (3.5)		3.53%	-0.2[-1.39,0.99]
Kuopio Reduced & Mod 1993	41	26 (4)	41	26.3 (3.6)		1.95%	-0.3[-1.95,1.35]
Kuopio Reduced Fat 1993	40	26.2 (3.2)	12	25.7 (4.2)		0.84%	0.5[-2.07,3.07]
Moy 2001	117	-0.1 (1)	118	0.2 (2)		15.19%	-0.31[-0.71,0.09]
Simon Low Fat Breast CA	34	23.8 (4.7)	38	27.4 (4.9)		1.11%	-3.6[-5.82,-1.38]
Strychar 2009	15	-0.2 (1)	15	0.6 (0.6)		10.18%	-0.8[-1.39,-0.21]
WHI 2006	16230	0 (3.2)	24943	0.3 (3.1)		26.32%	-0.27[-0.33,-0.21]
WHT:FSMP 2003	1094	-0.7 (1.2)	646	-0.1 (1.4)		24.86%	-0.6[-0.73,-0.47]
WINS 1993	755	26.8 (5.6)	1230	27.6 (5.4)		12.34%	-0.8[-1.3,-0.3]
Total ***	**18483**		**27220**			**100%**	**-0.5[-0.74,-0.26]**

Heterogeneity: Tau^2=0.06; Chi^2=35.05, df=9(P<0.0001); I^2=74.32%

Test for overall effect: Z=4.07(P<0.0001)

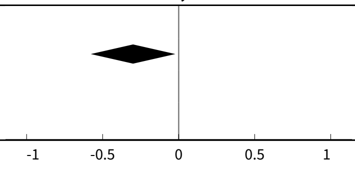
Favours reduced fat -4 -2 0 2 4 Favours moderate fat

Analysis 1.3. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 3 Waist circumference, cm.

Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
WHI 2006	6154	1.6 (8.6)	9517	1.9 (8.8)		100%	-0.3[-0.58,-0.02]

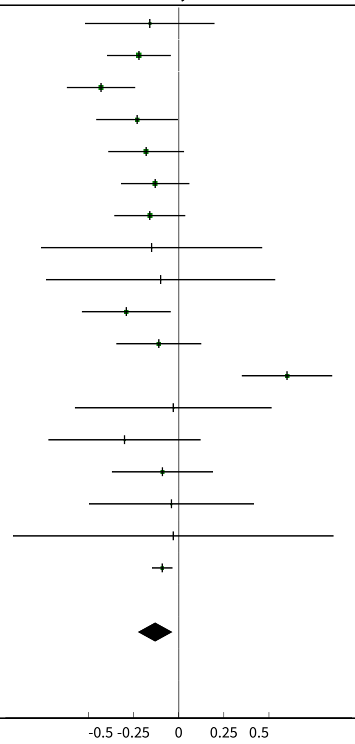
Favours reduced fat -1 -0.5 0 0.5 1 Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Weight	Mean Difference Random, 95% CI
Total ***	**6154**		**9517**		**100%**	**-0.3[-0.58,-0.02]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.11(P=0.03)						



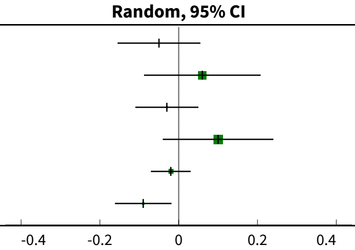
Analysis 1.4. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 4 LDL cholesterol, mmol/L.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	51	-0.3 (0.6)	52	-0.2 (1.2)	4.39%	-0.16[-0.52,0.2]
beFIT 1997	217	4.2 (0.9)	192	4.4 (0.9)	8.1%	-0.22[-0.4,-0.04]
DEER 1998 exercise men	48	-0.5 (0.5)	47	-0.1 (0.5)	7.78%	-0.43[-0.62,-0.24]
DEER 1998 exercise women	43	-0.4 (0.6)	43	-0.1 (0.5)	6.89%	-0.23[-0.46,-0]
DEER 1998 no exercise men	49	-0.3 (0.5)	46	-0.1 (0.6)	7.28%	-0.18[-0.39,0.03]
DEER 1998 no exercise wom	46	-0.2 (0.5)	45	-0.1 (0.4)	7.78%	-0.13[-0.32,0.06]
Kentucky Low Fat 1990	47	-0.6 (0.6)	51	-0.4 (0.4)	7.6%	-0.16[-0.36,0.04]
Kuopio Reduced & Mod 1993	41	4.2 (0.9)	12	4.4 (1)	2.03%	-0.15[-0.76,0.46]
Kuopio Reduced Fat 1993	40	4.3 (1)	12	4.4 (1)	1.92%	-0.1[-0.73,0.53]
Moy 2001	117	-0.7 (1.1)	118	-0.4 (0.8)	6.45%	-0.29[-0.54,-0.04]
MSFAT 1995	117	3.7 (1)	103	3.8 (0.8)	6.69%	-0.11[-0.35,0.13]
Pilkington 1960	12	1.8 (0.4)	23	1.2 (0.3)	6.36%	0.6[0.35,0.85]
Rivellese 1994	27	4.8 (0.9)	17	4.9 (0.9)	2.45%	-0.03[-0.57,0.51]
Simon Low Fat Breast CA	34	2.8 (0.8)	37	3.1 (1)	3.57%	-0.3[-0.72,0.12]
Sondergaard 2003	63	3 (0.7)	52	3.1 (0.8)	5.75%	-0.09[-0.37,0.19]
Strychar 2009	15	-0.2 (0.7)	15	-0.2 (0.6)	3.19%	-0.04[-0.5,0.42]
WHEL 2007	1308	2.9 (11.9)	1313	3 (11.3)	1.07%	-0.03[-0.92,0.86]
WHI 2006	1133	-0.3 (0.8)	1699	-0.2 (0.8)	10.69%	-0.09[-0.15,-0.03]
Total ***	**3408**		**3877**		**100%**	**-0.13[-0.23,-0.03]**
Heterogeneity: Tau²=0.02; Chi²=48.57, df=17(P<0.0001); I²=65%						
Test for overall effect: Z=2.64(P=0.01)						



Analysis 1.5. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 5 HDL cholesterol, mmol/L.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	51	0 (0.1)	52	0.1 (0.4)	1.72%	-0.05[-0.16,0.06]
BDIT Pilot Studies 1996	53	1.6 (0.4)	57	1.6 (0.4)	0.87%	0.06[-0.09,0.21]
Bloemberg 1991	39	-0 (0.2)	40	0 (0.2)	2.97%	-0.03[-0.11,0.05]
de Bont 1981 non-obese	70	-0.1 (0.4)	65	-0.2 (0.4)	0.97%	0.1[-0.04,0.24]
DEER 1998 exercise men	48	0 (0.1)	47	0 (0.1)	7.43%	-0.02[-0.07,0.03]
DEER 1998 exercise women	43	-0 (0.2)	43	0.1 (0.2)	3.68%	-0.09[-0.16,-0.02]



Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
DEER 1998 no exercise men	49	-0 (0.1)	46	-0 (0.1)		9.69%	-0.01[-0.05,0.03]
DEER 1998 no exercise wom	46	0 (0.2)	45	0 (0.2)		4.13%	-0.02[-0.09,0.05]
Kentucky Low Fat 1990	47	0 (0.1)	51	0 (0.1)		6.17%	0[-0.06,0.06]
Kuopio Reduced & Mod 1993	41	1.4 (0.3)	12	1.5 (0.4)		0.34%	-0.1[-0.34,0.14]
Kuopio Reduced Fat 1993	40	1.4 (0.3)	12	1.5 (0.4)		0.32%	-0.15[-0.39,0.09]
Moy 2001	117	0 (0.3)	118	0 (0.2)		4.47%	0.04[-0.03,0.1]
MSFAT 1995	117	1.3 (0.3)	103	1.4 (0.4)		1.98%	-0.06[-0.16,0.04]
Rivellese 1994	27	1.2 (0.3)	17	1.1 (0.2)		0.98%	0.1[-0.04,0.24]
Simon Low Fat Breast CA	34	1.4 (0.6)	38	1.6 (0.6)		0.28%	-0.12[-0.38,0.14]
Sondergaard 2003	63	1.3 (0.4)	52	1.2 (0.4)		1.06%	0.02[-0.11,0.15]
Strychar 2009	15	0.1 (0.3)	15	-0 (0.2)		0.61%	0.07[-0.11,0.25]
WHEL 2007	1308	1.5 (4.7)	1313	1.5 (4.3)		0.16%	-0.08[-0.43,0.27]
WHI 2006	1133	-0 (0.2)	1699	-0 (0.3)		52.19%	-0.01[-0.03,0.01]
Total ***	**3341**		**3825**			**100%**	**-0.01[-0.03,0]**
Heterogeneity: Tau²=0; Chi²=18.03, df=18(P=0.45); I²=0.15%							
Test for overall effect: Z=1.61(P=0.11)							

Favours moderate fat -0.4 -0.2 0 0.2 0.4 Favours reduced fat

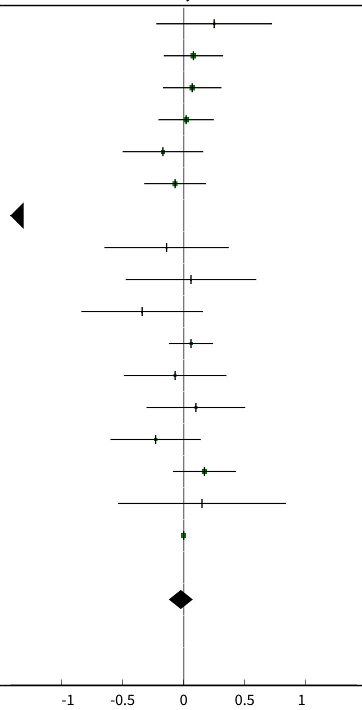
Analysis 1.6. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 6 Total cholesterol, mmol/L.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	51	-0.2 (0.8)	52	-0.1 (1.3)		3.23%	-0.05[-0.46,0.36]
BDIT Pilot Studies 1996	54	5.1 (0.8)	61	5.4 (0.8)		4.98%	-0.24[-0.54,0.06]
Bloemberg 1991	39	-0.3 (0.9)	40	-0 (0.8)		3.93%	-0.3[-0.66,0.06]
de Bont 1981 non-obese	70	-0.9 (1.1)	65	-0.3 (1)		4.1%	-0.62[-0.97,-0.27]
DEER 1998 exercise men	48	-0.5 (0.5)	47	-0.1 (0.5)		7.26%	-0.4[-0.61,-0.19]
DEER 1998 exercise women	43	-0.4 (0.6)	43	0.2 (0.6)		6.41%	-0.6[-0.84,-0.36]
DEER 1998 no exercise men	49	-0.3 (0.5)	46	-0.1 (0.6)		7.18%	-0.24[-0.45,-0.03]
DEER 1998 no exercise wom	46	-0.2 (0.5)	45	-0 (0.5)		7.25%	-0.17[-0.38,0.04]
Kentucky Low Fat 1990	47	-0.6 (0.6)	51	-0.4 (0.6)		6.54%	-0.17[-0.41,0.07]
Kuopio Reduced & Mod 1993	41	6.2 (1.1)	12	6.5 (1.1)		1.4%	-0.27[-0.96,0.42]
Kuopio Reduced Fat 1993	40	6.4 (1.2)	12	6.5 (1.1)		1.33%	-0.16[-0.87,0.55]
MSFAT 1995	117	5.6 (1.1)	103	5.8 (1)		5.54%	-0.14[-0.42,0.14]
Pilkington 1960	12	5.7 (0.9)	23	5.4 (0.9)		1.74%	0.23[-0.38,0.84]
Polyp Prevention 1996	370	-0.1 (0.8)	374	-0.1 (0.8)		10.64%	-0.06[-0.17,0.05]
Rivellese 1994	27	6.8 (0.8)	17	6.6 (0.6)		3.37%	0.15[-0.25,0.55]
Simon Low Fat Breast CA	34	4.9 (0.9)	38	5.2 (0.2)		5.07%	-0.34[-0.64,-0.04]
Sondergaard 2003	63	5 (0.8)	52	5.1 (1)		4.46%	-0.13[-0.46,0.2]
Strychar 2009	15	-0.1 (0.7)	15	-0.2 (0.7)		2.64%	0.12[-0.35,0.59]
WHEL 2007	1308	5.1 (11.9)	1313	5 (11.9)		0.83%	0.08[-0.83,0.99]
WHI 2006	1133	-0.3 (0.8)	1699	-0.2 (0.8)		12.09%	-0.09[-0.15,-0.02]
Total ***	**3607**		**4108**			**100%**	**-0.2[-0.29,-0.11]**
Heterogeneity: Tau²=0.01; Chi²=40.91, df=19(P=0); I²=53.55%							
Test for overall effect: Z=4.55(P<0.0001)							

Favours reduced fat -0.5 -0.25 0 0.25 0.5 Favours moderate fat

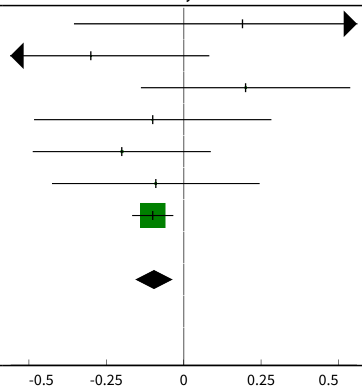
Analysis 1.7. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 7 Triglycerides, mmol/L.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	51	0.4 (0.7)	52	0.1 (1.6)		3.38%	0.25[-0.22,0.72]
de Bont 1981 non-obese	70	-0 (0.8)	65	-0.1 (0.6)		7.99%	0.08[-0.16,0.32]
DEER 1998 exercise men	48	-0.1 (0.6)	47	-0.1 (0.6)		8.11%	0.07[-0.17,0.31]
DEER 1998 exercise women	43	-0.1 (0.6)	43	-0.1 (0.5)		8.54%	0.02[-0.21,0.25]
DEER 1998 no exercise men	49	-0.1 (0.7)	46	0.1 (0.9)		5.67%	-0.17[-0.5,0.16]
DEER 1998 no exercise wom	46	-0 (0.7)	45	0 (0.5)		7.67%	-0.07[-0.32,0.18]
Kentucky Low Fat 1990	47	-1 (2)	51	1.1 (2)		1.4%	-2.11[-2.91,-1.31]
Kuopio Reduced & Mod 1993	41	1.2 (0.6)	12	1.4 (0.8)		3.02%	-0.14[-0.65,0.37]
Kuopio Reduced Fat 1993	40	1.4 (0.8)	12	1.4 (0.8)		2.79%	0.06[-0.47,0.59]
Moy 2001	117	-0.4 (2)	118	-0.1 (1.9)		3.12%	-0.34[-0.84,0.16]
MSFAT 1995	117	1.3 (0.8)	103	1.2 (0.6)		10.19%	0.06[-0.12,0.24]
Rivellese 1994	27	1.5 (0.7)	17	1.6 (0.7)		4.07%	-0.07[-0.49,0.35]
Simon Low Fat Breast CA	34	1.4 (1.1)	37	1.3 (0.6)		4.31%	0.1[-0.3,0.5]
Sondergaard 2003	63	1.5 (1)	52	1.8 (1)		4.87%	-0.23[-0.6,0.14]
Strychar 2009	15	0.1 (0.5)	15	-0 (0.2)		7.53%	0.17[-0.09,0.43]
WHEL 2007	1308	1.2 (7.8)	1313	1 (10)		1.82%	0.15[-0.54,0.84]
WHI 2006	1133	0 (0)	1699	0 (0)		15.54%	0[-0,0]
Total ***	**3249**		**3727**			**100%**	**-0.02[-0.12,0.08]**
Heterogeneity: Tau²=0.02; Chi²=36.35, df=16(P=0); I²=55.98%							
Test for overall effect: Z=0.47(P=0.64)							



Analysis 1.8. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 8 Total cholesterol/HDL.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	51	-0.3 (1)	52	-0.5 (1.7)		1.24%	0.19[-0.35,0.73]
DEER 1998 exercise men	48	-0.6 (0.9)	47	-0.3 (1)		2.5%	-0.3[-0.68,0.08]
DEER 1998 exercise women	43	-0.2 (0.8)	43	-0.4 (0.8)		3.21%	0.2[-0.14,0.54]
DEER 1998 no exercise men	49	-0.2 (0.9)	46	-0.1 (1)		2.5%	-0.1[-0.48,0.28]
DEER 1998 no exercise wom	46	-0.2 (0.7)	45	0 (0.7)		4.44%	-0.2[-0.49,0.09]
Strychar 2009	15	-0.2 (0.6)	15	-0.1 (0.4)		3.26%	-0.09[-0.43,0.25]
WHI 2006	1133	-0.2 (0.8)	1699	-0.1 (1)		82.85%	-0.1[-0.17,-0.03]
Total ***	**1385**		**1947**			**100%**	**-0.1[-0.16,-0.04]**
Heterogeneity: Tau²=0; Chi²=5.61, df=6(P=0.47); I²=0%							
Test for overall effect: Z=3.1(P=0)							

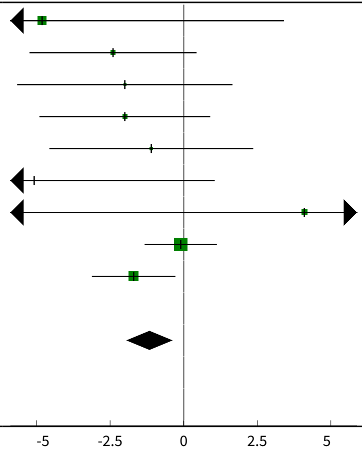


Analysis 1.9. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 9 Systolic blood pressure, mmHg.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	51	-3.5 (17.7)	52	1.3 (24.4)		0.92%	-4.81[-13.03,3.41]
DEER 1998 exercise men	48	-3 (6.8)	47	-0.6 (7.3)		7.72%	-2.4[-5.24,0.44]
DEER 1998 exercise women	43	-3.1 (8.4)	43	-1.1 (8.9)		4.65%	-2[-5.66,1.66]
DEER 1998 no exercise men	49	-1.7 (6.4)	46	0.3 (7.9)		7.39%	-2[-4.9,0.9]
DEER 1998 no exercise wom	46	-3.5 (9.2)	45	-2.4 (7.6)		5.18%	-1.1[-4.56,2.36]
Kuopio Reduced & Mod 1993	41	-2.6 (11.2)	37	2.5 (15.8)		1.65%	-5.08[-11.22,1.06]
Strychar 2009	15	3.9 (14.4)	15	-0.2 (21.1)		0.37%	4.1[-8.83,17.03]
WHI 2006	1133	-2.2 (16.3)	1699	-2.1 (16.4)		41.23%	-0.1[-1.33,1.13]
WHT:FSMP 2003	1101	-3.1 (14.5)	648	-1.4 (14.7)		30.88%	-1.7[-3.12,-0.28]
Total ***	**2527**		**2632**			**100%**	**-1.16[-1.95,-0.37]**

Heterogeneity: Tau^2=0; Chi^2=7.64, df=8(P=0.47); I^2=0%

Test for overall effect: Z=2.89(P=0)



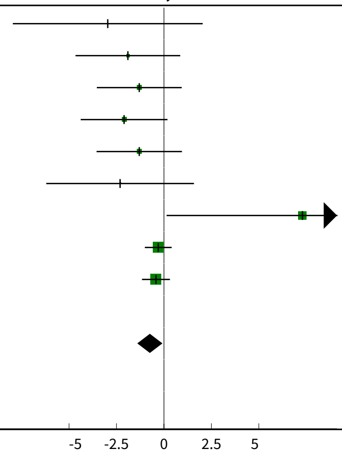
Favours reduced fat | Favours moderate fat

Analysis 1.10. Comparison 1 Fat reduction versus usual fat diet, adult RCTs, Outcome 10 Diastolic blood pressure, mmHg.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	51	-7.2 (12)	52	-4.2 (13.9)		1.7%	-2.96[-7.96,2.04]
DEER 1998 exercise men	48	-3 (6.6)	47	-1.1 (7.1)		5.23%	-1.9[-4.66,0.86]
DEER 1998 exercise women	43	-2.7 (4.6)	43	-1.4 (5.9)		7.59%	-1.3[-3.54,0.94]
DEER 1998 no exercise men	49	-0.3 (5.2)	46	1.8 (6.1)		7.3%	-2.1[-4.39,0.19]
DEER 1998 no exercise wom	46	-1.9 (5)	45	-0.6 (5.9)		7.51%	-1.3[-3.55,0.95]
Kuopio Reduced & Mod 1993	41	-0.9 (7.1)	37	1.4 (10)		2.76%	-2.31[-6.2,1.58]
Strychar 2009	15	4.7 (11)	15	-2.6 (8.9)		0.84%	7.3[0.14,14.46]
WHI 2006	1133	-2.6 (9.4)	1699	-2.3 (9.4)		34.09%	-0.3[-1.01,0.41]
WHT:FSMP 2003	1101	-1.1 (7.4)	648	-0.6 (7.7)		32.98%	-0.42[-1.16,0.32]
Total ***	**2527**		**2632**			**100%**	**-0.74[-1.4,-0.08]**

Heterogeneity: Tau^2=0.21; Chi^2=10.43, df=8(P=0.24); I^2=23.32%

Test for overall effect: Z=2.2(P=0.03)



Favours reduced fat | Favours moderate fat

Comparison 2. Fat reduction versus usual fat diet, adult RCTs - subgrouping

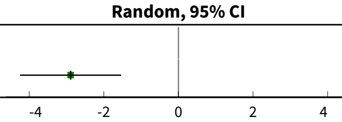
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Weight - subgrouped by duration of advice	30		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 6 to < 12 months	16	5305	Mean Difference (IV, Random, 95% CI)	-1.74 [-2.34, -1.13]
1.2 12 to < 24 months	18	51367	Mean Difference (IV, Random, 95% CI)	0.00 [-2.51, -1.48]
1.3 24 to < 60 months	10	49286	Mean Difference (IV, Random, 95% CI)	-1.18 [-1.65, -0.70]
1.4 60+ months	4	40838	Mean Difference (IV, Random, 95% CI)	-0.68 [-1.66, 0.29]
2 Weight, subgrouped by control group fat intake	29	54335	Mean Difference (IV, Fixed, 95% CI)	-1.01 [-1.15, -0.86]
2.1 > 35%E from fat	13	45103	Mean Difference (IV, Fixed, 95% CI)	-0.91 [-1.07, -0.75]
2.2 > 30% to 35%E from fat	11	7123	Mean Difference (IV, Fixed, 95% CI)	-0.84 [-1.21, -0.48]
2.3 > 25% to 30%E from fat	5	2109	Mean Difference (IV, Fixed, 95% CI)	-2.97 [-3.60, -2.34]
3 Weight, subgrouped by sex	30		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Studies of women only	17	50154	Mean Difference (IV, Random, 95% CI)	-1.42 [-1.93, -0.91]
3.2 Studies of men only	6	1719	Mean Difference (IV, Random, 95% CI)	-2.74 [-4.32, -1.17]
3.3 Studies of men and women	7	2492	Mean Difference (IV, Random, 95% CI)	-1.09 [0.00, -0.18]
4 Weight, subgrouped by year of first publication of results	30		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 1960s	3	1450	Mean Difference (IV, Random, 95% CI)	-4.10 [-8.06, -0.14]
4.2 1970s	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 1980s	3	288	Mean Difference (IV, Random, 95% CI)	-0.91 [-1.80, -0.01]
4.4 1990s	16	5941	Mean Difference (IV, Random, 95% CI)	-1.94 [-2.62, -1.25]
4.5 2000s	8	46686	Mean Difference (IV, Random, 95% CI)	-0.94 [-1.59, -0.29]
4.6 2010s	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Weight, subgrouped by difference in %E from fat be-	32	57583	Mean Difference (IV, Random, 95% CI)	-1.54 [-1.97, -1.12]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
tween control and reduced fat groups				
5.1 Up to 5%E from fat	8	4567	Mean Difference (IV, Random, 95% CI)	-0.16 [-0.91, 0.59]
5.2 5% to < 10%E from fat	14	44356	Mean Difference (IV, Random, 95% CI)	-2.11 [-2.87, -1.35]
5.3 10% to < 15%E from fat	5	8311	Mean Difference (IV, Random, 95% CI)	-1.34 [-1.70, -0.98]
5.4 15+%E from fat	4	319	Mean Difference (IV, Random, 95% CI)	-3.89 [-8.76, 0.99]
5.5 Unknown difference in %E from fat	1	30	Mean Difference (IV, Random, 95% CI)	-2.43 [-4.20, -0.66]
6 Weight - subgrouped by advice vs provided	29		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 Dietary advice	25	52594	Mean Difference (IV, Random, 95% CI)	-1.55 [-2.00, -1.10]
6.2 Advice plus supplements	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Diet provided	4	1741	Mean Difference (IV, Random, 95% CI)	-0.72 [-1.34, -0.10]
7 Weight subgrouped by fat goals	29		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 30%E from fat goal	5	1628	Mean Difference (IV, Random, 95% CI)	-0.96 [-1.66, -0.26]
7.2 25% to < 30%E from fat goal	6	509	Mean Difference (IV, Random, 95% CI)	-2.45 [-4.27, -0.64]
7.3 20% to < 25%E from fat goal	6	43878	Mean Difference (IV, Random, 95% CI)	-0.90 [-1.24, -0.55]
7.4 15% to < 20%E from fat goal	8	7860	Mean Difference (IV, Random, 95% CI)	-1.28 [-2.19, -0.37]
7.5 10% to < 15%E from fat goal	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.6 No specific goal stated	4	460	Mean Difference (IV, Random, 95% CI)	-2.49 [-5.03, 0.05]
8 Weight, kg subgrouped of above below 30%E from fat	24		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 Int achieved > 30%E from fat	8	1767	Mean Difference (IV, Random, 95% CI)	-0.83 [-1.28, -0.37]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.2 Int achieved 30%E from fat or less	16	50099	Mean Difference (IV, Random, 95% CI)	-1.11 [-1.62, -0.60]
9 Weight, kg subgrouped by BMI baseline	28	53147	Mean Difference (IV, Random, 95% CI)	-1.54 [-1.97, -1.12]
9.1 BMI at baseline < 25	10	1781	Mean Difference (IV, Random, 95% CI)	-0.96 [-1.69, -0.22]
9.2 BMI at baseline ≥ 25 to 29.9	17	51297	Mean Difference (IV, Random, 95% CI)	-1.83 [-2.38, -1.28]
9.3 BMI at baseline ≥ 30	1	69	Mean Difference (IV, Random, 95% CI)	-1.80 [-3.48, -0.12]
10 Weight, kg subgrouped by healthy vs patient	30	53647	Mean Difference (IV, Random, 95% CI)	-1.54 [-1.97, -1.12]
10.1 Healthy - not recruited on the basis of risk factors or disease	6	45032	Mean Difference (IV, Random, 95% CI)	-0.98 [-1.56, -0.41]
10.2 Recruited on basis of risk factors, e.g. lipids, BMI, hormonal levels, breast CA risk	14	2166	Mean Difference (IV, Random, 95% CI)	-2.18 [-3.17, -1.20]
10.3 People with disease such as DM, MI, cancer, polyps	10	6449	Mean Difference (IV, Random, 95% CI)	-1.20 [-1.85, -0.56]
11 Weight, kg subgrouped by energy reduction in int group	26	53459	Mean Difference (IV, Random, 95% CI)	-1.52 [-1.97, -1.07]
11.1 E intake same or greater in low fat group	6	3352	Mean Difference (IV, Random, 95% CI)	-0.51 [-1.49, 0.47]
11.2 E intake 1 to 100 kcal/d less in low fat group	5	2398	Mean Difference (IV, Random, 95% CI)	-1.49 [-2.92, -0.06]
11.3 E intake 101 to 200 kcal/d less in low fat group	6	43755	Mean Difference (IV, Random, 95% CI)	-1.14 [-2.24, -0.04]
11.4 E intake > 201 kcal/d less in low fat group	9	3954	Mean Difference (IV, Random, 95% CI)	-2.23 [-2.97, -1.49]

Analysis 2.1. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 1 Weight - subgrouped by duration of advice.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.1.1 6 to < 12 months							
Auckland reduced fat 1999	66	-3 (4.4)	70	-0.1 (3.6)		9.41%	-2.89[-4.24,-1.54]

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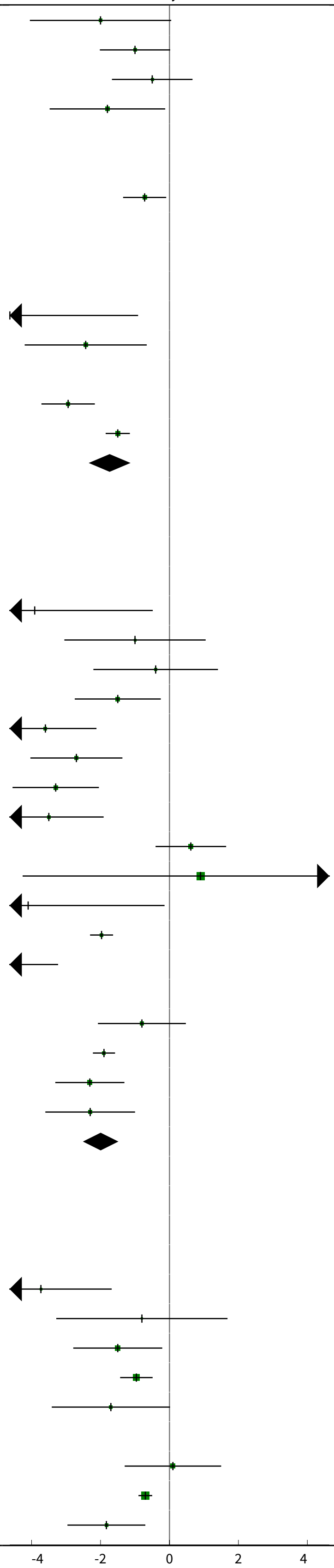
Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
BDIT Pilot Studies 1996	100	58 (7)	106	60 (8)		5.86%	-2[-4.05,0.05]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		11.8%	-1[-2.02,0.02]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		10.68%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		7.53%	-1.8[-3.48,-0.12]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		14.9%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	689	-1.9 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Simon Low Fat Breast CA	67	63.8 (10.4)	76	68.5 (12.3)		2.31%	-4.63[-8.35,-0.91]
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		7.06%	-2.43[-4.2,-0.66]
Veterans Dermatology 1994	57	-3.5 (0)	58	1.5 (0)			Not estimable
WHT Feasibility 1990	179	-3.2 (3.7)	113	-0.2 (3)		13.74%	-2.94[-3.71,-2.17]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		16.71%	-1.5[-1.85,-1.15]
Subtotal ***	**2705**		**2600**			**100%**	**-1.74[-2.34,-1.13]**
Heterogeneity: Tau²=0.54; Chi²=31.06, df=9(P=0); I²=71.02%							
Test for overall effect: Z=5.61(P<0.0001)							
2.1.2 12 to < 24 months							
Auckland reduced fat 1999	66	-3.3 (5.5)	70	0.6 (13.5)		1.9%	-3.91[-7.33,-0.49]
BDIT Pilot Studies 1996	100	59 (7)	106	60 (8)		4.15%	-1[-3.05,1.05]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		4.86%	-0.4[-2.21,1.41]
Canadian DBCP 1997	385	61.4 (8.6)	397	62.9 (9.2)		7.07%	-1.5[-2.75,-0.25]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		6.04%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		6.68%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		7.05%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		5.62%	-3.5[-5.09,-1.91]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		8.19%	0.62[-0.4,1.64]
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.92%	0.9[-4.26,6.06]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		1.49%	-4.1[-8.06,-0.14]
Polyp Prevention 1996	975	-2 (4.1)	989	0 (3.5)		11.52%	-1.97[-2.3,-1.64]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.89%	-8.5[-13.77,-3.23]
Veterans Dermatology 1994	57	-2 (0)	58	1 (0)			Not estimable
WHEL 2007	1463	73 (17.2)	1484	73.8 (18.1)		6.95%	-0.8[-2.08,0.48]
WHI 2006	17026	74 (16.5)	24977	75.9 (16.5)		11.56%	-1.9[-2.22,-1.58]
WHT Feasibility 1990	177	-2.9 (4.8)	110	-0.6 (3.8)		8.3%	-2.31[-3.31,-1.31]
WINS 1993	854	-2.3 (15.1)	1310	0 (15.1)		6.82%	-2.3[-3.6,-1]
Subtotal ***	**21477**		**29890**			**100%**	**-2[-2.51,-1.48]**
Heterogeneity: Tau²=0.57; Chi²=55.86, df=16(P<0.0001); I²=71.35%							
Test for overall effect: Z=7.6(P<0.0001)							
2.1.3 24 to < 60 months							
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		4.51%	-3.73[-5.78,-1.68]
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		3.25%	-0.8[-3.28,1.68]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		9.22%	-1.5[-2.79,-0.21]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		22.47%	-0.96[-1.43,-0.49]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		6.06%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	57	-2 (0)	58	0.5 (0)			Not estimable
WHEL 2007	1355	74.2 (18.8)	1363	74.1 (18.5)		8.23%	0.1[-1.3,1.5]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		27.45%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		10.96%	-1.83[-2.96,-0.7]



Study or subgroup	Reduced fat		Usual fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)		7.85%	-1.8[-3.25,-0.35]
Subtotal ***	**20084**		**29202**			**100%**	**-1.18[-1.65,-0.7]**
Heterogeneity: Tau²=0.2; Chi²=18.01, df=8(P=0.02); I²=55.58%							
Test for overall effect: Z=4.86(P<0.0001)							
2.1.4 60+ months							
Auckland reduced fat 1999	51	1.1 (4.6)	52	1.3 (4.9)		17.48%	-0.2[-2.03,1.63]
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		22.12%	0.4[-1.08,1.88]
WHI 2006	14409	75.6 (16.8)	22321	76.2 (16.6)		42.53%	-0.6[-0.95,-0.25]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)		17.86%	-2.7[-4.5,-0.9]
Subtotal ***	**16154**		**24684**			**100%**	**-0.68[-1.66,0.29]**
Heterogeneity: Tau²=0.55; Chi²=7.17, df=3(P=0.07); I²=58.17%							
Test for overall effect: Z=1.37(P=0.17)							
Test for subgroup differences: Chi²=8.59, df=1 (P=0.04), I²=65.06%							
				Favours reduced fat	-4 -2 0 2 4	Favours moderate fat	

Analysis 2.2. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 2 Weight, subgrouped by control group fat intake.

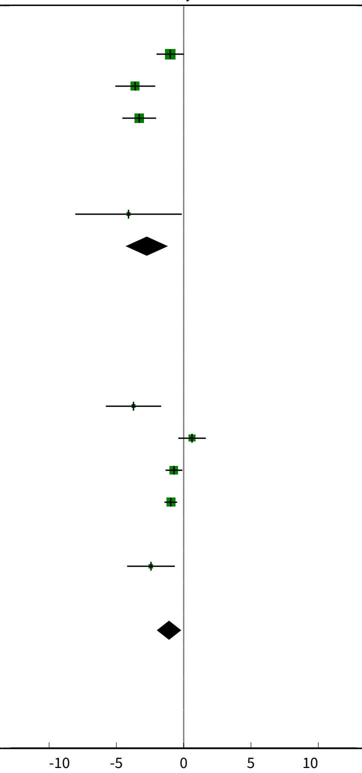
Study or subgroup	Reduced fat		Usual fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
2.2.1 > 35%E from fat							
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		0.33%	-0.8[-3.28,1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		1.97%	-1[-2.02,0.02]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		1.5%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		0.73%	-1.8[-3.48,-0.12]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		5.23%	-0.72[-1.34,-0.1]
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		0.13%	-4.1[-8.06,-0.14]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Veterans Dermatology 1994	57	-2 (0)	58	0.5 (0)			Not estimable
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		51.49%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		1.6%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		16.6%	-1.5[-1.85,-1.15]
Subtotal ***	**18409**		**26694**			**79.57%**	**-0.91[-1.07,-0.75]**
Heterogeneity: Tau²=0; Chi²=22.12, df=8(P=0); I²=63.84%							
Test for overall effect: Z=11.14(P<0.0001)							
2.2.2 > 30% to 35%E from fat							
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		0.48%	-3.73[-5.78,-1.68]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		0.63%	-0.4[-2.21,1.41]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		1.23%	-1.5[-2.79,-0.21]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		1.95%	0.62[-0.4,1.64]
NDHS Open 1st L&M 1968	332	-2.4 (0)	689	-1.9 (0)			Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.08%	0.9[-4.26,6.06]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		9.2%	-0.96[-1.43,-0.49]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.07%	-8.5[-13.77,-3.23]
				Favours reduced fat	-10 -5 0 5 10	Favours moderate fat	

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		0.69%	-1.7[-3.41,0.01]
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		0.93%	0.4[-1.08,1.88]
Subtotal ***	**3339**		**3784**			**15.27%**	**-0.84[-1.21,-0.48]**
Heterogeneity: Tau²=0; Chi²=29.11, df=8(P=0); I²=72.52%							
Test for overall effect: Z=4.52(P<0.0001)							
2.2.3 > 25% to 30%E from fat							
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		0.93%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		1.15%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		1.3%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		0.81%	-3.5[-5.09,-1.91]
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)		0.98%	-1.8[-3.25,-0.35]
Subtotal ***	**884**		**1225**			**5.16%**	**-2.97[-3.6,-2.34]**
Heterogeneity: Tau²=0; Chi²=4.06, df=4(P=0.4); I²=1.38%							
Test for overall effect: Z=9.25(P<0.0001)							
Total ***	**22632**		**31703**			**100%**	**-1.01[-1.15,-0.86]**
Heterogeneity: Tau²=0; Chi²=94.79, df=22(P<0.0001); I²=76.79%							
Test for overall effect: Z=13.8(P<0.0001)							
Test for subgroup differences: Chi²=39.5, df=1 (P<0.0001), I²=94.94%							
			Favours reduced fat		-10 -5 0 5 10	Favours moderate fat	

Analysis 2.3. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 3 Weight, subgrouped by sex.

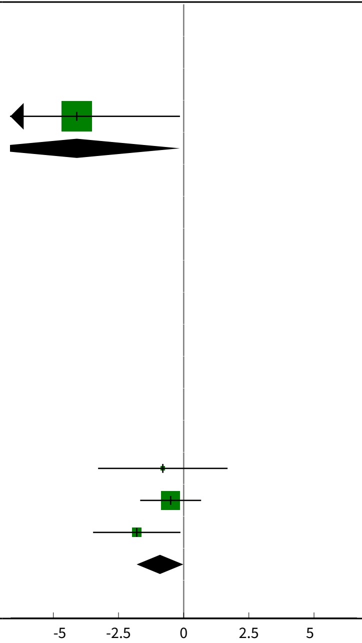
Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.3.1 Studies of women only							
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		3.27%	-0.8[-3.28,1.68]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		5.15%	-0.4[-2.21,1.41]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		7.53%	-1.5[-2.79,-0.21]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		8.25%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		5.66%	-1.8[-3.48,-0.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		7.29%	-2.7[-4.03,-1.37]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		6.03%	-3.5[-5.09,-1.91]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.92%	0.9[-4.26,6.06]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.88%	-8.5[-13.77,-3.23]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		5.5%	-1.7[-3.41,0.01]
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		6.53%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		14.22%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		8.49%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		13.6%	-1.5[-1.85,-1.15]
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)		6.7%	-1.8[-3.25,-0.35]
Subtotal ***	**20734**		**29420**			**100%**	**-1.42[-1.93,-0.91]**
Heterogeneity: Tau²=0.47; Chi²=50.41, df=14(P<0.0001); I²=72.23%							
Test for overall effect: Z=5.47(P<0.0001)							
			Favours reduced fat		-10 -5 0 5 10	Favours moderate fat	

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Weight	Mean Difference Random, 95% CI
2.3.2 Studies of men only						
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)	31.68%	-1[-2.02,0.02]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)	27.6%	-3.6[-5.08,-2.12]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)	29.67%	-3.3[-4.55,-2.05]
NDHS Open 1st L&M 1968	332	-2.4 (0)	689	-1.9 (0)		Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)		Not estimable
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)	11.04%	-4.1[-8.06,-0.14]
Subtotal ***	**659**		**1060**		**100%**	**-2.74[-4.32,-1.17]**
Heterogeneity: Tau²=1.77; Chi²=12.43, df=3(P=0.01); I²=75.86%						
Test for overall effect: Z=3.41(P=0)						
2.3.3 Studies of men and women						
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)	11.73%	-3.73[-5.78,-1.68]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)	21.39%	0.62[-0.4,1.64]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)	25.79%	-0.72[-1.34,-0.1]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)	27.22%	-0.96[-1.43,-0.49]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)		Not estimable
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)	13.87%	-2.43[-4.2,-0.66]
Veterans Dermatology 1994	57	-2 (0)	58	0.5 (0)		Not estimable
Subtotal ***	**1254**		**1238**		**100%**	**-1.09[-2,-0.18]**
Heterogeneity: Tau²=0.73; Chi²=18.91, df=4(P=0); I²=78.85%						
Test for overall effect: Z=2.35(P=0.02)						
Test for subgroup differences: Chi²=3.21, df=1 (P=0.2), I²=37.63%						



Analysis 2.4. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 4 Weight, subgrouped by year of first publication of results.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Weight	Mean Difference Random, 95% CI
2.4.1 1960s						
NDHS Open 1st L&M 1968	332	-2.4 (0)	689	-1.9 (0)		Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)		Not estimable
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)	100%	-4.1[-8.06,-0.14]
Subtotal ***	**523**		**927**		**100%**	**-4.1[-8.06,-0.14]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.03(P=0.04)						
2.4.2 1970s						
Subtotal ***	**0**		**0**			**Not estimable**
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.4.3 1980s						
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)	12.97%	-0.8[-3.28,1.68]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)	58.55%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)	28.48%	-1.8[-3.48,-0.12]
Subtotal ***	**146**		**142**		**100%**	**-0.91[-1.8,-0.01]**
Heterogeneity: Tau²=0; Chi²=1.56, df=2(P=0.46); I²=0%						



Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Test for overall effect: Z=1.99(P=0.05)							
2.4.4 1990s							
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		5.32%	-3.73[-5.78,-1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		8.35%	-1[-2.02,0.02]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		7.51%	-1.5[-2.79,-0.21]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		6.92%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		7.37%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		7.63%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		6.59%	-3.5[-5.09,-1.91]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		8.34%	0.62[-0.4,1.64]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		9.45%	-0.72[-1.34,-0.1]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		9.79%	-0.96[-1.43,-0.49]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		1.44%	-8.5[-13.77,-3.23]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		6.23%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	57	-2 (0)	58	0.5 (0)			Not estimable
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		8.01%	-1.83[-2.96,-0.7]
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)		7.03%	-1.8[-3.25,-0.35]
Subtotal ***	**2806**		**3135**			**100%**	**-1.94[-2.62,-1.25]**
Heterogeneity: Tau²=1.18; Chi²=63.84, df=13(P<0.0001); I²=79.64%							
Test for overall effect: Z=5.56(P<0.0001)							
2.4.5 2000s							
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		9.48%	-0.4[-2.21,1.41]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		1.52%	0.9[-4.26,6.06]
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		9.77%	-2.43[-4.2,-0.66]
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		12.47%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		34.48%	-0.7[-0.9,-0.5]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		32.28%	-1.5[-1.85,-1.15]
Subtotal ***	**19172**		**27514**			**100%**	**-0.94[-1.59,-0.29]**
Heterogeneity: Tau²=0.31; Chi²=21.66, df=5(P=0); I²=76.92%							
Test for overall effect: Z=2.83(P=0)							
2.4.6 2010s							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Chi²=7.18, df=1 (P=0.07), I²=58.2%							

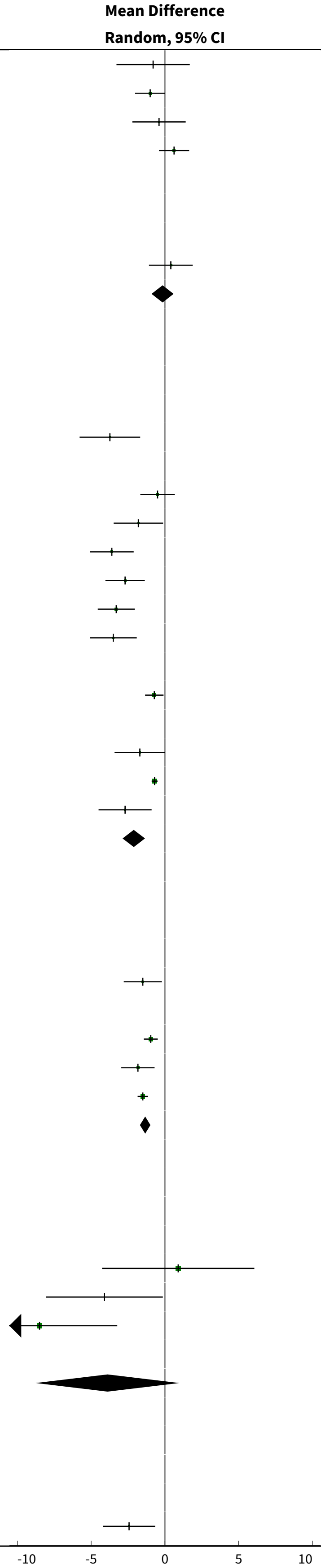
Favours reduced fat -5 -2.5 0 2.5 5 Favours moderate fat

Analysis 2.5. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 5 Weight, subgrouped by difference in %E from fat between control and reduced fat groups.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.5.1 Up to 5%E from fat							

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Weight	Mean Difference Random, 95% CI
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)	2.13%	-0.8[-3.28,1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)	5.46%	-1[-2.02,0.02]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)	3.25%	-0.4[-2.21,1.41]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)	5.45%	0.62[-0.4,1.64]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)		Not estimable
NDHS Open 1st L&M 1968	332	-2.4 (0)	689	-1.9 (0)		Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)		Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)	4.03%	0.4[-1.08,1.88]
Subtotal ***	**2080**		**2487**		**20.32%**	**-0.16[-0.91,0.59]**
Heterogeneity: Tau²=0.21; Chi²=5.71, df=4(P=0.22); I²=29.92%						
Test for overall effect: Z=0.42(P=0.68)						
2.5.2 5% to < 10%E from fat						
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)	2.77%	-3.73[-5.78,-1.68]
beFIT 1997	217	-2.7 (0)	192	0 (0)		Not estimable
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)	4.96%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)	3.55%	-1.8[-3.48,-0.12]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)	4.03%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)	4.45%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)	4.7%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)	3.75%	-3.5[-5.09,-1.91]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)		Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)	6.81%	-0.72[-1.34,-0.1]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)		Not estimable
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)	3.46%	-1.7[-3.41,0.01]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)	7.85%	-0.7[-0.9,-0.5]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)	3.27%	-2.7[-4.5,-0.9]
Subtotal ***	**17492**		**26864**		**49.61%**	**-2.11[-2.87,-1.35]**
Heterogeneity: Tau²=1.17; Chi²=61.75, df=10(P<0.0001); I²=83.81%						
Test for overall effect: Z=5.45(P<0.0001)						
2.5.3 10% to < 15%E from fat						
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)	4.58%	-1.5[-2.79,-0.21]
Mastopathy Diet 1988	1491	-2.1 (0)	1676	0 (0)		Not estimable
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)	7.27%	-0.96[-1.43,-0.49]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)	5.09%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)	7.58%	-1.5[-1.85,-1.15]
Subtotal ***	**4306**		**4005**		**24.52%**	**-1.34[-1.7,-0.98]**
Heterogeneity: Tau²=0.04; Chi²=4.08, df=3(P=0.25); I²=26.43%						
Test for overall effect: Z=7.36(P<0.0001)						
2.5.4 15+%E from fat						
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)	0.62%	0.9[-4.26,6.06]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)	1%	-4.1[-8.06,-0.14]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)	0.6%	-8.5[-13.77,-3.23]
Veterans Dermatology 1994	57	-2 (0)	58	0.5 (0)		Not estimable
Subtotal ***	**150**		**169**		**2.22%**	**-3.89[-8.76,0.99]**
Heterogeneity: Tau²=12.6; Chi²=6.26, df=2(P=0.04); I²=68.06%						
Test for overall effect: Z=1.56(P=0.12)						
2.5.5 Unknown difference in %E from fat						
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)	3.33%	-2.43[-4.2,-0.66]



Favours reduced fat | Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Subtotal ***	**15**		**15**			**3.33%**	**-2.43[-4.2,-0.66]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.69(P=0.01)							
Total ***	**24043**		**33540**			**100%**	**-1.54[-1.97,-1.12]**
Heterogeneity: Tau²=0.58; Chi²=99.49, df=23(P<0.0001); I²=76.88%							
Test for overall effect: Z=7.14(P<0.0001)							
Test for subgroup differences: Chi²=16.03, df=1 (P=0), I²=75.04%							

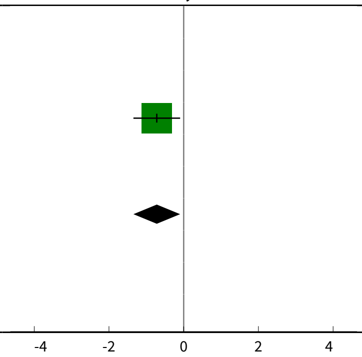
Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 2.6. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 6 Weight - subgrouped by advice vs provided.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.6.1 Dietary advice							
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		3.11%	-3.73[-5.78,-1.68]
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		2.4%	-0.8[-3.28,1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		6%	-1[-2.02,0.02]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		3.63%	-0.4[-2.21,1.41]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		5.07%	-1.5[-2.79,-0.21]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		5.47%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		3.95%	-1.8[-3.48,-0.12]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		4.48%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		4.93%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		5.19%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		4.18%	-3.5[-5.09,-1.91]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		5.98%	0.62[-0.4,1.64]
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.71%	0.9[-4.26,6.06]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		1.14%	-4.1[-8.06,-0.14]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		7.89%	-0.96[-1.43,-0.49]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.68%	-8.5[-13.77,-3.23]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		3.85%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	57	-2 (0)	58	0.5 (0)			Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		4.48%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		8.48%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		5.61%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		8.2%	-1.5[-1.85,-1.15]
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)		4.58%	-1.8[-3.25,-0.35]
Subtotal ***	**21953**		**30641**			**100%**	**-1.55[-2,-1.1]**
Heterogeneity: Tau²=0.62; Chi²=93.93, df=21(P<0.0001); I²=77.64%							
Test for overall effect: Z=6.7(P<0.0001)							
2.6.2 Advice plus supplements							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

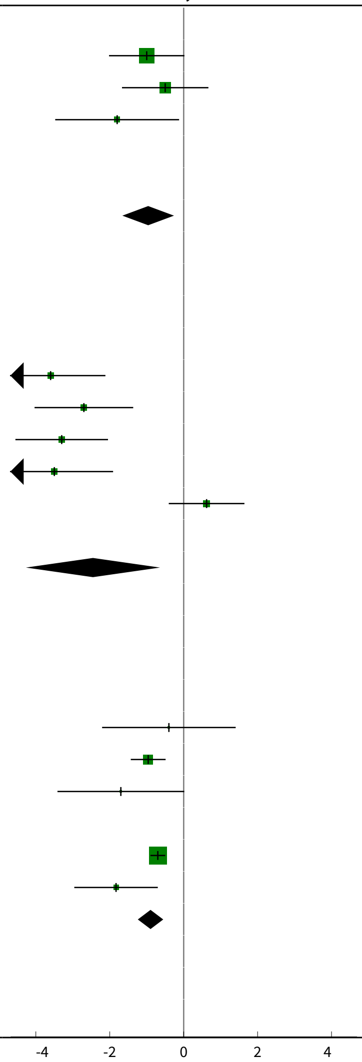
Favours reduced fat -4 -2 0 2 4 Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.6.3 Diet provided							
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		100%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	689	-1.9 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Subtotal ***	**679**		**1062**			**100%**	**-0.72[-1.34,-0.1]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.26(P=0.02)							
Test for subgroup differences: Chi²=4.42, df=1 (P=0.04), I²=77.37%							



Analysis 2.7. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 7 Weight subgrouped by fat goals.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.7.1 30%E from fat goal							
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		46.93%	-1[-2.02,0.02]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		35.7%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		17.37%	-1.8[-3.48,-0.12]
NDHS Open 1st L&M 1968	332	-2.4 (0)	689	-1.9 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Subtotal ***	**620**		**1008**			**100%**	**-0.96[-1.66,-0.26]**
Heterogeneity: Tau²=0; Chi²=1.57, df=2(P=0.46); I²=0%							
Test for overall effect: Z=2.69(P=0.01)							
2.7.2 25% to < 30%E from fat goal							
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		19.54%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		20.03%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		20.3%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		19.16%	-3.5[-5.09,-1.91]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		20.97%	0.62[-0.4,1.64]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Subtotal ***	**260**		**249**			**100%**	**-2.45[-4.27,-0.64]**
Heterogeneity: Tau²=3.81; Chi²=38.25, df=4(P<0.0001); I²=89.54%							
Test for overall effect: Z=2.65(P=0.01)							
2.7.3 20% to < 25%E from fat goal							
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		3.44%	-0.4[-2.21,1.41]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		29.74%	-0.96[-1.43,-0.49]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		3.8%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	57	-2 (0)	58	0.5 (0)			Not estimable
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		54.88%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		8.15%	-1.83[-2.96,-0.7]
Subtotal ***	**17567**		**26311**			**100%**	**-0.9[-1.24,-0.55]**
Heterogeneity: Tau²=0.05; Chi²=5.77, df=4(P=0.22); I²=30.67%							
Test for overall effect: Z=5.11(P<0.0001)							



Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual fat N	Usual fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.7.4 15% to < 20%E from fat goal							
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		9.49%	-0.8[-3.28,1.68]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		19.47%	-1.5[-2.79,-0.21]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		2.85%	0.9[-4.26,6.06]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		2.75%	-8.5[-13.77,-3.23]
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		17.32%	0.4[-1.08,1.88]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		30.43%	-1.5[-1.85,-1.15]
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)		17.7%	-1.8[-3.25,-0.35]
Subtotal ***	**3957**		**3903**			**100%**	**-1.28[-2.19,-0.37]**
Heterogeneity: Tau²=0.68; Chi²=14.21, df=6(P=0.03); I²=57.79%							
Test for overall effect: Z=2.75(P=0.01)							
2.7.5 10% to < 15%E from fat goal							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.7.6 No specific goal stated							
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		34.74%	-3.73[-5.78,-1.68]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		43.75%	-0.72[-1.34,-0.1]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		21.51%	-4.1[-8.06,-0.14]
Subtotal ***	**228**		**232**			**100%**	**-2.49[-5.03,0.05]**
Heterogeneity: Tau²=3.74; Chi²=9.9, df=2(P=0.01); I²=79.79%							
Test for overall effect: Z=1.92(P=0.05)							
Test for subgroup differences: Chi²=4.52, df=1 (P=0.34), I²=11.43%							

Favours reduced fat -4 -2 0 2 4 Favours moderate fat

Analysis 2.8. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 8 Weight, kg subgrouped of above below 30%E from fat.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.8.1 Int achieved > 30%E from fat							
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		3.4%	-0.8[-3.28,1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		20.16%	-1[-2.02,0.02]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		15.34%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		7.46%	-1.8[-3.48,-0.12]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		53.65%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Subtotal ***	**864**		**903**			**100%**	**-0.83[-1.28,-0.37]**
Heterogeneity: Tau²=0; Chi²=1.82, df=4(P=0.77); I²=0%							
Test for overall effect: Z=3.54(P=0)							
2.8.2 Int achieved 30%E from fat or less							

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		4.51%	-3.73[-5.78,-1.68]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		5.4%	-0.4[-2.21,1.41]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		8.09%	-1.5[-2.79,-0.21]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		10.02%	0.62[-0.4,1.64]
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.92%	0.9[-4.26,6.06]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		1.51%	-4.1[-8.06,-0.14]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		14.72%	-0.96[-1.43,-0.49]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.89%	-8.5[-13.77,-3.23]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		5.79%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)			Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		6.94%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		16.41%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		9.21%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		15.59%	-1.5[-1.85,-1.15]
Subtotal ***	**20865**		**29234**			**100%**	**-1.11[-1.62,-0.6]**
Heterogeneity: Tau²=0.4; Chi²=49.41, df=12(P<0.0001); I²=75.71%							
Test for overall effect: Z=4.26(P<0.0001)							
Test for subgroup differences: Chi²=0.65, df=1 (P=0.42), I²=0%							

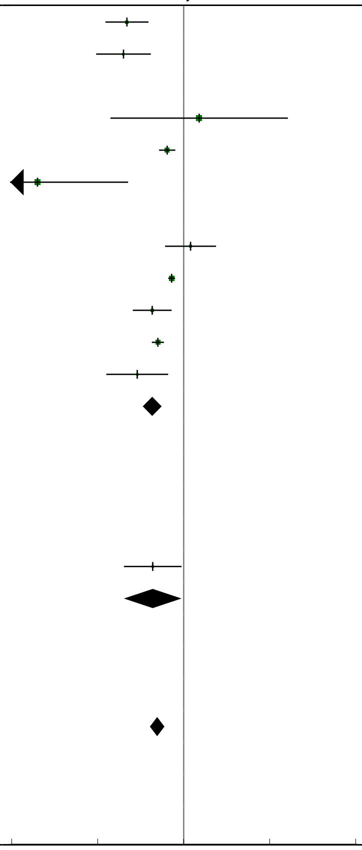
Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 2.9. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 9 Weight, kg subgrouped by BMI baseline.

Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
2.9.1 BMI at baseline < 25							
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		2.13%	-0.8[-3.28,1.68]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		4.58%	-1.5[-2.79,-0.21]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		4.96%	-0.5[-1.67,0.67]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		5.45%	0.62[-0.4,1.64]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		6.81%	-0.72[-1.34,-0.1]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		1%	-4.1[-8.06,-0.14]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		3.33%	-2.43[-4.2,-0.66]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		3.46%	-1.7[-3.41,0.01]
Subtotal ***	**862**		**919**			**31.71%**	**-0.96[-1.69,-0.22]**
Heterogeneity: Tau²=0.54; Chi²=15.75, df=7(P=0.03); I²=55.57%							
Test for overall effect: Z=2.55(P=0.01)							
2.9.2 BMI at baseline ≥ 25 to 29.9							
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		2.77%	-3.73[-5.78,-1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		5.46%	-1[-2.02,0.02]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		3.25%	-0.4[-2.21,1.41]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		4.03%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		4.45%	-2.7[-4.03,-1.37]

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

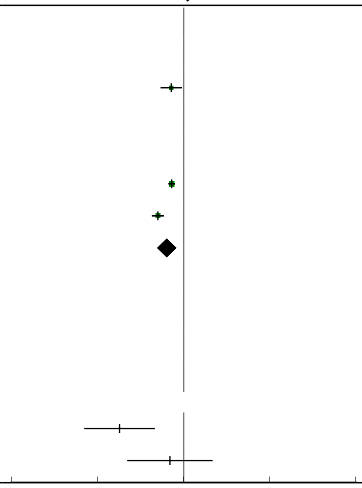
Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Weight	Mean Difference Random, 95% CI
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)	4.7%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)	3.75%	-3.5[-5.09,-1.91]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)		Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)	0.62%	0.9[-4.26,6.06]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)	7.27%	-0.96[-1.43,-0.49]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)	0.6%	-8.5[-13.77,-3.23]
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)		Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)	4.03%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)	7.85%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)	5.09%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)	7.58%	-1.5[-1.85,-1.15]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)	3.27%	-2.7[-4.5,-0.9]
Subtotal ***	**21190**		**30107**		**64.74%**	**-1.83[-2.38,-1.28]**
Heterogeneity: Tau^2=0.67; Chi^2=81.09, df=14(P<0.0001); I^2=82.73%						
Test for overall effect: Z=6.51(P<0.0001)						
2.9.3 BMI at baseline ≥ 30						
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)	3.55%	-1.8[-3.48,-0.12]
Subtotal ***	**34**		**35**		**3.55%**	**-1.8[-3.48,-0.12]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.11(P=0.04)						
Total ***	**22086**		**31061**		**100%**	**-1.54[-1.97,-1.12]**
Heterogeneity: Tau^2=0.58; Chi^2=99.49, df=23(P<0.0001); I^2=76.88%						
Test for overall effect: Z=7.14(P<0.0001)						
Test for subgroup differences: Chi^2=3.58, df=1 (P=0.17), I^2=44.14%						



Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 2.10. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 10 Weight, kg subgrouped by healthy vs patient.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Weight	Mean Difference Random, 95% CI
2.10.1 Healthy - not recruited on the basis of risk factors or disease						
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)		Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)	6.81%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)		Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)		Not estimable
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)	7.85%	-0.7[-0.9,-0.5]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)	7.58%	-1.5[-1.85,-1.15]
Subtotal ***	**18331**		**26701**		**22.24%**	**-0.98[-1.56,-0.41]**
Heterogeneity: Tau^2=0.22; Chi^2=15.38, df=2(P=0); I^2=87%						
Test for overall effect: Z=3.35(P=0)						
2.10.2 Recruited on basis of risk factors, e.g. lipids, BMI, hormonal levels, breast CA risk						
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)	2.77%	-3.73[-5.78,-1.68]
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)	2.13%	-0.8[-3.28,1.68]



Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		5.46%	-1[-2.02,0.02]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		4.58%	-1.5[-2.79,-0.21]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		4.03%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		4.45%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		4.7%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		3.75%	-3.5[-5.09,-1.91]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		5.45%	0.62[-0.4,1.64]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.62%	0.9[-4.26,6.06]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.6%	-8.5[-13.77,-3.23]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		5.09%	-1.83[-2.96,-0.7]
Subtotal * **	**1102**		**1064**			**43.64%**	**-2.18[-3.17,-1.2]**
Heterogeneity: Tau²=2.11; Chi²=52.62, df=11(P<0.0001); I²=79.1%							
Test for overall effect: Z=4.35(P<0.0001)							
2.10.3 People with disease such as DM, MI, cancer, polyps							
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		3.25%	-0.4[-2.21,1.41]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		4.96%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		3.55%	-1.8[-3.48,-0.12]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		1%	-4.1[-8.06,-0.14]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		7.27%	-0.96[-1.43,-0.49]
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		3.33%	-2.43[-4.2,-0.66]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		3.46%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)			Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		4.03%	0.4[-1.08,1.88]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)		3.27%	-2.7[-4.5,-0.9]
Subtotal * **	**2883**		**3566**			**34.13%**	**-1.2[-1.85,-0.56]**
Heterogeneity: Tau²=0.37; Chi²=14.33, df=8(P=0.07); I²=44.19%							
Test for overall effect: Z=3.67(P=0)							
Total * **	**22316**		**31331**			**100%**	**-1.54[-1.97,-1.12]**
Heterogeneity: Tau²=0.58; Chi²=99.49, df=23(P<0.0001); I²=76.88%							
Test for overall effect: Z=7.14(P<0.0001)							
Test for subgroup differences: Chi²=4.31, df=1 (P=0.12), I²=53.57%							

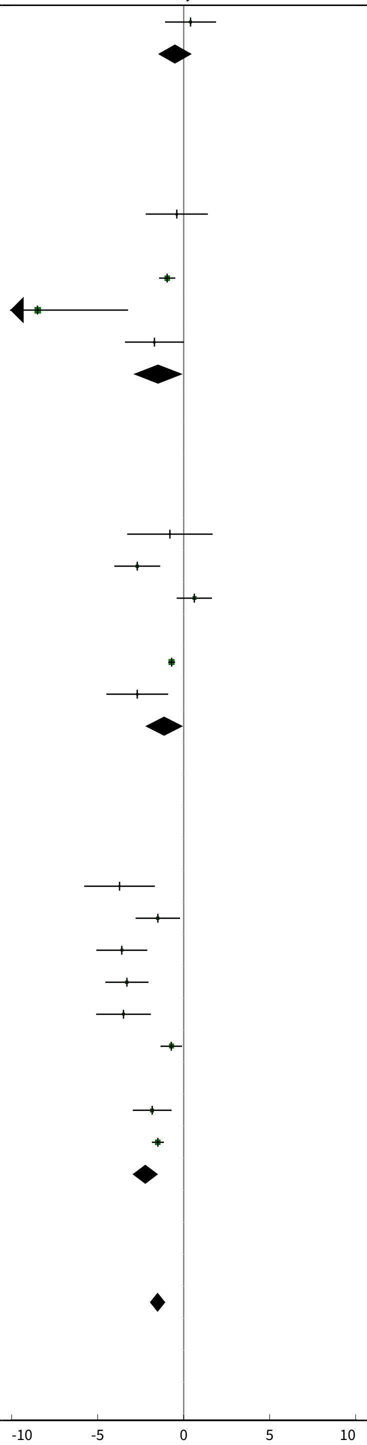
Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 2.11. Comparison 2 Fat reduction versus usual fat diet, adult RCTs - subgrouping, Outcome 11 Weight, kg subgrouped by energy reduction in int group.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.11.1 E intake same or greater in low fat group							
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		5.51%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		3.95%	-1.8[-3.48,-0.12]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.7%	0.9[-4.26,6.06]

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		4.49%	0.4[-1.08,1.88]
Subtotal ***	**1655**		**1697**			**14.65%**	**-0.51[-1.49,0.47]**
Heterogeneity: Tau²=0.26; Chi²=4.01, df=3(P=0.26); I²=25.17%							
Test for overall effect: Z=1.02(P=0.31)							
2.11.2 E intake 1 to 100 kcal/d less in low fat group							
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		3.63%	-0.4[-2.21,1.41]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		8%	-0.96[-1.43,-0.49]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.67%	-8.5[-13.77,-3.23]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		3.85%	-1.7[-3.41,0.01]
Subtotal ***	**1169**		**1229**			**16.16%**	**-1.49[-2.92,-0.06]**
Heterogeneity: Tau²=1.24; Chi²=8.86, df=3(P=0.03); I²=66.14%							
Test for overall effect: Z=2.04(P=0.04)							
2.11.3 E intake 101 to 200 kcal/d less in low fat group							
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		2.39%	-0.8[-3.28,1.68]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		4.95%	-2.7[-4.03,-1.37]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		6.03%	0.62[-0.4,1.64]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)			Not estimable
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		8.62%	-0.7[-0.9,-0.5]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)		3.65%	-2.7[-4.5,-0.9]
Subtotal ***	**17181**		**26574**			**25.64%**	**-1.14[-2.24,-0.04]**
Heterogeneity: Tau²=1.08; Chi²=19.74, df=4(P=0); I²=79.74%							
Test for overall effect: Z=2.03(P=0.04)							
2.11.4 E intake > 201 kcal/d less in low fat group							
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		3.1%	-3.73[-5.78,-1.68]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		5.09%	-1.5[-2.79,-0.21]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		4.49%	-3.6[-5.08,-2.12]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		5.22%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		4.18%	-3.5[-5.09,-1.91]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		7.5%	-0.72[-1.34,-0.1]
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)			Not estimable
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		5.65%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		8.33%	-1.5[-1.85,-1.15]
Subtotal ***	**2218**		**1736**			**43.56%**	**-2.23[-2.97,-1.49]**
Heterogeneity: Tau²=0.77; Chi²=31.77, df=7(P<0.0001); I²=77.97%							
Test for overall effect: Z=5.89(P<0.0001)							
Total ***	**22223**		**31236**			**100%**	**-1.52[-1.97,-1.07]**
Heterogeneity: Tau²=0.6; Chi²=94.69, df=20(P<0.0001); I²=78.88%							
Test for overall effect: Z=6.61(P<0.0001)							
Test for subgroup differences: Chi²=8.07, df=1 (P=0.04), I²=62.84%							



Favours reduced fat | Favours moderate fat

Comparison 3. Fat reduction versus usual fat diet, adult RCTs - sensitivity analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Weight, kg - removing studies with more attention to low fat arms	8	1537	Mean Difference (IV, Random, 95% CI)	-1.25 [-2.09, -0.41]
2 Weight, kg - removing studies with dietary interventions other than fat	22	5516	Mean Difference (IV, Random, 95% CI)	-1.92 [-2.57, -1.26]
3 Weight, kg - fixed-effect analysis	30	54005	Mean Difference (IV, Fixed, 95% CI)	-1.02 [-1.16, -0.87]
4 Weight, kg - removing WHI	29	12294	Mean Difference (IV, Random, 95% CI)	-1.64 [-2.12, -1.16]
5 Weight, kg - removing studies without good allocation concealment	11	49617	Mean Difference (IV, Random, 95% CI)	-0.95 [-1.40, -0.51]

Analysis 3.1. Comparison 3 Fat reduction versus usual fat diet, adult RCTs - sensitivity analyses, Outcome 1 Weight, kg - removing studies with more attention to low fat arms.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		25.18%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		16.64%	-1.8[-3.48,-0.12]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		38.59%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		4.14%	-4.1[-8.06,-0.14]
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		15.45%	-2.43[-4.2,-0.66]
Total * **	**752**		**785**			**100%**	**-1.25[-2.09,-0.41]**
Heterogeneity: Tau²=0.38; Chi²=7.19, df=4(P=0.13); I²=44.39%							
Test for overall effect: Z=2.91(P=0)							

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 3.2. Comparison 3 Fat reduction versus usual fat diet, adult RCTs - sensitivity analyses, Outcome 2 Weight, kg - removing studies with dietary interventions other than fat.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		4.57%	-3.73[-5.78,-1.68]
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		3.78%	-0.8[-3.28,1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		6.94%	-1[-2.02,0.02]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		6.29%	-1.5[-2.79,-0.21]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		6.59%	-0.5[-1.67,0.67]

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Weight	Mean Difference Random, 95% CI
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)	5.39%	-1.8[-3.48,-0.12]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)	5.84%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)	6.19%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)	6.39%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)	5.58%	-3.5[-5.09,-1.91]
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)	6.93%	0.62[-0.4,1.64]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)	7.76%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)		Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)		Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)	1.34%	0.9[-4.26,6.06]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)	2.05%	-4.1[-8.06,-0.14]
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)	1.3%	-8.5[-13.77,-3.23]
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)	5.17%	-2.43[-4.2,-0.66]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)	5.3%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)		Not estimable
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)	6.68%	-1.83[-2.96,-0.7]
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)	5.92%	-1.8[-3.25,-0.35]
Total ***	**2548**		**2968**		**100%**	**-1.92[-2.57,-1.26]**

Heterogeneity: $Tau^2=1.33$; $Chi^2=66.85$, df=18(P<0.0001); $I^2=73.08\%$

Test for overall effect: Z=5.76(P<0.0001)

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 3.3. Comparison 3 Fat reduction versus usual fat diet, adult RCTs - sensitivity analyses, Outcome 3 Weight, kg - fixed-effect analysis.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Weight	Mean Difference Fixed, 95% CI
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)	0.48%	-3.73[-5.78,-1.68]
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)	0.33%	-0.8[-3.28,1.68]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)	1.95%	-1[-2.02,0.02]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)	0.62%	-0.4[-2.21,1.41]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)	1.22%	-1.5[-2.79,-0.21]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)	1.49%	-0.5[-1.67,0.67]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)	0.72%	-1.8[-3.48,-0.12]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)	0.92%	-3.6[-5.08,-2.12]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)	1.14%	-2.7[-4.03,-1.37]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)	1.29%	-3.3[-4.55,-2.05]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)	0.8%	-3.5[-5.09,-1.91]
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)		Not estimable
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)	1.94%	0.62[-0.4,1.64]
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)		Not estimable
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)	5.2%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)		Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)		Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)	0.08%	0.9[-4.26,6.06]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)	0.13%	-4.1[-8.06,-0.14]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)	9.15%	-0.96[-1.43,-0.49]

Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.07%	-8.5[-13.77,-3.23]
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		0.65%	-2.43[-4.2,-0.66]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		0.69%	-1.7[-3.41,0.01]
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)			Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		0.92%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		51.16%	-0.7[-0.9,-0.5]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		1.59%	-1.83[-2.96,-0.7]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		16.49%	-1.5[-1.85,-1.15]
WINS 1993	698	-1.8 (15.1)	1044	0 (15.1)		0.97%	-1.8[-3.25,-0.35]
Total * **	**22628**		**31377**			**100%**	**-1.02[-1.16,-0.87]**

Heterogeneity: Tau²=0; Chi²=97.25, df=23(P<0.0001); I²=76.35%

Test for overall effect: Z=13.98(P<0.0001)

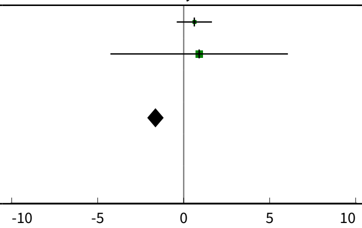
Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Analysis 3.4. Comparison 3 Fat reduction versus usual fat diet, adult RCTs - sensitivity analyses, Outcome 4 Weight, kg - removing WHI.

Study or subgroup	Reduced fat N	Reduced fat Mean(SD)	Usual or modified fat N	Usual or modified fat Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Simon Low Fat Breast CA	34	63.4 (11.1)	38	71.9 (11.7)		0.74%	-8.5[-13.77,-3.23]
Pilkington 1960	12	66.7 (5.9)	23	70.8 (5.2)		1.23%	-4.1[-8.06,-0.14]
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		3.21%	-3.73[-5.78,-1.68]
DEER 1998 exercise men	48	-4.2 (4.2)	47	-0.6 (3.1)		4.48%	-3.6[-5.08,-2.12]
DEER 1998 no exercise wom	46	-2.7 (3.5)	45	0.8 (4.2)		4.21%	-3.5[-5.09,-1.91]
DEER 1998 no exercise men	49	-2.8 (3.5)	46	0.5 (2.7)		5.11%	-3.3[-4.55,-2.05]
DEER 1998 exercise women	43	-3.1 (3.7)	43	-0.4 (2.5)		4.88%	-2.7[-4.03,-1.37]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)		3.72%	-2.7[-4.5,-0.9]
Strychar 2009	15	-0.8 (3)	15	1.6 (1.8)		3.78%	-2.43[-4.2,-0.66]
WHT Feasibility 1990	159	-1.9 (4.9)	102	-0.1 (4.3)		5.47%	-1.83[-2.96,-0.7]
de Bont 1981 obese	34	-2.7 (3.6)	35	-0.9 (3.5)		4%	-1.8[-3.48,-0.12]
Swedish Breast CA 1990	63	-0.4 (5.5)	106	1.3 (5.5)		3.91%	-1.7[-3.41,0.01]
WHT:FSMP 2003	1325	-1.8 (4)	883	-0.3 (4.2)		7.56%	-1.5[-1.85,-1.15]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		5%	-1.5[-2.79,-0.21]
Bloemberg 1991	39	-0.9 (2.7)	40	0.1 (1.9)		5.8%	-1[-2.02,0.02]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		7.32%	-0.96[-1.43,-0.49]
BDIT Pilot Studies 1996	76	59.6 (7.3)	78	60.4 (8.4)		2.52%	-0.8[-3.28,1.68]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		6.95%	-0.72[-1.34,-0.1]
de Bont 1981 non-obese	36	-0.4 (2.8)	29	0.1 (2)		5.35%	-0.5[-1.67,0.67]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		3.7%	-0.4[-2.21,1.41]
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Veterans Dermatology 1994	38	-2 (0)	58	0.5 (0)			Not estimable
Rivellese 1994	27	-1.8 (0)	17	-1.6 (0)			Not estimable
Diet and Hormone Study 2003	81	-0.7 (0)	96	-0.1 (0)			Not estimable
MeDiet 2006	51	-1.3 (0)	55	-0.6 (0)			Not estimable
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)			Not estimable
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		4.48%	0.4[-1.08,1.88]

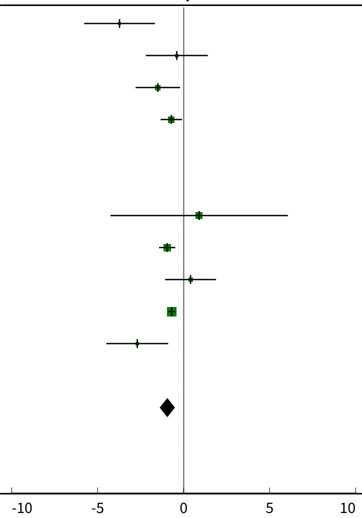
Favours reduced fat -10 -5 0 5 10 Favours moderate fat

Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Kentucky Low Fat 1990	47	1.1 (2.5)	51	0.4 (2.7)		5.79%	0.62[-0.4,1.64]
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.77%	0.9[-4.26,6.06]
Total ***	**6019**		**6275**			**100%**	**-1.64[-2.12,-1.16]**
Heterogeneity: Tau²=0.75; Chi²=79.26, df=22(P<0.0001); I²=72.24%							
Test for overall effect: Z=6.73(P<0.0001)							



Analysis 3.5. Comparison 3 Fat reduction versus usual fat diet, adult RCTs - sensitivity analyses, Outcome 5 Weight, kg - removing studies without good allocation concealment.

Study or subgroup	Reduced fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Auckland reduced fat 1999	48	-1.6 (5.4)	51	2.1 (5)		4.05%	-3.73[-5.78,-1.68]
BRIDGES 2001	48	0.1 (4.9)	46	0.5 (4.1)		5.03%	-0.4[-2.21,1.41]
Canadian DBCP 1997	388	62 (9.1)	401	63.5 (9.4)		8.49%	-1.5[-2.79,-0.21]
MSFAT 1995	117	0.4 (2.4)	103	1.1 (2.4)		18.86%	-0.72[-1.34,-0.1]
NDHS Open 1st L&M 1968	332	-2.4 (0)	348	-1.9 (0)			Not estimable
NDHS Open 2nd L&M 1968	179	-1.8 (0)	215	-1.2 (0)			Not estimable
Nutrition & Breast Health	47	67.3 (13.8)	50	66.4 (12)		0.72%	0.9[-4.26,6.06]
Polyp Prevention 1996	943	-0.6 (5.2)	943	0.3 (5.2)		22.48%	-0.96[-1.43,-0.49]
WHEL 2007	1308	74.1 (19.5)	1313	73.7 (19.2)		6.91%	0.4[-1.08,1.88]
WHI 2006	16297	-0.8 (10.1)	25056	-0.1 (10.1)		28.38%	-0.7[-0.9,-0.5]
WINS 1993	386	-2.7 (15.3)	998	0 (15.3)		5.07%	-2.7[-4.5,-0.9]
Total ***	**20093**		**29524**			**100%**	**-0.95[-1.4,-0.51]**
Heterogeneity: Tau²=0.17; Chi²=17.72, df=8(P=0.02); I²=54.85%							
Test for overall effect: Z=4.2(P<0.0001)							

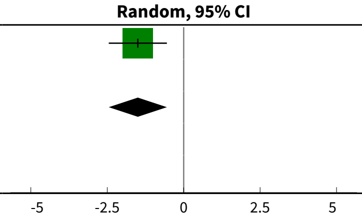


Comparison 4. Fat reduction versus usual fat, child RCTs

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 BMI, kg/m2 - in child RCTs	1	191	Mean Difference (IV, Random, 95% CI)	-1.5 [-2.45, -0.55]

Analysis 4.1. Comparison 4 Fat reduction versus usual fat, child RCTs, Outcome 1 BMI, kg/m2 - in child RCTs.

Study or subgroup	Low fat		Usual or modified fat		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
VYRONAS 2009	98	23.3 (2.8)	93	24.8 (3.8)		100%	-1.5[-2.45,-0.55]
Total ***	**98**		**93**			**100%**	**-1.5[-2.45,-0.55]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.09(P=0)							



ADDITIONAL TABLES

Table 1. Characteristics and results of included cohort studies in adults (all or a majority of participants recruited as adults)

Study	Participants at baseline	+ / 0 / -	Results and/or estimate of effect?
CARDIA Ludwig 1999 (1) **USA**	2909 healthy black and white young adults **Baseline age:** 18 to 30 yrs **Follow-up:** 10 yrs **%E from fat:** unclear (lower quintile < 30, upper > 41.7) **BMI:** unclear	**+** (weight) in black men and women **0** (weight) in white men and women	Adjusted means of 10-year body weight according to quintiles of total fat as a percentage of total energy. P for trend 0.32 in white men and women (quintile 1 weight 168.6 lb, quintile 5 weight 169.4 lb), 0.03 for black men and women (quintile 1 weight 182.1 lb, quintile 5 weight 185.7 lb)
Danish Diet Cancer & Health Study Halkjaer 2009 (2-4) **Denmark**	22,570 women and 20,126 men **Baseline age:** 50 to 64 yrs **Follow-up:** 5 yrs **%E from fat:** unclear (approx 32% in women, 33% in men) **BMI:** median 24.7 women, 26.1 men	**0** (Δ waist) women **0** (Δ waist) men	Association between total fat intake at baseline and change in waist circumference over 5 years suggested no statistically significant effects in women (mean change in waist circumference -0.03 cm/MJ/d total fat, 95% CI -0.20 to 0.14) or men (mean change in waist circumference 0.06 cm/MJ/d total fat, 95% CI -0.05 to 0.17)
	12,353 women and 10,080 men **Baseline age:** 50 to 60 yrs **Follow-up:** 5 yrs **%E from fat:** median 33.8% women, 35.2% in men **BMI:** median 24.4 women, 25.8 men	**0** (Δ waist circumference) **0** (Δ body weight)	Macronutrient energy substitution where energy from protein was replaced by fat or carbohydrate. Multiple linear regression investigated the association between dietary protein in relation to change in body weight or waist circumference over 5 years. No statistically significant effect of replacing 5%E from fat with protein on change in body weight (8.0 g/year, 95% CI -16.6 to 32.5, P value = 0.525) or waist circumference (0.1 mm/year, 95% CI -0.3 to 0.4, P value = 0.799)

Table 1. Characteristics and results of included cohort studies in adults (all or a majority of participants recruited as adults) *(Continued)*

Danish MONICA **Iqbal 2006 (5)** **Denmark**	900 women and 862 men **Baseline age:** 30 to 60 yrs **Follow-up:** 5 yrs **%E from fat:** 43.8% (SD 6.5 women, 42.7 (SD 6.3) men **BMI:** 23.4 (SD 3.7 women, 25.1 (SD 3.3) men	**0** (Δ weight) women **0** (Δ weight) men	Regression assessment of total fat as %E and other dietary factors as a function of change in body weight suggested no significant effects of %E from fat on 5-year change in body weight in women (unadjusted beta 0.47, SE 0.89, P value = 0.60, adjusted beta 0.86, SE 0.92, P value = 0.35) or men (unadjusted beta -0.14, SE 0.69, P value = 0.84, adjusted beta 0.11, SE 0.69, P value = 0.87)
Diabetes Control & Complications Trial (DCCT) & EDIC **Cundiff 2012 (6)** **USA**	1055 women and men with diabetes, HbA1c ≤ 9.5 **Baseline age:** 13 to 39 yrs (mean 27.4) **Follow-up:** 14 to 19 yrs (mean 16.4 yrs) **%E from fat:** 36.2% (90% CI 26.6 to 45.1) **BMI:** 23.4 (90% CI 19.4 to 27.9)	**0** (Δ BMI/year)	Multiple regression analyses generated the formula linking macronutrient intake and exercise at baseline with change in BMI per year. Univariate analyses suggested no relationship between total fat (as %E) and change in BMI per year (β 0.04 kg/m^2/year, P value = 0.22), and only total fat minus polyunsaturated fat (%E, not total fat) was included in the formula predicting BMI change per year
EPIC-PANACEA **Vergnaud 2013 (7)** **Europe** (10 countries) **EPIC** **Beulens 2014 (8)** **Europe** (15 cohorts)	373,803 men and women from the general European population **Baseline age:** 25 to 70 yrs **Follow-up:** 5 yrs (2 to 11) **%E from fat:** mean 35.4 (SD unclear) **BMI:** mean 25.6 women, 26.7 men (SDs unclear)	**0** (Δ weight) when replacing fat with CHO in women or men **-** (Δ weight) when replacing fat with protein in women or men	Multivariate substitution models were performed to estimate weight change associated with replacement of 5%E of one macronutrient with another. 5% greater proportion of E from fat at the expense of carbohydrate was not associated with weight change in women or men (P value = 0.36, P value = 0.73). Replacing 5%E from protein with fat was associated with weight reduction in women (β 0.4 kg/5 years, P value < 0.0001) and men (β 0.3 kg/5 years, P value = 0.003)
	6192 people with type 2 diabetes **Baseline age:** unclear **Follow-up:** 5 yrs **%E from fat:** unclear **BMI:** unclear	**-** (Δ weight) when replacing CHO with total fat	Linear regression was used to explore the relationship between replacement of CHO with total fat (and also MUFA and PUFA) and 5-year weight change. This is an abstract so results reported as "5-year weight change decreased when carbohydrates were substituted with total fat" (no further details)
Health Professionals Follow-Up Study (HPFUS) **Coakley 1998 (9)** **USA**	19,478 male health professionals **Baseline age:** 45 to 75 yrs **Follow-up:** 4 yrs **%E from fat:** unclear, energy adjusted fat intake mean 69.6 g/d (SD 13.8)	**+** (Δ weight) 45 to 54 yrs men **+** (Δ weight) 55 to 64 yrs men **0** (Δ weight) 65+ yrs men	Multivariate regression analyses determined whether total fat intake and other habits were predictive of 4-year weight change, and found that a change of adjusted fat intake of 10 g/d predicted 0.10 kg of weight change over 4 years (P value < 0.001 for ages 45 to 54 and 55 to 64 years, P value > 0.05 for age 65+)

Table 1. Characteristics and results of included cohort studies in adults (all or a majority of participants recruited as adults) *(Continued)*

	BMI: unclear		
Melbourne Collaborative Cohort Study (MCCS) **MacInnis 2013 (10)** **Australia**	5879 healthy Australian-born non-smokers **Baseline age:** 40 to 69 yrs **Follow-up:** 11.7 yrs **%E from fat**: 33% (SD 6) women, 33 (SD 5) men **BMI:** unclear	**+** (weight) overall **+** (waist circumference) overall **+** (weight) 40 to 49 yrs **0** (weight) 50 to 59 yrs **0** (weight) 60 to 69 yrs **+** (waist) 40 to 49 yrs **+** (waist) 50 to 59 yrs **0** (waist) 60 to 69 yrs	Multivariable linear regression was used to predict waist circumference and weight at 12-year follow-up. Higher percentage of energy from fat at baseline was associated with weight (0.26 kg per 10%E from fat, P value = 0.03) and waist circumference (0.85 cm per 10%E from fat, P value < 0.001) in the whole sample. When assessed in age bands, total fat was associated with weight in those aged 40 to 49 years at baseline (P value = 0.002), but not in those aged 50 to 59 (P value = 0.94) or 60 to 69 years (P value = 0.79), and with waist circumference in those aged 40 to 49 (P value < 0.001) and 50 to 59 (P value = 0.01), but not in those aged 60 to 69 (P value = 0.14)
Memphis **Klesges 1992 (11-13)** **USA**	152 women and 142 men (Caucasian health professionals) **Baseline age:** 24 to 52 yrs **Follow-up:** 2 yrs **%E from fat:** mean 36.8 (SD 6.1) women, 36.0 (SD 5.4) men **BMI:** mean 24.8 (SD 5.0) women, 27.8 (SD 4.3) men	**+** (Δ weight) women **0** (Δ weight) men **0** (Δ waist) women **-** (Δ waist) men	Stepwise multivariate regression analyses assessed whether various lifestyle factors were predictive of weight change over 2 years. Percentage of energy as fat was predictive of weight change in women (coefficient 0.53, SE 0.16, P value = 0.0010) but not in men (exact data not provided) Hierarchical linear regression assessed the effects of lifestyle factors on change in waist circumference over 2 years, and found no significant effect in women (coefficient -0.04, P value = 0.50) but a statistically significant negative relationship in men (coefficient -0.05, P value = 0.04)
NHANES Follow-up **Kant 1995 (14)** **USA**	4567 women and 2580 men **Baseline age:** 25 to 74 yrs **Follow-up:** mean 10.6 (SD 5) yrs **%E from fat:** mean 36.4 (SD 5.0) women, 37.0 (SD 10.1) men **BMI:** mean 25.2 (SD 5.0) women, 25.9 (SD 5.0) men	**+** (Δ weight) < 50 yrs women **0** (Δ weight) 50+ yrs women **0** (Δ weight) < 50 yrs men **0** (Δ weight) 50+ yrs men	Univariate regression analyses assessed whether fat as %E is predictive of 10-year weight change and found no significant effects in women (Beta -0.011, SE 0.017, P value = 0.51) or men (Beta 0.043, SE 0.022, P value = 0.06). Effects were similar in multivariate regression in women (Beta -0.033, SE 0.019, P value = 0.08 for women overall, Beta -0.053, SE 0.025, P value = 0.04 for women aged < 50 yrs, Beta -0.019, SE 0.030, P value = 0.55 for women aged 50+) or men (Beta 0.021, SE 0.022, P value = 0.33 for men overall, Beta -0.004, SE 0.028, P value = 0.88 for men aged < 50 yrs, Beta -0.058, SE 0.035, P value = 0.10 for men aged 50+)
Nurses' Health Study **Colditz 1990 (15)** **Field 2007 (16)** **USA**	31,940 women (nurses) **Baseline age:** 30 to 55+ **Follow-up:** 8 yrs **%E from fat:** unclear	**0** (Δ weight) women	Correlation between total fat (g/d) and weight gain over subsequent 4 years (beta -0.0007, t -0.4), not statistically significant

Table 1. Characteristics and results of included cohort studies in adults (all or a majority of participants recruited as adults) *(Continued)*

	BMI: unclear		
	41,518 women (nurses) **Baseline age:** 41 to 68 yrs (mean 53.7, SD 7.1 yrs) **Follow-up:** 8 yrs **%E from fat:** 32.8 (SD 5.6) **BMI:** 25.0 (SD 4.5)	**? unclear** (Δ weight) women	Association between a 1% difference in total fat as %E and weight change (in pounds over 8 years) was modelled using linear regression. There was a weak relationship between total fat and weight change (β 0.11 lb/1% total fat difference, P value < 0.0001 stated in text, but no statistical significance indicated in table)
Pawtucket HHP **Parker 1997 (17)** **USA**	289 women and 176 men **Baseline age:** 18 to 64 yrs **Follow-up:** 4 yrs **%E from fat:** unclear **BMI:** mean 26.5 (SD 5.0)	**0** (Δ weight) women and men	Multiple regression assessed association of weight change with different nutrients at baseline. Found no effect of total fat in grams on weight change over 4 years (coefficient 2.30, P value = 0.71)
San Luis Valley Diabetes Study (SLVDS) **Mosca 2004 (18)** **USA**	433 women and 349 men - non-diabetic, Hispanic and non-Hispanic white **Baseline age:** 20 to 74 yrs **Follow-up:** 14 yrs **%E from fat:** mean 38.3 (SD 8.9) white women, 37.2 (8.9) Hispanic women, 38.9 (8.7) white men, 37.8 (9.8) Hispanic men **BMI:** mean 24.3 (SD 4.4) white women, 25.0 (4.6) Hispanic women, 25.7 (3.3) white men, 24.7 (3.8) Hispanic men	**+** (Δ weight) overall (includes women and men, Hispanic and non-Hispanic white)	Linear mixed model (random-effects, PROC MIXED in SAS) was used to assess whether those who generally consume a relatively high fat diet gain more weight over time. They found a significant association between %E from total fat and weight change between participants (β 0.012, P value = 0.0178) after adjusting for potential confounders
SEASONS **Ma 2005 (19)** **USA**	275 healthy women and 297 healthy men **Baseline age:** 20 to 70 yrs **Follow-up:** 1 yr **%E from fat:** mean 36.7 (SD 9.0) **BMI:** mean 27.4 (SD 5.5)	**0** (BMI) women and men – with no energy adjustment	Regression analyses to assess effects of total fat %E on BMI. Longitudinal effect was not statistically significant (coefficient 0.005, P value = 0.07)
Women's Gothenburg **Lissner 1997 (20)** **Sweden**	361 women **Baseline age:** 38 to 60 yrs **Follow-up:** 6 yrs **%E from fat:** mean 34.1 (SD 4.0) lower fat group,	**+** (Δ weight) sedentary **0** (Δ weight) moderate **0** (Δ weight) active	Multivariate regression used to test for interactive effects of dietary fat intake on weight change over 6 years. A significant effect of high vs low %E from fat was found in sedentary women (high fat women gained 2.64 kg while low fat women lost 0.64 kg over 6 years, P value = 0.03) but this was lost with further energy adjustment. No effects were seen in more active women (2 categories),

Table 1. Characteristics and results of included cohort studies in adults (all or a majority of participants recruited as adults) *(Continued)*

	42.3 (SD 3.0) higher fat group **BMI:** mean 24.6 (SD 4.1) lower fat group, 24.1 (SD 4.1) higher fat group		where those with low and high fat intakes all gained 1 to 2 kg on average

Key:
+ = positive relationship found between fat intake and weight outcome.
0 = no relationship found between fat intake and weight outcome.
- = negative (inverse) relationship found between fat intake and weight outcome.
Abbreviations: BMI: body mass index; CHO: carbohydrates; CI: confidence interval; MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid; SD: standard deviation; SE: standard error.
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Table 2. Characteristics and results of included cohort studies in children and young people (including all cohorts where assessment began in childhood or adolescence)

Study	Participants at baseline	+ / 0 / -	Results and/or estimate of effect
Adelaide Nutrition Study **Magarey 2001 (1)** **Australia**	243 boys and girls **Age:** diet analysed at 2, 4, 6, 8, 11, 13 and 15 years old **Follow-up:** assessed for each gap (e.g. 2 to 4 years, 2 to 6 years, 2 to 8 years, 4 to 6 years etc), 2 to 13 years **%E from fat:** boys aged 2 yrs 38.4 (SD 5.8), girls aged 2 38.1 (SD 13.4), boys aged 15 33.2 (SD 5.6), girls aged 15 yrs 34.4 (SD 5.6) **BMI:** boys aged 2 yrs 16.8 (SD 1.7), girls aged 2 16.5 (SD 1.4), boys aged 15 20.2 (SD 2.6), girls aged 15 yrs 21.4 (SD 4.1)	0 (BMI) for 20 of 21 possible age gaps 0 (triceps skinfold) for 21 of 21 possible age gaps 0 (sub-scapular skinfold) for 20 of 21 possible age gaps	**Single dietary assessment for each of 21 analyses** **Analysis:** multiple regression analysis was used to predict whether body fatness at a specific age was predicted by macronutrient intake at previous ages. For BMI only one of 21 possible gaps showed a statistically significant relationship between total fat intake as a percentage of energy and later BMI (a significant relationship, P value < 0.01, was only seen between fat at age 6 and BMI at age 8). For triceps skinfold none of 21 possible gaps showed a statistically significant relationship between total fat intake as a percentage of energy and later triceps skinfold. For subscapular skinfold only one of 21 possible gaps showed a statistically significant relationship between total fat intake as a percentage of energy and later sub-scapular skinfold (a significant relationship, P value < 0.01, was only seen between fat at age 2 and skinfold at age 15)
Amsterdam Growth & Health Long. Study (AGAHLS) **Twisk 1998, Koppes 2009 (2;3)** **Netherlands**	83 boys (then men) and 98 girls (then women) **Age:** recruited aged 13, diet analysed at ages 13, 14, 15, 16, 21, 27 **Follow-up:** 14 yrs (age 27) **%E from fat:** not reported **BMI:** boys aged 13 yrs 17.3 (SD 1.6), girls 18.1 (SD 2.1), men aged 27 yrs 22.6 (SD 2.2), women 21.9 (SD 2.5)	0 (sum of 4 skinfolds) 0 (BMI) Both for absolute fat intake and %E from fat	**Multiple dietary assessments** **Analysis:** first order auto-regressive model (fatness at each time point related to exposure at the previous time point) estimated by generalised estimating equations. There was no relationship between total fat intake (absolute, g/d) and later fatness as assessed by sum of four skinfolds (P value = 0.41) or BMI (P value = 0.23), or between fat intake as %E and later fatness as assessed by sum of four skinfolds (P value = 0.92) or BMI (P value = 0.69)
	168 boys (then men) and 182 girls (then women) **Age:** recruited aged 13 (SD 0.7), diet analysed at ages 13, 14, 15, 16, 21, 27, 32, 36 **Follow-up:** 23 yrs (age 36) **%E from fat:** not reported **BMI:** as above	0 (high %body fat at age 36), 0 of 14 analyses 0 (% body fatness) in men or women	**Multiple dietary assessments** **Analysis:** generalised estimating equation regression analyses found that dietary fat intake (%E) at ages 13, 14, 15, 16, 21, 27 or 32 did not predict high body fatness (> 25% for men, > 35% for women, assessed by DEXA at 36 years) in either men or women (in any of 7 analyses in men or 7 in women). Regression coefficients using all available data gathered between ages 13 and 36 found no relationship between %E from fat and sum of skinfolds in either men (P value = 0.42) or women (P value = 0.89)
Bogaert 2003 (4) **Australia**	29 boys and 30 girls **Age:** recruited aged 6 to 9 yrs, mean 8.6 (SE 0.2) yrs **Follow-up:** at 6 and 12 mo **%E from fat:** 33.5 (SD 0.8) in boys aged < 8 yrs, 31.7 (SD 2.7)	0 (Δ BMI)	**Single dietary assessment** **Analysis:** correlations were calculated to assess the relation between %E from fat at baseline and BMI z-score change from baseline to 12 months. No "positive relation" was found

Table 2. Characteristics and results of included cohort studies in children and young people (including all cohorts where assessment began in childhood or adolescence) *(Continued)*

	girls < 8 yrs, 37.5 (SD 1.2) boys aged 8+ yrs, 33.6 (SD 1.7) girls aged 8+ yrs **BMI:** z scores boys mean 0.3 (SE 0.1), girls mean 0.5 (SE 0.3)		
Carruth and Skinner 2001 (5;6) **USA**	29 white boys and 24 girls **Age:** recruited at 24 months, diet assessed at 24 to 32, 28 to 36, 42, 48, 54, 60 months old **Follow-up:** body fat assessed at 70 months **%E from fat:** 31% boys, 32% girls at 27 months, 31% boys, 33% girls at 60 months **BMI:** 15.7 (SD 1.2) in boys and 15.4 (SD 1.0) in girls at 60 months	+ (%body fat) + (g body fat)	**Multiple dietary assessments** **Analysis:** regression analyses (general linear models) of total fat intake (averaging over 6 dietary assessments aged 27 to 60 months) predicted body fat at 70 months (assessed as %body fat, P value = 0.02 and grams of body fat, P value = 0.01, both assessed by DEXA)
	37 white boys and 33 girls **Age:** recruited at 24 months (except 2 joined at 1 year, 6 joined at 2 years from similar study), diet assessed at 2.0, 2.3, 2.7, 3.0, 3.5, 4.0, 4.5, 5.0, 6.0, 7.0, 8.0 yrs old **Follow-up:** BMI assessed at 8 yrs **%E from fat:** mean 32% (SD not stated) **BMI:** 16.5 in boys and 16.2 in girls at 2 yrs, 16.8 in boys and 17.1 in girls at 8 yrs	+ (BMI) by g/d of fat + (BMI) by %E from fat	**Multiple dietary assessments** **Analysis:** forward stepwise regression was used to assess the relationship between dietary fat (averaged from 9 sets of 3-day dietary data from ages 2 to 8) and BMI at age 8 years. Whether assessing fat as g/d (P value = 0.004) or %E from fat (P value = 0.010) there was a significant relationship (adjusted for BMI at 2 years and adiposity rebound age)
Davison 2001 (7) **USA**	197 non-Hispanic white girls **Age:** 5.4 (0.4) yrs **Follow-up:** 2 yrs (age 7.3 ±0.3) **%E from fat:** 31 (SD unclear) **BMI:** 15.8 (1.4)	+ (Δ BMI)	**Single dietary assessment** **Analysis:** in hierarchical regression models, girls' fat intake (as %E) at 5 yrs had a significant relationship with change in BMI from 5 to 7 years, P value = 0.02
Etude Longitud. Alimentation Nutrition Croissance des Enfants (ELANCE) **Rolland-Cachera 2013 (8)**	40 boys and 33 girls whose diets were assessed at 2 yrs **Age:** 2 yrs **Follow-up:** 18 years (age 20) **%E from fat:** 31.9 (SD 5.7) boys, 32.8 (SD 4.5) girls	0 (BMI) 0 (% triceps skinfold) - (% sub-scapular skinfold) - (fat mass)	**Single dietary assessment** (for this analysis) Analysis: association between dietary intake at 2 years and adult body composition was analysed using linear regression models. No statistically significant relationships were found between %E from fat at 2 years and BMI (P value = 0.23), % triceps skinfold (P value = 0.19), or fat-free mass (P value = 0.98) at age 20. Greater total fat intake predicted lower %

Table 2. Characteristics and results of included cohort studies in children and young people (including all cohorts where assessment began in childhood or adolescence) *(Continued)*

France	**BMI:** unclear		subscapular skinfold (P value = 0.03) and fat mass (P value = 0.04). All data presented from the adjusted models
European Youth Heart Study **Brixval 2009 (9)** **Denmark**	171 girls and 137 boys (but total of 384 stated also, numbers vary between tables) **Age:** boys 9.7 (SD 0.4) yrs, girls 9.6 (SD0.4) yrs **Follow-up:** 6 years (age 15 to 16) **%E from fat:** 32.1 (SD 6.6) boys, 33.3 (SD 6.7) girls **BMI:** 17.1 (SD 2.0) boys, 17.2 (SD 2.4) girls	0 (Δ BMI z-score) boys 0 (Δ BMI z-score) girls	**Single dietary assessment.** **Analysis:** examined the associations between dietary fat intake at 9 years and subsequent 6-year weight development using regression analysis. None of the regression models (various levels of adjustment) suggested that fat %E was associated with change in BMI over 6 years (in boys P value = 0.27, girls P value = 0.75 in the most adjusted model)
Klesges 1995 (10) **USA**	110 boys and 93 girls **Age:** 3 to 5 yrs (boys 4.4 (0.5), girls 4.3 (0.5) **Follow-up**: 2 yrs **%E from fat:** boys and girls 33.0 (5.0) **BMI:** boys 16.1 (1.4), girls 16.1 (1.2)	0 /+ /0/0 (Δ BMI)	**Multiple dietary assessments** **Analysis:** assessed whether baseline %E from fat, change from baseline to 1 year, 1 yr to 2 yrs, or baseline to 2 yrs (along with other variables) predicted change in BMI over 2 yrs Multiple regression analysis suggested lower baseline %E from fat correlated to lower BMI change (regression coefficient = 0.034, P value = 0.05 – marginal significance) at 2 yrs, 0.17 k/m^{2}per 5% more E from fat Change in %E from fat over the last year was correlated with BMI change (regression *numbers not legible, probably P value = 0.01*), 0.20 kg/m^2 per 5%E from fat change. Change in %E from fat from baseline to 1 yr, and baseline to 2 yrs did not predict change in BMI
Obesity & Metabolic Disorders Cohort in Children (OMDCC) **Lee 2012 (11)** **Korea**	1504 1st and 4th grade children **Age:** 7.3 (SD 0.3) in 1st graders, 10.0 (SD 0.4) years in 4th graders **Follow-up:** 2 years **%E from fat**: 26.6 (SD 4.9) in 1st graders, 25.2 (SD 5.1) in 4th graders **BMI:** 16.0 (SD 2.3) in 1st graders, 18.1 (SD 3.0) in 4th graders	0 (Δ BMI)	**Single dietary assessment** Multiple linear regression modelling assessed relationships between baseline environmental factors, parental and lifestyle habits and change in BMI over 2 years. They found no statistically significant relationship between fat intake and change in BMI over 2 years (P value = 0.104)
Trial of Activity for Adolescent Girls (TAAG)	265 girls in 8th grade **Age:** mean 13.9 (SD 0.4) yrs	0 (BMI percentile) - (% body fat)	**Single dietary assessment** Multivariable random coefficients model designed to examine whether habitual physical activity, diet

Table 2. Characteristics and results of included cohort studies in children and young people (including all cohorts where assessment began in childhood or adolescence) *(Continued)*

Cohen 2014 (12) **USA**	**Follow-up**: 2 and 3 yrs **%E from fat:** unclear **BMI:** mean 22.1 (SD 5.2)		and environmental exposure were predictive of future weight gain or percentage body fat. The multivariate model found no relationship between fat calories at baseline and BMI percentile (P value = 0.16), but suggested a reduction in % body fat associated with increased fat calories (P value = 0.03)
Viva la Familia Study **Butte 2007 (13)** **USA**	1030 Hispanic boys and girls (unclear how many of each) **Age:** unclear, 4 to 19 yrs? **Follow-up**: 1 yr **%E from fat**: 34.0 (6.0) **BMI:** not stated	+ (Δ weight)	**Single dietary assessment** **Analysis:** %E from fat was positively correlated with 1 yr weight gain (kg/y). For 798 participants generalised estimating equations (GEE) suggested coefficient 0.044, SD 0.018, P value = 0.014

Key:
+ = positive ss relationship found between fat intake and weight outcome.
0 = no ss relationship found between fat intake and weight outcome.
- = negative (inverse) ss relationship found between fat intake and weight outcome.
Abbreviations: BMI: body mass index; DEXA: dual energy X-ray absorptiometry; SD: standard deviation; SE: standard error; ss: statistically significant
References for this table:
(1) Magarey AM, Daniels LA, Boulton TJC, Cockington RA. Does fat intake predict adiposity in healthy children and adolescents aged 2-15 y? A longitudinal analysis. *European Journal of Clinical Nutrition* 2001;55:471-81.
(2) Twisk JWR, Kempner HCG, van Mechelen W, Post GB, van Lenthe FJ. Body fatness: longitudinal relationship of body mass index and the sum of skinfolds with other risk factors for coronary heart disease. *International Journal of Obesity* (Lond) 1998;22:915-22.
(3) Koppes LLJ, Boon N, Nooyens ACJ, van Mechelen W, Saris WHM. Macronutrient distribution over a period of 23 years in relation to energy intake and body fatness. *British Journal of Nutrition* 2009;101:108-15.
(4) Bogaert N, Steinbeck KS, Baur LA, Brock K, Bermingham MA. Food, activity and family - environmental vs biochemical predictors of weight gain in children. *European Journal of Clinical Nutrition* 2003;57:1242-9.
(5) Carruth BR, Skinner JD. The role of dietary calcium and other nutrients in moderating body fat in preschool children. *International Journal of Obesity* (Lond) 2001;25:559-66.
(6) Skinner JD, Bounds W, Carruth BR, Morris M, Ziegler P. Predictors of children's body mass index: a longitudinal study of diet and growth in children aged 2-8 years. *International Journal of Obesity* (Lond) 2004;28:476-82.
(7) Davison KK, Birch LL. Child and parent characteristics as predictors of change in girls' body mass index. *International Journal of Obesity* (Lond) 2001;25:1834-42.
(8) Rolland-Cachera MF, Maillot M, Deheeger M, Souberbielle JC, Peneau S, Hercberg S, et al. Association of nutrition in early life with body fat and serum leptin at adult age. *International Journal of Obesity* 2013 Aug;37(8):1116-22.
(9) Brixval CS, Anderson LB, Heitmann BL. Fat intake and weight development from 9 to 16 years of age: the European Youth Heart Study - a Longitudinal Study. *Obesity Facts* 2009;3:166-70.
(10) Klesges RC, Klesges LM, Eck LH, Shelton ML. A longitudinal analysis of accelerated weight gain in preschool children. *Pediatrics* 1995;95:126-30.
(11) Lee HH, Park HA, Kang JH, Cho YG, Park JK, Lee R, et al. Factors related to body mass index and body mass index change in Korean children: preliminary results from the obesity and metabolic disorders cohort in childhood. *Korean Journal of Family Medicine* 2012 May;33(3):134-43.
(12) Cohen DAG. Energy balance in adolescent girls: The trial of activity for adolescent girls cohort. *Obesity* (Silver Spring) 2014;22(3):772-80.
(13) Butte NF, Cai G, Cole SA, Wilson TA, Fisher JO, Zakeri IF, et al. Metabolic and behavioral predictors of weight gain in Hispanic children: The Viva la Familia Study. *American Journal of Clinical Nutrition* 2007;85:1478-85.

Table 3. Excluded child RCTs

Study	Reason for exclusion
Alexy U, Reinehr T, et al. (2006). Positive changes of dietary habits after an outpatient training program for overweight children. *Nutrition Research* 26(5): 202-8	Weight loss intention

Table 3. Excluded child RCTs *(Continued)*

Amesz EMS. Optimal growth and lower fat mass in preterm infants fed a protein-enriched postdischarge formula. *Journal of Pediatric Gastroenterology and Nutrition*. 2010;50(2):200-7	Includes infants
Anand SS, Davis AD, et al. (2007). A family-based intervention to promote healthy lifestyles in an aboriginal community in Canada. *Canadian Journal of Public Health Revue Canadienne de Sante Publique*. 98(6): 447-52	Weight loss intention
Angelopoulos PD, Milionis HJ, et al. (2009). Changes in BMI and blood pressure after a school based intervention: the CHILDREN study. *European Journal of Public Health* 19(3): 319-25	Multifactorial intervention
Burrows TJ. Long-term changes in food consumption trends in overweight children in the HIKCUPS intervention. Journal of Pediatric Gastroenterology and Nutrition. 2011;53(5):543-7	All obese or overweight at baseline
Dal Molin Netto B, Landi Masquio DC, Da Silveira Campos RM, De Lima Sanches P, Campos Corgosinho F, Tock L, et al. The high glycemic index diet was an independent predictor to explain changes in agouti-related protein in obese adolescents. Nutricion Hospitalaria. 2014;29(2):305-14	Obese adolescents
Evans RK, Franco RL, et al. (2009). Evaluation of a 6-month multi-disciplinary healthy weight management program targeting urban, overweight adolescents: effects on physical fitness, physical activity, and blood lipid profiles. *International Journal of Pediatric Obesity* 4(3): 130-3	Multifactorial intervention, weight loss goal
Forneris T, Fries E, et al. (2010). Results of a rural school-based peer-led intervention for youth: goals for health. *Journal of School Health* 80(2): 57-65	No relevant outcomes
Garnett SPB. Researching Effective Strategies to Improve Insulin Sensitivity in Children and Teenagers - RESIST. A randomised control trial investigating the effects of two different diets on insulin sensitivity in young people with insulin resistance and/or pre-diabetes. *BMC Public Health*. 2010;10(pp 575):2010. **2.** Garnett SPD. Optimum macronutrient content of the diet for adolescents with pre-diabetes; RESIST a randomised control trial ACTRN12608000416392. *Endocrine Reviews*. 2012;Conference(var.pagings)	All obese or overweight at baseline
Hernandez TLA. Women with gestational diabetes randomised to a low-carbohydrate/higher fat diet demonstrate greater insulin resistance and infant adiposity. *Diabetes*. 2013;Conference(var.pagings):July	Effect on infants
Horan MKM. The association of maternal characteristics and macronutrient intake in pregnancy with neonatal body composition. *Archives of Disease in Childhood: Fetal and Neonatal Edition*. 2014;Conference(var.pagings):June	Infants
Jebb SA, Frost G, et al. (2007). The RISCK study: Testing the impact of the amount and type of dietary fat and carbohydrate on metabolic risk. *Nutrition Bulletin* 32(2): 154-6	Design paper
Kaitosaari T, Ronnemaa T, et al. (2006). Low-saturated fat dietary counselling starting in infancy improves insulin sensitivity in 9-year-old healthy children: the Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) study. *Diabetes Care* 29(4): 781-5	No relevant outcomes
Lagstrom H, Hakanen M, et al. (2008) Growth patterns and obesity development in overweight or normal-weight 13-year-old adolescents: the STRIP study. *Pediatrics* 122(4): e876-83	No relevant exposures
Mirza NM, Palmer MG, Sinclair KB, McCarter R, He J, Ebbeling CB, et al. Effects of a low glycemic load or a low-fat dietary intervention on body weight in obese Hispanic American children and adolescents: a randomised controlled trial. *American Journal of Clinical Nutrition*. 2013;97(2):276-85	All obese at baseline
Mobley CCS. Effect of nutrition changes on foods selected by students in a middle school-based diabetes prevention intervention program: The HEALTHY experience. *Journal of School Health*. 2012;82(2):82-90	No total fat intake assessment

Table 3. Excluded child RCTs *(Continued)*

Niinikoski H, Lagstrom H, Jokinen E, Siltala M, Ronnemaa T, Viikari J, et al. Impact of repeated dietary counselling between infancy and 14 years of age on dietary intakes and serum lipids and lipoproteins: the STRIP study. *Circulation*. 2007;116(9):1032-40	Aim to reduce saturated fat not total fat
Ramon-Krauel MS. A low-glycemic-load versus low-fat diet in the treatment of fatty liver in obese children. *Childhood Obesity*. 2013;9(3):252-60	All obese at baseline
Shalitin S, Ashkenazi-Hoffnung L, et al. (2010). Effects of a twelve-week randomised intervention of exercise and/or diet on weight loss and weight maintenance, and other metabolic parameters in obese preadolescent children. *Hormone Research* 72(5): 287-301	Weight loss/unsuitable exposures
Sharma SF. One-year change in energy and macronutrient intakes of overweight and obese inner-city African American children: Effect of community-based Taking Action Together type 2 diabetes prevention program. *Eating Behaviors*. 2012;13(3):271-4	All obese or overweight at baseline
Singhal A, Kennedy K, Lanigan J, Fewtrell M, Cole TJ, Stephenson T, et al. Nutrition in infancy and long-term risk of obesity: evidence from 2 randomised controlled trials. *American Journal of Clinical Nutrition*. 2010;92(5):1133-44	Infants
Thakwalakwa C, Ashorn P, Phuka J, Cheung YB, Briend A, Puumalainen T, et al. A lipid-based nutrient supplement but not corn-soy blend modestly increases weight gain among 6- to 18-month-old moderately underweight children in rural Malawi. *Journal of Nutrition* 2010;140(11):2008-13	Duration < 26 weeks
Williamson DA, Han H, Johnson WD, Martin CK, Newton RL, Jr. Modification of the school cafeteria environment can impact childhood nutrition. Results from the Wise Mind and LA Health studies. *Appetite*. 2013;61(1):77-84	Weight loss aimed
Williamson DA, Copeland AL, et al. (2007). Wise Mind project: a school-based environmental approach for preventing weight gain in children. *Obesity* 15(4): 906-17	Multifactorial intervention

Table 4. Excluded adult cohort studies

Study	Reason for exclusion
Adams T, Rini A (2007). Predicting 1-year change in body mass index among college students. *Journal of American College Health* 55(6): 361-5	No relevant exposures
Aerenhouts D, Deriemaeker P, Hebbelinck M, Clarys P, Aerenhouts D, Deriemaeker P, et al. Energy and macronutrient intake in adolescent sprint athletes: a follow-up study. *Journal of Sports Sciences*. 2011;29(1):73-82	No relationship between total fat and body fatness
Ahluwalia N, Ferrieres J, et al. (2009). Association of macronutrient intake patterns with being overweight in a population-based random sample of men in France. *Diabetes & Metabolism* 35(2): 129-36	Invalid study design
Aljadani HM, Patterson A, Sibbritt D, Hutchesson MJ, Jensen ME, Collins CE. Diet quality, measured by fruit and vegetable intake, predicts weight change in young women. *Journal of Obesity*. 2013;2013:525161	No relevant outcomes
Almoosawi S, Prynne CJ, Hardy R, Stephen AM. Time-of-day and nutrient composition of eating occasions: prospective association with the metabolic syndrome in the 1946 British birth cohort. *International Journal of Obesity*. 2013;37(5):725-31	No total fat assessment

Table 4. Excluded adult cohort studies *(Continued)*

Al-Sarraj T, Saadi H, et al. (2010). Metabolic syndrome prevalence, dietary intake, and cardiovascular risk profile among overweight and obese adults 18-50 years old from the United Arab Emirates. *Metabolic Syndrome & Related Disorders* 8(1): 39-46	Cross-sectional study
Althuizen E, van Poppel MN, de Vries JH, Seidell JC, van MW, Althuizen E, et al. Postpartum behaviour as predictor of weight change from before pregnancy to one year postpartum. *BMC Public Health*. 2011;11:165	Total fat assessment is not baseline
Bailey BWS. Dietary predictors of visceral adiposity in overweight young adults. *British Journal of Nutrition.* 2010;103(12):1702-5	Cross-sectional
Berg CM, Lappas G, et al. (2008). Food patterns and cardiovascular disease risk factors: the Swedish INTERGENE research program. *American Journal of Clinical Nutrition* 88(2): 289-97	Invalid study design
Bes-Rastrollo M, van Dam RM, et al. (2008) Prospective study of dietary energy density and weight gain in women. *American Journal of Clinical Nutrition* 88(3): 769-77	Not total fat to body fatness
Black MHW. High-fat diet is associated with obesity-mediated insulin resistance and beta-cell dysfunction in Mexican Americans. *Journal of Nutrition*. 2013;143(4):479-85. 2. Black MHW. Variants in PPARG interact with high-fat diet to influence longitudinal decline in beta-cell function in Mexican Americans at risk for type 2 diabetes (T2D). *Diabetes*. 2014;Conference(var.pagings):June	Not prospective
Bujnowski D, Xun P, Daviglus ML, Van HL, He K, Stamler J, et al. Longitudinal association between animal and vegetable protein intake and obesity among men in the United States: the Chicago Western Electric Study. *Journal of the American Dietetic Association*. 2011;111(8):1150-5	No total fat intake assessment
Carvalho LKB. Annual variation in body fat is associated with systemic inflammation in chronic kidney disease patients Stages 3 and 4: A longitudinal study. *Nephrology Dialysis Transplantation*. 2012;27(4):1423-8	No total fat assessment and chronic kidney disease
Castellanos DC, Connell C, Lee J. Factors affecting weight gain and dietary intake in Latino males residing in Mississippi: a preliminary study. *Hispanic Health Care International*. 2011;9(2):91-8	Cross-sectional
Chang A, Van Horn L, Jacobs Jr DR, Liu K, Muntner P, Newsome B, et al. Lifestyle-related factors, obesity, and incident microalbuminuria: the CARDIA (Coronary Artery Risk Development in Young Adults) Study. *American Journal of Kidney Diseases*. 2013;62(2):267-75	Assesses dietary patterns
Chopra VP. Dietary factors affecting weight gain in midlife women. *FASEB Journal*. 2013;Conference(var.pagings):April	All overweight or obese at baseline
de Groot S, Post MW, Snoek GJ, Schuitemaker M, van der Woude LH. Longitudinal association between lifestyle and coronary heart disease risk factors among individuals with spinal cord injury. *Spinal Cord*. 2013;51(4):314-8	No total fat assessment
de Koning L, Malik VS, Kellogg MD, Rimm EB, Willett WC, Hu FB. Sweetened beverage consumption, incident coronary heart disease, and biomarkers of risk in men. *Circulation*. 2012;125(14):1735-41	No body fatness outcomes
Dujmovic M, Kresic G, Mandic ML, Kenjeric D, Cvijanovic O, Dujmovic M, et al. Changes in dietary intake and body weight in lactating and non-lactating women: prospective study in northern coastal Croatia. *Collegium Antropologicum*. 2014;38(1):179-87	Follow-up < 1 year
Eghtesadi SS-K. Dietary patterns predicting changes in obesity indices (BMI,WC,WHR) in longitudinal Tehran lipid and glucose study. *Annals of Nutrition and Metabolism*. 2013;Conference(var.pagings):2013	No total fat intake assessment
Erber E, Hopping BN, Grandinetti A, Park SY, Kolonel LN, Maskarinec G. Dietary patterns and risk for diabetes: the multiethnic cohort. *Diabetes Care*. 2010;33(3):532-8	No total fat intake assessment and no body fatness outcomes

Table 4. Excluded adult cohort studies *(Continued)*

Ericson U, Rukh G, Stojkovic I, Sonestedt E, Gullberg B, Wirfalt E, et al. Sex-specific interactions between the IRS1 polymorphism and intakes of carbohydrates and fat on incident type 2 diabetes. *American Journal of Clinical Nutrition*. 2013;97(1):208-16	Cross-sectional
Hairston KGV. Lifestyle factors and 5-year abdominal fat accumulation in a minority cohort: The IRAS family study. *Obesity*. 2012;20(2):421-7	No total fat intake assessment
Heppe DHMV. Maternal milk consumption, fetal growth, and the risks of neonatal complications: The Generation R Study. *American Journal of Clinical Nutrition*. 2011;94(2):501-9	Fetal growth assessment
Holmberg S, Thelin A, Holmberg S, Thelin A. High dairy fat intake related to less central obesity: a male cohort study with 12 years' follow-up. *Scandinavian Journal of Primary Health Care*. 2013;31(2):89-94	No total fat intake assessment
Ibe YT. Food groups and weight gain in Japanese men. *Clinical Obesity*. 2014;4(3):157-64	No relationship between total fat and body fatness assessed
Jaacks LMG. Age, period and cohort effects on adult body mass index and overweight from 1991 to 2009 in China: The China Health And Nutrition Survey. *International Journal of Epidemiology*. 2013;42(3):828-37	No total fat intake assessment
Jaakkola JH. Eating behavior influences diet, weight, and central obesity in women after pregnancy. *Nutrition*. 2013;29(10):1209-13	No total fat intake assessment
Jarvandi S, Gougeon R, Bader A, Dasgupta K, Jarvandi S, Gougeon R, et al. Differences in food intake among obese and non-obese women and men with type 2 diabetes. *Journal of the American College of Nutrition*. 2011;30(4):225-32	Cross-sectional
Johns DJ, Ambrosini GL, Jebb SA, Sjöström L, Carlsson LMS, Lindroos AK. Tracking of an energy-dense, high saturated fat, low-fibre dietary pattern, foods and nutrient composition over 10 years in the severely obese. *Journal of Human Nutrition & Dietetics*. 2011;24(4):391-2. 2. Johns DJ, Lindroos AK, Jebb SA, Sjostrom L, Carlsson LM, Ambrosini GL, et al. Tracking of a dietary pattern and its components over 10-years in the severely obese. *PLoS One* [Electronic Resource]. 2014;9(5):e97457	No relevant outcomes
Kimokoti RWG. Dietary patterns of women are associated with incident abdominal obesity but not metabolic syndrome. *Journal of Nutrition*. 2012;142(9):1720-7. 2. Kimokoti RWN. Diet quality, physical activity, smoking status, and weight fluctuation are associated with weight change in women and men. *Journal of Nutrition*. 2010;140(7):1287-93	No total fat intake assessment
Kirk JK, Craven T, Lipkin EW, Katula J, Pedley C, O'Connor PJ, et al. Longitudinal changes in dietary fat intake and associated changes in cardiovascular risk factors in adults with type 2 diabetes: the ACCORD trial. *Diabetes Research & Clinical Practice*. 2013;100(1):61-8	Compares PEP score, not total fat
Ko GTC, Chan JCN, et al. (2007). Associations between dietary habits and risk factors for cardiovascular diseases in a Hong Kong Chinese working population--the "Better Health for Better Hong Kong" (BHBHK) health promotion campaign. *Asia Pacific Journal of Clinical Nutrition* 16(4): 757-65	No relevant exposures
Laatikainen T, Philpot B, Hankonen N, Sippola R, Dunbar JA, Absetz P, et al. Predicting changes in lifestyle and clinical outcomes in preventing diabetes: The Greater Green Triangle Diabetes Prevention Project. *Preventive Medicine*. 2012;54(2):157-61	No relevant outcomes
Manios Y, Kourlaba G, Grammatikaki E, Androutsos O, Ioannou E, Roma-Giannikou E, et al. Comparison of two methods for identifying dietary patterns associated with obesity in preschool children: the GENESIS study. *European Journal of Clinical Nutrition*. 2010;64(12):1407-14	Cross-sectional
Meidtner KF. Variation in genes related to hepatic lipid metabolism and changes in waist circumference and body weight. *Genes and Nutrition*. 2014;9(2)	No total fat intake assessment

Table 4. Excluded adult cohort studies *(Continued)*

Mejean C, Macouillard P, Castetbon K, Kesse-Guyot E, Hercberg S, Mejean C, et al. Socio-economic, demographic, lifestyle and health characteristics associated with consumption of fatty-sweetened and fatty-salted foods in middle-aged French adults. *British Journal of Nutrition*. 2011;105(5):776-86	No total fat intake assessment
Mirmiran PB. Association between dietary phytochemical index and 3-year changes in weight, waist circumference and body adiposity index in adults: Tehran Lipid and Glucose study. *Nutrition and Metabolism*. 2012(9):108	No assessment of total fat on body fatness
Moran LJ, Ranasinha S, Zoungas S, McNaughton SA, Brown WJ, Teede HJ, et al. The contribution of diet, physical activity and sedentary behaviour to body mass index in women with and without polycystic ovary syndrome. *Human Reproduction*. 2013;28(8):2276-83	Cross-sectional
Mozaffarian D, Cao H, King IB, Lemaitre RN, Song X, Siscovick DS, et al. Circulating palmitoleic acid and risk of metabolic abnormalities and new-onset diabetes. *American Journal of Clinical Nutrition*. 2010;92(6):1350-8	No body fatness outcomes
Naniwadekar AS. Nutritional assessment of patients with chronic pancreatitis and impact of dietary advice. *Gastroenterology*. 2010;Conference(var.pagings):S393	Pancreatitis patients
Neeland IJT. Dysfunctional adiposity and the risk of prediabetes and type 2 diabetes in obese adults. *JAMA - Journal of the American Medical Association*. 2012;308(11):1150-9	No total fat intake assessment
Niu J, Seo DC, Niu J, Seo DC. Central obesity and hypertension in Chinese adults: a 12-year longitudinal examination. *Preventive Medicine*. 2014;62:113-8	No relevant outcomes
Noori N, Dukkipati R, Kovesdy CP, Sim JJ, Feroze U, Murali SB, et al. Dietary omega-3 fatty acid, ratio of omega-6 to omega-3 intake, inflammation, and survival in long-term hemodialysis patients. *American Journal of Kidney Diseases*. 2011;58(2):248-56	No total fat assessment and haemodialysis patients
Plotnikoff RC, Karunamuni N, et al. (2009) An examination of the relationship between dietary behaviours and physical activity and obesity in adults with type 2 diabetes. *Canadian Journal of Diabetes* 33(1): 27-34	No relevant exposures
Qi QR. Consumption of branched chain amino acids and risk of coronary heart disease in us men and women. *Circulation*. 2013;Conference(var.pagings)	No total fat intake on weight assessment
Quatromoni PA, Pencina M, Cobain MR, Jacques PF, D'Agostino RB. Dietary quality predicts adult weight gain: findings from the Framingham Offspring Study. *Obesity* (Silver Spring, Md). 2006;14(8):1383-91	No relevant outcomes
Rautiainen SW. Dairy consumption and risk of becoming overweight or obese in middle-aged and older women. *Circulation*. 2014;Conference(var.pagings):25	No total fat intake assessment
Rukh G, Sonestedt E, Melander O, Hedblad B, Wirfalt E, Ericson U, et al. Genetic susceptibility to obesity and diet intakes: association and interaction analyses in the Malmo Diet and Cancer Study. *Genes & Nutrition*. 2013;8(6):535-47 **2.** Rukh GS. Genetic susceptibility for obesity increases the risk of type 2 diabetes and is modified by macronutrient intakes. *Diabetologia*. 2010;Conference(var.pagings):September **3.** Rukh GS. Genetic susceptibility to obesity associates with type 2 diabetes and interacts with dietary intake to predispose for obesity. *Obesity Reviews*. 2010;Conference(var.pagings):July	Not prospective
Sammel MD, Grisson JA, Freeman EW, Hollander L, Liu L, Liu S, et al. Weight gain among women in the late reproductive years. *Family Practice* 2003; 20: 401–9	No total fat assessment
Sanchez-Villegas A, Bes-Rastrollo M, Martinez-Gonzalez MA, Serra-Majem L. Adherence to a Mediterranean dietary pattern and weight gain in a follow-up study: the SUN cohort. *International Journal of Obesity* 2006; 30: 350–8	No relevant outcomes

Table 4. Excluded adult cohort studies *(Continued)*

Sayon-Orea CB-R. Longitudinal association between yogurt consumption and weight gain, and the risk of overweight/obesity: The SUN cohort study. *Obesity Facts*. 2014;Conference(var.pagings):May	No total fat intake assessment
Scholz U, Ochsner S, Hornung R, Knoll N, Scholz U, Ochsner S, et al. Does social support really help to eat a low-fat diet? Main effects and sex differences of received social support within the Health Action Process Approach. Applied Psychology. 2013;*Health and Well-being*. 5(2):270-90	All obese or overweight at baseline
Schulz M, Kroke A, Liese AD, Hoffmann K, Bergmann MM, Boeing H. Food groups as predictors for short-term weight changes in men and women of the EPIC Potsdam cohort. *Journal of Nutrition* 2002; 132: 1335–40	No total fat assessment
Sherafat-Kazemzadeh R, Egtesadi S, Mirmiran P, Gohari M, Farahani SJ, Esfahani FH, et al. Dietary patterns by reduced rank regression predicting changes in obesity indices in a cohort study: Tehran Lipid and Glucose Study. *Asia Pacific Journal of Clinical Nutrition*. 2010;19(1):22-32.**2.** Sherafat-Kazemzadeh R, Egtesadi S, Mirmiran P, Hedayati M, Gohari M, Vafa M, et al. Predicting of changes in obesity indices regarding to dietary patterns in longitudinal Tehran lipid and glucose study. *Iranian Journal of Endocrinology & Metabolism*. 2010;12(2):197	No assessment of total fat on body fatness
Simpson A, Maynard V, Simpson A, Maynard V. A longitudinal study of the effect of Antarctic residence on energy dynamics and aerobic fitness. *International Journal of Circumpolar Health*. 2012;71:17227	No total fat intake assessment
Tanisawa KI. Strong influence of dietary intake and physical activity on body fatness in elderly Japanese men: age-associated loss of polygenic resistance against obesity. *Genes and Nutrition*. 2014;9(5)	Cross-sectional
Threapleton DE, Greenwood DC, Burley VJ, Aldwairji M, Cade JE, Threapleton DE, et al. Dietary fibre and cardiovascular disease mortality in the UK Women's Cohort Study. *European Journal of Epidemiology*. 2013;28(4):335-46	No total fat intake assessment
Vadiveloo M, Scott M, Quatromoni P, Jacques P, Parekh N, Vadiveloo M, et al. Trends in dietary fat and high-fat food intakes from 1991 to 2008 in the Framingham Heart Study participants. *British Journal of Nutrition*. 2014;111(4):724-34. **2.** Vadiveloo MS. Increases in dietary fat intake among the Framingham heart study participants: Trends from 1991-2008. *Circulation*. 2012;Conference(var.pagings)	No assessment of total fat on body fatness
Verheijden MW, van der Veen JE, van Zadelhoff WM, Bakx C, Koelen MA, van den Hoogen HJ, et al. Nutrition guidance in Dutch family practice: behavioral determinants of reduction of fat consumption. *American Journal of Clinical Nutrition*. 2003;77(4 Suppl):1058s-64s	No relevant outcomes
Wang HT. Longitudinal association between dairy consumption and changes of body weight and waist circumference: The Framingham Heart Study.*International Journal of Obesity*. 2014;38(2):299-305	No total fat intake assessment
Wolongevicz DM, Zhu L, Pencina MJ, Kimokoti RW, Newby PK, D'Agostino RB, et al. Diet quality and obesity in women: the Framingham Nutrition Studies. *British Journal of Nutrition*. 2010;103(8):1223-9	No relevant outcomes
Yadav VM. Effects of a low fat plant based diet in multiple sclerosis (MS): results of a 1-year long randomised controlled (RC) study. Neurology. 2014;Conference(var.pagings)	Multiple sclerosis patients
Yin JQ. Maternal diet, breastfeeding and adolescent body composition: A 16-year prospective study. *European Journal of Clinical Nutrition*. 2012;66(12):1329-34	No total fat intake assessment
Yoshimura YK. Relations of nutritional intake to age, sex and body mass index in Japanese elderly patients with type2 diabetes: The Japanese Elderly Diabetes Intervention Trial. *Geriatrics and Gerontology International*. 2012;12(SUPPL.1):29-40	Cross-sectional

Table 4. Excluded adult cohort studies *(Continued)*

Younossi ZMS. Prevalence and independent predictors of non-alcoholic fatty liver disease (NAFLD) in lean U.S population. *Hepatology*. 2011;Conference(var.pagings):October	NAFLD
Yuan BD. Study on transition of dietary patterns in Jiangsu province, 1989-2009, China. *FASEB Journal*. 2011;Conference(var.pagings):April. **2.** Yuan BD. Nutrition transition in Jiangsu, China, 1989-2009. *Annals of Nutrition and Metabolism*. 2013;Conference(var.pagings):2013	No total fat intake assessment
Zamora D, Gordon-Larsen P, Jacobs DR, Jr., Popkin BM, Zamora D, Gordon-Larsen P, et al. Diet quality and weight gain among black and white young adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study (1985-2005). *American Journal of Clinical Nutrition*. 2010;92(4):784-93	No assessment of total fat on body fatness
Zelber-Sagi SL. Non-alcoholic fatty liver disease (NAFLD) independently predicts type-2 diabetes and pre-diabetes during a seven-year prospective follow-up. *Journal of Hepatology*. 2012;Conference(var.pagings):April	No relevant outcomes

Table 5. Excluded child cohort studies

Study	Reason for exclusion
Alexy U, Libuda L, Mersmann S, Kersting M, Alexy U, Libuda L, et al. Convenience foods in children's diet and association with dietary quality and body weight status. *European Journal of Clinical Nutrition*. 2011;65(2):160-6	Not longitudinal
Ambrosini GLE. Identification of a dietary pattern prospectively associated with increased adiposity during childhood and adolescence. *International Journal of Obesity* (2005). 2012;36(10):1299-305. **2.**Ambrosini GLE. Tracking a dietary pattern associated with increased adiposity in childhood and adolescence. *Obesity*. 2014;22(2):458-65. **3.** Ambrosini GLL. An energy-dense, high fat, low fibre dietary pattern is prospectively associated with greater adiposity in adolescent girls in the Avon longitudinal study of parents and children. *Obesity Reviews*. 2010;Conference(var.pagings):July	No total fat intake assessment
Barton AJ, Gilbert L, et al. (2006). Cardiovascular risk in Hispanic and non-Hispanic preschoolers. *Nursing Research* 55(3): 172-9	Cross-sectional study
Berz JP, Singer MR, Guo X, Daniels SR, Moore LL, Berz JPB, et al. Use of a DASH food group score to predict excess weight gain in adolescent girls in the National Growth and Health Study. *Archives of Pediatrics & Adolescent Medicine*. 2011;165(6):540-6	No total fat assessment
Bigornia SJL. Dairy intakes at age 10 years do not adversely affect risk of excess adiposity at 13 years. *Journal of Nutrition*. 2014;144(7):1081-90	No total fat assessment
Boreham C, Twisk J, van Mechelen W, Savage M, Strain J, Cran G. Relationships between the development of biological risk factors for coronary heart disease and lifestyle parameters during adolescence: The Northern Ireland Young Hearts Project. *Public Health*. 1999;113(1):7-12	No relevant outcomes
Burke V, Beilin LJ, Simmer K, Oddy WH, Blake KV, Doherty D, et al. Predictors of body mass index and associations with cardiovascular risk factors in Australian children: a prospective cohort study.*International Journal of Obesity* (Lond). 2005;29(1):15-23	No baseline fat intake
Burke V, Beilin LJ, et al. (2006). Television, computer use, physical activity, diet and fatness in Australian adolescents. *International Journal of Pediatric Obesity* 1(4): 248-55	Cross-sectional study
Chaput J-P, Tremblay A, et al. (2008). A novel interaction between dietary composition and insulin secretion: effects on weight gain in the Quebec Family Study. *American Journal of Clinical Nutrition* 87(2): 303-9	No relevant exposures

Table 5. Excluded child cohort studies *(Continued)*

Davis JN, Alexander KE, et al. Inverse relation between dietary fiber intake and visceral adiposity in overweight Latino youth. *American Journal of Clinical Nutrition* 2009; 90(5): 1160-6	Unsuitable analyses
Deshmukh UJ. Growth and body composition changes in Indian undernourished children. *Annals of Nutrition and Metabolism*. 2013;Conference(var.pagings):2013	No relevant outcomes
Dubois L, Farmer A, et al. (2007). Regular sugar-sweetened beverage consumption between meals increases risk of overweight among preschool-aged children. *Journal of the American Dietetic Association* 107(6): 924-34	Invalid study design
Elliott SAT. Associations of body mass index and waist circumference with: energy intake and percentage energy from macronutrients, in a cohort of Australian children. *Nutrition Journal*. 2011;10(1)	Cross-sectional
Enes CC, Slater B, Enes CC, Slater B. Variation in dietary intake and physical activity pattern as predictors of change in body mass index (BMI) Z-score among Brazilian adolescents. *Revista Brasileira de Epidemiologia*. 2013;16(2):493-501	Not prospective
Faith MS, Dennison BA, et al. (2006). Fruit juice intake predicts increased adiposity gain in children from low-income families: weight status-by-environment interaction. *Pediatrics* 118(5): 2066-75	No relevant exposures
Frohnert BIJ. Relation between serum free fatty acids and adiposity, insulin resistance, and cardiovascular risk factors from adolescence to adulthood. *Diabetes*. 2013;62(9):3163-9	No total fat assessment
Heppe DH, Kiefte-de Jong JC, Durmus B, Moll HA, Raat H, Hofman A, et al. Parental, fetal, and infant risk factors for preschool overweight: the Generation R Study. *Pediatric Research*. 2013;73(1):120-7	No total fat intake assessment
Hooley M, Skouteris H, Millar L, Hooley M, Skouteris H, Millar L. The relationship between childhood weight, dental caries and eating practices in children aged 4-8 years in Australia, 2004-2008. *Pediatric Obesity*. 2012;7(6):461-70	No total fat intake assessment
Hopkins DS. The effect on growth of using cows milk as the main drink for infants. *Annals of Nutrition and Metabolism*. 2011;Conference(var.pagings):October	Infants
Huh SYR. Prospective association between milk intake and adiposity in preschool-aged children. *Journal of the American Dietetic Association.* 2010;110(4):563-70	No total fat intake assessment
Humenikova L, Gates GE (2007). Dietary intakes, physical activity, and predictors of child obesity among 4-6th graders in the Czech Republic. *Central European Journal of Public Health* 15(1): 23-8	Cross-sectional
Isharwal S, Arya S, et al. (2008). Dietary nutrients and insulin resistance in urban Asian Indian adolescents and young adults. *Annals of Nutrition & Metabolism* 52(2): 145-51	Invalid study design
Kagura J, Feeley AB, Micklesfield LK, Pettifor JM, Norris SA, Kagura J, et al. Association between infant nutrition and anthropometry, and pre-pubertal body composition in urban South African children. *Journal of Developmental Origins of Health and Disease*. 2012;3(6):415-23	No total fat intake assessment
Khalil HM. Developmental trajectories of body mass index (BMI) from birth to late childhood and their relation with paternal and child nutrients intake. *Obesity Facts*. 2014;Conference(var.pagings):May	No relevant outcomes
Labayen I, Ruiz JR, Ortega FB, Huybrechts I, Rodríguez G, Jiménez-Pavón D, et al. High fat diets are associated with higher abdominal adiposity regardless of physical activity in adolescents; the HELENA study. *Clinical Nutrition*. 2014;33(5):859-66	Cross-sectional
Li SF. Dairy consumption with onset of overweight and obesity among U.S. adolescents.*FASEB Journal*. 2014;Conference(var.pagings)	No total fat intake assessment

Table 5. Excluded child cohort studies *(Continued)*

Magnussen CG, Thomson R, Cleland VJ, Ukoumunne OC, Dwyer T, Venn A, et al. Factors affecting the stability of blood lipid and lipoprotein levels from youth to adulthood: evidence from the Childhood Determinants of Adult Health Study. *Archives of Pediatrics & Adolescent Medicine*. 2011;165(1):68-76	No relevant outcomes
Manios Y. (2006). Design and descriptive results of the "Growth, Exercise and Nutrition Epidemiological Study in preSchoolers": The GENESIS Study. *BMC Public Health* 6(32)	No fat to weight relationship
Mete MS. Dietary patterns and depression in a population with high prevalence of obesity: The strong heart family study. *Circulation*. 2012;Conference(var.pagings)	No total fat intake assessment
Millar L, Rowland B, Nichols M, Swinburn B, Bennett C, Skouteris H, et al. Relationship between raised BMI and sugar sweetened beverage and high fat food consumption among children. *Obesity*. 2014;22(5):E96-103. **2.** Millar LMR. Sugar sweetened beverage and high fat food consumption are related to raised BMI z-scores among a cohort of Australian children from 4 to 10 years of age. *Obesity Facts*. 2013;Conference(var.pagings):May.	No total fat assessment
Oldewage-Theron W, Napier C, Egal A. Dietary fat intake and nutritional status indicators of primary school children in a low-income informal settlement in the Vaal region... [corrected] [published erratum appears in S AFR J CLIN NUTR 2011; 24(3):164]. *South African Journal of Clinical Nutrition*. 2011;24(2):99-104	Cross-sectional
Pala VL. Dietary patterns and longitudinal change in body mass in European children: a follow-up study on the IDEFICS multicenter cohort. *European Journal of Clinical Nutrition*. 2013;67(10):1042-9	No total fat intake assessment
Pan A, Malik VS, Hao T, Willett WC, Mozaffarian D, Hu FB, et al. Changes in water and beverage intake and long-term weight changes: results from three prospective cohort studies. *International Journal of Obesity*. 2013;37(10):1378-85	No total fat intake assessment
Puengputtho WL. Salt intake and salt reduction in secondary school-age students of Princess Chulabhorn's College Chiangrai (Regional science school). *Annals of Nutrition and Metabolism*. 2013;Conference(var.pagings):2013	No total fat intake on weight assessment
Riedel CV. Interactions of genetic and environmental risk factors with respect to body fat mass in children: Results from the ALSPAC study. *Obesity*. 2013;21(6):1238-42	No total fat intake assessment
Scharf RJ, Demmer RT, Deboer MD. Longitudinal evaluation of milk type consumed and weight status in preschoolers. *Archives of Disease in Childhood*. 2013;98(5):335-40	No total fat intake assessment
Serra-Majem L, Aranceta-Bartrina J, et al. Prevalence and determinants of obesity in Spanish children and young people. *British Journal of Nutrition*. 2006;96 Suppl 1: S67-72	Cross-sectional
Vazaiou AP. Protein intake of toddlers in Greece and its nutritional consequences. *Hormone Research in Paediatrics*. 2011;Conference(var.pagings):October	No assessment of total fat on body fatness
Weijs PJM. High beverage sugar as well as high animal protein intake at infancy may increase overweight risk at 8 years: a prospective longitudinal pilot study. *Nutrition Journal*. 2011;10(1)	Infants
Williams CL, Strobino BA. Childhood diet, overweight, and CVD risk factors: the Healthy Start project. *Preventive Cardiology*. 2008;11(1):11-20	No relevant outcomes
Wosje KS, Khoury PR, Claytor RP, Copeland KA, Hornung RW, Daniels SR, et al. Dietary patterns associated with fat and bone mass in young children. *American Journal of Clinical Nutrition*. 2010;92(2):294-303	No total fat intake assessment
Yin JQ. Maternal diet, breastfeeding and adolescent body composition: A 16-year prospective study. *European Journal of Clinical Nutrition*. 2012;66(12):1329-34	No total fat intake assessment

Table 5. Excluded child cohort studies *(Continued)*

Zaki MH. Identifying obesogenic dietary factors among Egyptian obese adolescents. *Annals of Nutrition and Metabolism*. 2013;Conference(var.pagings):2013	No relevant outcomes
Zhang ZG. Added sugar intake and lipids profile among us adolescents: Nhanes 2005-2010. *Circulation*. 2014;Conference(var.pagings):25	Cross-sectional

Table 6. Risk of bias of included adult cohort studies

Study	Number lost to follow-up	Baseline similarity by total fat intake, funding, control groups	Adjustments (where stratified not counted as not being adjusted)*	Method of assessment	Risk of bias**
CARDIA Ludwig 1999 (1) **USA**	5111 attended original screening, 3609 attended at years 1, 7 and 10, 2909 included in analysis **43% lost or not analysed** **Reasons:** exclusion of those who were pregnant or lactating, with diabetes, on lipid or BP medication or with extreme dietary factors	**Different**. Those with lower total fat intake were more likely to be women, non-smokers, more physically active, with higher alcohol and vitamin supplement intake **Funded by**: NHLBI, NIDDKD **Control group:** internal	Weight was adjusted for baseline weight. Analysis adjusted for energy, sex, age, field centre, education, energy intake, physical activity, cigarette smoking, alcohol intake, vitamin supplement use. **All adjusted for**	**Interviewer- administered FFQ (700 foods)** **Single** (multiple dietary assessments – but appear to use baseline data only in analysis)	**High**
Danish Diet Cancer & Health Study Halkjaer 2009 (2-4) **Denmark**	57,043 at baseline, 44,897 re-assessed 5 years later **21% lost or not analysed** **Reasons:** 1781 had died, 435 emigrated, remainder did not want to participate or did not reply	Data not reported **Unclear** **Funded by:** National Danish Research Foundation, DiOGenes (EU funding) **Control group:** internal	BMI, energy, age, smoking, alcohol, wine, beer, spirits, sporting activity **Not adjusted for ethnicity, or socioeconomic status**	**192-item semi-quantitative FFQ checked by dietitian** **Single** dietary assessment used	**High**
	57,053 at baseline, 22,433 included in 5-year analysis. **61% lost or not analysed** **Reasons:** excluded aged ≥ 60 years (baseline) or ≥ 65 years (follow-up), did not attend follow-up, illness at baseline or during follow-up, average weight gain or loss > 5 kg/year or waist circumference > 7 cm/year, lack of blood sample or other baseline data	Data not reported. **Unclear** **Funded by:** National Danish Research Foundation, DiOGenes (EU funding) **Control group:** internal	Age, sex, physical activity, smoking, education, follow-up time, fibre intake, glycaemic index, hormone treatment and baseline body weight or waist circumference (analysed as %E from fat, so adjusted for E) **Not adjusted for ethnicity**	**192-item semi-quantitative FFQ checked by dietitian** **Single** dietary assessment used	**High**

Table 6. Risk of bias of included adult cohort studies *(Continued)*

Danish MONICA Iqbal 2006 (5) **Denmark**	2025 at baseline, 1762 re-assessed 5 years later **13% lost or not analysed** **Reasons:** missing or very high energy or unknown history of family obesity	Data not reported **Unclear** **Funded by:** Apotekerfonden & Danish Ministry for Health **Control group:** internal	Baseline BMI, age, physical activity, smoking, education level, cohort, volume, energy intake **Not adjusted for ethnicity**	**Weighed 7-day food record** **Single** dietary assessment used	**Moderate**
Diabetes Control & Complications Trial (DCCT) & EDIC **Cundiff 2012 (6)**	1441 at baseline, 1055 analysed at 14 to 19 years **27% lost or not analysed** **Reasons:** omitted 137 with HbA1c > 9.5, otherwise losses not described in this publication Note: also analysed FAO/WHO data from 167 countries, but these appear cross-sectional	Data not reported **Unclear** **Funded by:** Data collection by NIH, General Clinical Research Center Program (NCRR), analysis not funded **Control group:** internal	Energy, fibre, saturated, mono- and poly-unsaturated fat, alcohol, exercise (probably) **Not adjusted for age, sex, ethnicity or SES**	**1 week food record** (unclear whether recall or diary based) **Multiple** dietary assessments (baseline, 2, 5 yrs and completion averaged)	**High**
EPIC-PANACEA **Vergnaud 2013 (7)** **EPIC** **Beulens 2014 (8)**	521,448 recruited, 373,803 included in analysis **28% lost or not analysed** **Reasons:** omitted 23,713 with missing or implausible baseline data, 121,866 with missing follow-up weight, 2066 with implausible weight changes	Those with lower fat intake tended to be older, more physically active and less likely to smoke **Dissimilar** **Funded by:** EU and a wide range of charities and government funders **Control group:** internal	Adjusted for age, baseline BMI, study centre, weekday, season, total E (from non-alcohol sources, and from alcohol sources), smoking, education, physical activity **Not adjusted for ethnicity**	**Quant. dietary questionnaire of 88-266 items (country-specific)** **Single** dietary assessment used	**High**
	Unclear how many were included compared with recruited **unclear% lost or not analysed** **Reasons:** unclear	Data not reported **Unclear** **Funded by:** unclear **Control group:** internal	Adjustments unclear **Not adjusted for ... unclear**	Country-specific FFQs	**High**
Health Professionals Follow-Up Study (HPFUS)	36,353 returned 1992 questionnaires, of whom 19,478 were included in this analysis **46% lost or not analysed**	Data not reported **Unclear** **Funded by:** NIH and Centres for Disease Control	Baseline weight, energy, height, activity, TV viewing, high BP, high cholesterol	**FFQ** **Single** dietary assessment used	**High**

Table 6. Risk of bias of included adult cohort studies *(Continued)*

Coakley 1998 (9) **USA**	**Reasons:** 9345 had cancer, heart disease, diabetes or stroke, 7530 were missing key information	**Control group:** internal	**Not adjusted for ethnicity, socioeconomic status**		
Melbourne Collaborative Cohort Study (MCCS) **MacInnis 2013 (10)** **Australia**	Of 9066 at baseline, 5879 included in analyses. **35% lost or not analysed** **Reasons:** 656 died, 1894 declined, 21 did not have waist circumference or weight at follow-up, and 616 lost ≥ 5 kg weight so excluded	Data not reported **Unclear** **Funded by:** Cancer Council Victoria, VicHealth, National Health and Medical Research Council **Control group:** internal	Weight adjusted for baseline weight, waist for baseline waist circumference. All adjusted for sex, age, physical activity, alcohol, education, smoking, marital status, SES, total energy intake. **Not adjusted for ethnicity** (all described as "Australian-born" but > 20% born in Europe)	**Self administered 121-item FFQ developed for study** **Single** dietary assessment used	**High**
Memphis **Klesges 1992 (11-13)** **USA**	417 were enrolled, 294 were included in weight change analysis, and 230 in the waist circumference change analysis **29% lost or not analysed (weight), 45% (waist)** **Reasons:** "attrition" for weight change, no explanation of further losses for waist circumference data	Data not reported **Unclear** **Funded by:** NHLBI and Tennessee Centres of Excellence **Control group:** internal	Sex, age, pregnancy status, smoking, alcohol, family risk of obesity, energy intake, sports activity, work activity, leisure activity, change from baseline of energy, fat intake, activity, cigarettes **Not adjusted for socioeconomic status**	**Willett's FFQ** **Single** (multiple dietary assessments – but appear to be using baseline data in analysis)	**High**
NHANES Follow-up **Kant 1995 (14)** **USA**	14,407 were enrolled and eligible, 7147 were included in analysis. **50% lost or not analysed** **Reasons:** no dietary info, unsatisfactory 24-hour recalls, atypical intake, proxies, mistakes, pregnant or lactating participants, lack of weight data, death	Higher fat as %E associated with younger age, more smoking, higher levels of morbidity **Funded by:** unclear **Control group:** internal	Baseline age, race, education, BMI, energy intake, smoking, physical activity, duration of follow-up, alcohol, morbidity, special diet, parity **All adjusted for**	**24-hour dietary recall** **Single** dietary assessment used	**High**
Nurses' Health Study **Colditz 1990 (15)** **Field 2007 (16)** **USA**	Of 121,700 women enrolled, 38,724 were eligible for this study, 31,940 women included in analyses **17% lost or not analysed** **Reasons:** non-respondent or invalid FFQ	Data not reported **Unclear** **Funded by:** NIH **Control group:** internal	Age, BMI, energy intake **Not adjusted for ethnicity, physical activity, socioeconomic status**	**61-item FFQ** **Single** dietary assessment used	**High**
	Of 121,700 women enrolled, 41,518 included in analyses **66% lost or not analysed**	Greater fat intake associated with greater baseline weight	Age, baseline BMI, activity, menopausal status, smoking, protein intake, change in protein intake	**136-item FFQ in 1986** **Single** dietary assessment	**High**

Table 6. Risk of bias of included adult cohort studies *(Continued)*

	Reasons: of 121,700, 41,518 assessed in 1986 and at 8 years, were free of cancer, hypertension and diabetes, and eligible for this study	**Unclear** **Funded by:** Boston Obesity Nutrition Research Center and National Cancer Institute **Control group:** internal	**Not adjusted for ethnicity or SES**	used	
Pawtucket HHP **Parker 1997 (17)** **USA**	Of 1081 enrolled, FFQ administered to random sub-sample of 556, 465 included in analysis **16% lost or not analysed** **Reasons:** those excluded were those who did not attend both relevant appointments, and were more male, less educated, less active, greater BMI	Data not reported **Unclear** **Funded by:** NHLBI **Control group:** internal	Age, BMI, energy, smoking, activity **Not adjusted for sex, ethnicity or socioeconomic status**	**Willett's FFQ with categories added for fats, oils, sweets, snacks and dairy products** **Single** dietary assessment used	**High**
San Luis Valley Diabetes Study (SLVDS) **Mosca 2004 (18)** **USA**	Of 1351 enrolled, 782 "included in analysis", unclear how many in prospective analysis **unclear% lost or not analysed** **Reasons:** unclear how many lost and how many excluded. Of 1351, 1027 had and 782 continued to have normal glucose tolerance tests, 140 altered smoking status or became pregnant and were excluded. 782 completed visit 1, 536 visit 2 and 375 visit 3	Data not reported **Unclear** **Funded by:** not stated **Control group:** internal	Sex, ethnicity, physical activity, baseline BMI, age, smoking status, energy intake **Not adjusted for SES**	**24-hour diet recall** (bilingual interviewers) with visual aids for food portions	**High**
SEASONS **Ma 2005 (19)** **USA**	Of 1257 in original cohort, 641 completed baseline questionnaire and one blood draw, 572 included in analyses **11% lost or not analysed** **Reasons:** unclear, did not attend further appointments	Data not reported **Unclear** **Funded by:** NHLBI **Control group:** internal	None (but analysed as %E from fat, so energy adjusted for indirectly) **Not adjusted for age, sex, ethnicity, physical activity or socioeconomic status**	**7-day dietary recall** **Single** (Multiple dietary assessments – but appear to be using baseline data in analysis)	**High**
Women's Gothenburg **Lissner 1997 (20)** **Sweden**	Of 1462 in main cohort, 437 randomly selected and asked for dietary information, 361 included in analysis. **17% lost or not analysed Reasons:** 64 did not return for weight assessment, 12 had chronic illness so excluded	Higher fat as %E associated with younger age, higher energy intake, more walking and lifting at work, greater likelihood of being a smoker	Baseline body weight, activity, smoking, age, energy **Not adjusted for ethnicity or socioeconomic status**	**Dietary interview including frequency of 69 food items** **Single** dietary assessment used	**High**

Table 6. Risk of bias of included adult cohort studies *(Continued)*

		Funded by: Swedish Medical Research Council **Control group:** internal			

*Of age, sex, energy intake, ethnicity, physical activity (and/or TV watching) and socioeconomic (which includes educational) status.
**Moderate risk of bias was suggested where < 20% were lost to follow-up, up to two factors were unadjusted for in the design or analysis, and diet was assessed using a 24-hour recall or diet diary. All other studies were at high risk of bias.
Reference numbers relate to references below Table 1.
Abbreviations: BMI: body mass index; BP: blood pressure; FAO: Food and Agriculture Organization; FFQ: food frequency questionnaire; NIH: National Institutes of Health; NHLBI: National Heart, Lung and Blood Institute; NIDDKD: National Institute of Diabetes and Digestive and Kidney Diseases; SES: socioeconomic status; WHO: World Health Organization

Table 7. Risk of bias of included cohort studies in children and young people

Study	Number lost to follow-up	Baseline similarity, funding, control group	Adjustments*	Method of dietary assessment	Risk of bias**
Adelaide Nutrition Study **Magarey 2001 (1)** **Australia**	Of 500 recruited to ANS at birth only 130 were seen at age 11, so a further 113 from a separate cohort were added at age 11 **˜74% lost (varied for different follow-ups)** **Reason:** did not attend **Lost characteristics:** not stated	Data not reported Unclear **Funded by:** National Heart Foundation of Australia, Adelaide Children's Hospital Research Foundation, National Health and Medical Research Council of Australia **Control group:** internal	Adjusted for energy intake, previous adiposity, adiposity of parent at a specific age **Not adjusted for sex, ethnicity, physical activity or SES (4)**	**3-day weighed food record**	High
Amsterdam Growth & Health Long. Study (AGAHLS) **Twisk 1998, Koppes 2009 (2;3)** **Netherlands**	Of 307 13-year olds recruited 181 were reassessed at age 27 **41% lost** **Reason:** unclear **Lost characteristics:** "for the variables of interest no drop-out effects were observed"	Data not reported Unclear **Funded by:** Dutch Heart Foundation, Dutch Prevention Fund, Dutch Ministry of Wellbeing and Public Health, Dairy Foundation on Nutrition and Health, Netherlands Olympic Committee, Netherlands Sports Fed., no additional funding was stated for the	Adjusted for physical activity, smoking, alcohol, dietary energy and macronutrient intake. Did not adjust for sex, would have if appropriate. **Not adjusted for ethnicity, parental BMI, or SES (3)**	**Modified cross-check dietary history interview relating to previous month**	High
	Of 698 13-year olds recruited (those above plus another school with fewer assessments) 350 had complete data at age 36 **50% lost**		Carried out for boys and girls separately, at each age. Skinfold data (not % body fat) additionally adjusted for physical activity	As above	High

Table 7. Risk of bias of included cohort studies in children and young people *(Continued)*

	Reason: unclear **Lost characteristics:** girls who completed follow-up had slightly lower body fat %age, and boys who completed had lower tobacco and alcohol use at baseline	36-year old analysis **Control group:** internal	**Not adjusted for ethnicity, parental BMI, physical activity or SES (4)**		
Bogaert 2003 (4) **Australia**	Of 59 recruited, 41 were re-assessed at 12 months **31% lost** **Reason:** unclear **Lost characteristics:** unclear	Data not reported Unclear **Funded by:** Australian Rotary Health Found., Financial Markets Found. for Children, National Health & Medical Research Council **Control group**: internal	Adjustment not described (or not done) – unclear **Assume not adjusted for age, sex, ethnicity, parental BMI, physical activity or SES (6)**	2 food records and 1 24-hour recall from	High
Carruth & Skinner 2001 (5;6) **USA**	Of 72 recruited 53 took part at 70 months **26% lost** **Reason:** 7 parents declined, 7 not in area, 5 could not be scheduled in timeframe **Lost characteristics:** unclear	Data not reported **Unclear** **Funded by:** Gerber products, Tennessee Agricultural Experiment Station Control group: internal	Adjusted for BMI (all children white and of same age) **Not adjusted for sex, energy intake, parental BMI, physical activity or SES (5)**	3-day dietary intake interviews by dietitian	High
	62 of 72 recruited (98 recruited at 2 mo of age), plus 2 added at 1 year and 6 added at 2 years took part **unclear % lost** **Reason:** as above? **Lost characteristics:** unclear		Adjusted for BMI at 2 years and adiposity rebound age, assessed across ages 2 to 8, all children white and "predominantly middle or upper socioeconomic status" Factors assessed but found non-significant so not adjusted for included sex, TV-watching, parental BMI **All adjusted for (0)**	3-day dietary intake interviews	High
Davison 2001 (7)	197 participants at study entry, 192 re-assessed 2 years later **3% lost** **Reason:** unclear	Data not reported **Unclear** **Funded by:** NIH **Control group:** internal	BMI, levels of activity, familial risk of overweight, change in BMI (mother), enjoyment of activity (father), total energy intake (father), and girls' percentage fat intake (girls). **Not adjusted for SES (1)**	**24-hour dietary recall**	Moderate

Table 7. Risk of bias of included cohort studies in children and young people *(Continued)*

	Lost characteristics: none stated				
ELANCE **Rol-land-Cachera 2013 (8)** **France**	Unclear how many 10-month olds, but 222 attended at 10 months and either 2 or 4 years, 73 attended at 20 years, 68 included in analyses. > **67% lost** **Reason:** unclear **Lost characteristics:** "similar" between those lost to follow-up and those included	Data not reported **Unclear** **Funded by:** Institut Benjamin Delessert **Control group:** internal	Total energy intake, sex, breast feeding, mother's BMI, father's occupation **Not adjusted for ethnicity or physical activity (2)**	**Dietary history** (dietitian discussion of diet with parent over past month)	High
European Youth Heart Study **Brixval 2009 (9)** **Denmark**	384 of 589 baseline children attended follow-up, 308 in regression model **48% lost** **Reason:** "due to ethical consideration it was not permitted to contact subjects who decided not to participate at follow-up" **Lost characteristics:** not stated	Data not reported **Unclear** **Funded by:** not stated **Control group:** internal	Age, puberty status, total energy intake, parental income, activity, overweight parents, protein intake, birth weight. Presented by sex **Not adjusted for ethnicity (1)**	Interview and questionnaire of children and parents relating to past 24 hours	High
Klesges 1995 (10) **USA**	203 children at baseline, 146 at follow-up **28% lost** **Reason:** unclear **Lost characteristics:** "no significant differences" (P value > 0.15) in BMI, energy intake, fat as %E, physical activity, sex or familial obesity risk between those attending at 2 years and those not attending	Data not reported **Unclear** **Funded by:** National Heart Lung and Blood Institute **Control group:** internal	Age, sex, BMI, physical activity **Not adjusted for ethnicity, SES (2)**	Dietary FFQ	High
OMDCC Lee 2012 (11) **Korea**	2740+ baseline children (unclear), 1504 followed up **45% lost** **Reasons:** "analytic sample" – no reasons given **Lost characteristics**: unclear	Data not reported Unclear **Funded by:** unclear **Control group:** internal	Age, sex, sexual maturation, baseline BMI, exercise, TV time, sleep, parental BMI and education, energy intake, food habits and household income **Not adjusted for ethnicity (1)**	24-hour recall for 2 weekdays and 1 weekend day	High
TAAG	Of 303 randomly selected at baseline, 265 analysed	Data not reported	Age, ethnicity, physical activity	FFQ	High

Table 7. Risk of bias of included cohort studies in children and young people *(Continued)*

Cohen 2014 (12)	**13% lost** **Reasons:** 38 did not have complete data **Lost characteristics:** no difference in race, age, mother's education	**Unclear** **Funded by:** National Heart Lung and Blood Institute **Control group:** internal	**Not adjusted for energy intake, parental BMI or SES (3)**		
Viva la Familia Study Butte 2007 (13) **USA**	1030 at baseline, with 879 returning after 1 year **15% lost** **Reasons:** unclear **Lost characteristics:** none stated	Data not reported Unclear **Funded by:** NIH, USDA/ARS **Control group:** internal	Adjusted for sex, age, age squared, and Tanner stage and BMI status in Generalised Estimating Equations **Not adjusted for parental BMI, physical activity and SES (3)**	**24-hour recall**, measured by a registered dietitian	High

* Of age, sex, energy intake, ethnicity, parental BMI, physical activity (and/or TV watching) and socioeconomic (which includes educational) status
** Moderate risk of bias was suggested where < 20% were lost to follow-up, up to three factors were unadjusted for in the design or analysis, and diet was assessed using a 24-hour recall or diet diary. All other studies were at high risk of bias.
References are the same as those following Table 2.
Abbreviations: ANS: Adelaide Nutrition Study; BMI: body mass index; FFQ: food frequency questionnaire; NIH: National Institutes of Health; SES: socioeconomic status; USDA/ARS: US Department of Agriculture/ Agricultural Research Service.

Table 8. Subgrouping: effects on weight of reducing fat

Factor assessed	**Subgroup**	**Effect on weight, kg (95% CI)**	**Number of comparisons**	**Number of participants**	**I^2 for subgroup**	**Chi^2 test for subgroup differences**
Duration of dietary advice	6 to < 12 months	-1.7 (-2.3 to -1.1)	10	5305	71%	P value = 0.04
	12 to < 24 months	-2.0 (-2.5 to -1.5)	17	51367	71%	
	24 to < 60 months	-1.2 (-1.7 to -0.7)	9	49,286	56%	
	60+ months	-0.7 (-1.7 to 0.3)	4	40,838	58%	
Fat intake in the control group assessed during trial (equivalent to baseline fat intake)	> 35%E from fat	-0.9 (-1.1 to -0.8)	9	45,103	64%	P value < 0.00001
	> 30% to 35%E from fat	-0.8 (-1.2 to -0.5)	9	7123	73%	
	> 25% to 30%E from fat	-3.0 (-3.6 to -2.3)	5	2109	1%	
Sex	Women only	-1.4 (-1.9 to -0.9)	15	50,154	72%	P value = 0.20
	Men only	-2.7 (-4.3 to -1.2)	4	1719	76%	
	Mixed men and women	-1.1 (-2.0 to -0.2)	5	2492	79%	

Table 8. Subgrouping: effects on weight of reducing fat *(Continued)*

Year of first publication of the trial	1960s	-4.1 (-8.1 to -0.1)	1	1450	-	P value = 0.07
	1970s	-	0	0	-	
	1980s	-0.9 (-1.8 to -0.01)	3	288	0%	
	1990s	-1.9 (-2.6 to -1.3)	14	5941	80%	
	2000s	-0.9 (-1.6 to -0.3)	6	46,686	77%	
	2010s	-	0	0	-	
Difference in %E from fat between intervention and control groups	Up to 5%E from fat	-0.2 (-0.9 to 0.6)	5	4567	30%	P value = 0.003
	5 to < 10%E from fat	-2.1 (-2.9 to -1.4)	11	44,356	84%	
	10 to < 15%E from fat	-1.3 (-1.7 to -1.0)	4	8311	26%	
	15+%E from fat	-3.9 (-8.8 to 1.0)	3	319	68%	
Dietary advice or diet provided	Dietary advice	-1.6 (-2.0 to -1.1)	22	52,594	78%	P value = 0.04
	Diet provided	-0.7 (-1.3 to -0.1)	1	1741	-	
Dietary fat goals for intervention (these were not necessarily achieved)	30%E from fat	-1.0 (-1.7 to -0.3)	3	1628	0%	P value = 0.34
	25 to < 30%E from fat	-2.5 (-4.3 to -0.6)	5	509	90%	
	20 to < 25%E from fat	-0.9 (-1.2 to -0.6)	5	43,878	31%	
	15 to < 20%E from fat	-1.3 (-2.2 to -0.4)	7	7860	58%	
Total fat achieved in intervention group	> 30%E from fat	-0.8 (-1.3 to -0.4)	5	1767	0%	P value = 0.42
	≤ 30%E from fat	-1.1 (-1.6 to -0.6)	13	50,099	76%	
BMI at baseline (body mass index, kg/m^2)	< 25	-1.0 (-1.7 to -0.2)	8	1781	56%	P value = 0.17
	25 to < 30	-1.8 (-2.4 to -1.3)	15	51,297	83%	
	30+	-1.8 (-3.5 to -0.1)	1	69	-	
Baseline health of participants	Healthy	-1.0 (-1.6 to -0.4)	3	45,032	87%	P value = 0.12
	With risk factors	-2.2 (-3.2 to -1.2)	12	2166	79%	
	With disease	-1.2 (-1.9 to -0.6)	9	6449	44%	
Amount of energy reduction in the low fat arm	E intake the same or greater in low fat group	-0.5 (-1.5 to 0.5)	4	3352	25%	P value = 0.04
	1 to 100 kcal/d less in low fat arm	-1.5 (-2.9 to -0.1)	4	2398	66%	

Table 8. Subgrouping: effects on weight of reducing fat *(Continued)*

	101 to 200 kcal/d less in low fat arm	-1.1 (-2.2 to -0.04)	5	43,755	80%
	201+ kcal/d less in low fat arm	-2.2 (-3.0 to -1.5)	8	3954	78%

Note: studies that provide data at different time points or that fit into different categories have all been included, so studies may appear more than once in any series of subgroups.

Table 9. Data on dietary intake of energy, sugars, carbohydrate, protein and alcohol during the diet period of RCTs comparing low fat with usual fat intake

Trial	Energy intake (SD), kcal		Sugars intake, %E		CHO intake, %E		Protein intake, %E		Alcohol intake, %E		No. of participants	
	Int.	**Cont**	**Int.**	**Cont**	**Int.**	**Cont**	**Int.**	**Cont**	**Int.**	**Cont**	**Int.**	**Cont**
Auckland reduced fat, 1 yr	1887 (672)	2269 (750)	—	—	54.2 (10.5)	45.8 (10.9)	18.4 (3.5)	16.6 (3.9)	3.6 (7.0)	5.7 (7.0)	49	61
BDIT pilot studies, 9 yrs	1460 (376)	1578 (365)	—	—	49.6 (7.5)	46.9 (6.2)	15.5 (2.4)	15.3 (2.6)	2.3 (3.3)	1.7 (2.4)	76	81
BeFIT	(data not reported in control groups)											
Bloemberg, Δ to 6 mo	—	—	—	—	4.4 (6.5)	1.2 (6.1)	0.33 (2.9)	0.57 (1.7)	—	—	39	41
BRIDGES, 6 mo	-34 (79)	+ 22 (79)	—	—	—	—	—	—	—	—	48	46
Canadian DBCP, 2 yrs	1540 (317)	1759 (437)	—	—	60.3 (8.3)	48.8 (8.1)	18.0 (3.2)	16.9 (2.8)	—	—	104	100
De Bont, Δ to 6 mo	-98 (369)	-120 (485)	—	—	7.9 (9.5)	-0.1 (10.9)	2.4 (7.0)	1.7 (5.9)	-0.2 (1.6)	-0.4 (2.6)	71	65
DEER (diet alone), Δ to 1 yr	Women: -220 (356) Men: -285 (541)	Women: -19 (367) Men: -25 (482)	—	—	Women: +5.5 (8.0) Men: +8.0 (9.3)	Women: -0.2 (7.3) Men: +1.1 (6.6)	—	—	—	—	46, 49	45, 46
DEER (diet and ex), Δ to 1 yr	Women: -191 (343) Men: -167 (516)	Women: -54 (410) Men: +141 (437)	—	—	Women: +7.8 (6.2) Men: +9.3 (8.3)	Women: -0.3 (7.9) Men: +1.4 (6.3)	—	—	—	—	43, 48	43, 47
Diet and hormone study, 1 yr	1921 (386)	2063 (610)	—	—	64.3 (9.0)	54.6 (9.2)	14.5 (2.9)	14.1 (3.8)	est: 1 (2)	est: 1 (2)	81	96

Table 9. Data on dietary intake of energy, sugars, carbohydrate, protein and alcohol during the diet period of RCTs comparing low fat with usual fat intake *(Continued)*

Kentucky low fat, 1 yr	1882 (521)	2010 (528)	—	—	53 (8.9)	50 (7.9)	17 (3.4)	18 (4.3)	—	—	47	51
Kuopio, wks 14 to 28	AHA 1791 (382) Mono 1887 (478) Low fat 1648 (430)	1982 (406)	—	—	AHA 48 (5) Mono 47 (6) Low fat 51 (5)	46 (6)	AHA 17 (2) Mono 17 (20) Low fat 19 (3)	16 (2)	—	—	AHA 41 Mono 41 Low fat 40	37
Mastopathy diet, 6 mo	1491 (NR)	1676 (NR)	—	—	56.3 (NR)	48.1 (NR)	17.9 (NR)	15.8 (NR)	4.8 (NR)	4.2 (NR)	10	9
MeDiet, 6 mo	1676 (639)	1654 (498)	18.7 (6.9)	21.9 (9.2)	27.2 (17.0)	25.8 (11.0)	14.9 (4.7)	16.2 (5.1)	5.6 (11.1)	1.6 (2.2)	51?	55?
Moy, 2 yrs	1825 (NR)	2092 (NR)	—	—	—	—	—	—	—	—	117	118
MSFAT, 6 mo	2460 (NR)	2699 (NR)	—	—	47 (NR)	41 (NR)	16 (NR)	14 (NR)	3 (NR)	3 (NR)	117	103
NDHS open 1st 6 mo (for definitions of groups B, C and D see Characteristics of Included Studies)	B: 2154 (432)	C: 2262 (435) D: 2228 (456)	—	—	B: 48.7 (12.3)	C: 45.3 (12.1) D: 44.7 (11.7)	B: 18.6 (3.4)	C: 17.6 (3.1) D: 17.4 (3.1)	B: 3.7 (3.7)	C: 3.6 (4.0) D: 3.8 (4.0)	B: 339	C: 355 D: 346
NDHS open 2nd 6 mo (for definitions of groups BC, F and G see Characteristics of Included Studies)	BC: 2249 (492)	F: 2196 (427) G: 2169 (420)	—	—	BC: 45.7 (12.7)	F: 44.1 (11.1) G: 43.3 (11.4)	BC: 17.3 (3.5)	F: 7.3 (3.0) G: 17.7 (2.9)	BC: 3.5 (4.2)	F: 4.2 (4.0) G: 4.0 (4.5)	BC: 491	F: 214 G: 194
Nutrition and breast health, 1 yr	1780 and 1960	1571 and 1687	—	—	—	—	—	—	—	—	23 and 25	24 and 23
Nutrition education study, 6 to 9 mo	1534 (448)	1721 (620)	—	—	43.4 (9.5)	41.5 (8.9)	19.9 (3.7)	18.7 (4.4)	4.5 (7.2)	4.8 (9.3)	224	69

Table 9. Data on dietary intake of energy, sugars, carbohydrate, protein and alcohol during the diet period of RCTs comparing low fat with usual fat intake *(Continued)*

Pilkington, 1 yr	NR	NR	—	—	—	—	—	—	—	—	12	23
Polyp prevention trial, yr 4	1978 (471)	2030 (518)	—	—	58.3 (7.4)	47.1 (7.2)	17.3 (2.5)	16.5 (2.4)	—	—	605	581
Rivellese, 6 mo	NR	NR	14	10	55	48	18	16	—	—	27	17
Simon low fat, 1 yr	1570 (NR)	1594 (NR)	—	—	—	—	—	—	—	—	65	68
Sondergaard, 12 mo	—	—	—	—	52.3 (6.4)	48.5 (8.7)	17.0 (2.9)	16.6 (3.1)	4.5 (5.3)	6.4 (7.4)	62	51
Strychar, 6 mo	NR	NR	—	—	—	—	—	—	—	—	15	15
Swedish breast CA, Δ to 2 yrs	-215 (P value < 0.01)	-143 (P value < 0.01)	+4.8 (P value < 0.01)	+1.4 (P value < 0.01)	+11.0 (P value < 0.01)	+2.7 (P value < 0.01)	+1.7 (P value < 0.01)	+0.3 (P value > 0.05)	+0.2 (P value > 0.05)	+0.4 (P value > 0.05)	63	106
Veteran's dermatology, during trial	1995 (564)	2196 (615)	—	—	60.3 (6.3)	44.6 (6.9)	17.7 (2.2)	15.7 (2.4)	3.2 (3.4)	3.2 (3.9)	57?	58?
WHEL, 1 yr	1664 (345)	1635 (384)	—	—	65.3 (8.5)	57.1 (9.3)	—	—	—	—	197	196
WHI, 7.5 yrs	1446 (510)	1564 (595)	—	—	52.7 (9.8)	44.7 (8.5)	—	—	—	—	14246	22083
WHT: feasibility, 2 yrs	1356 (358)	1617 (391)	—	—	59.0 (8.8)	46.9 (8.9)	19.2 (3.9)	16.8 (3.8)	—	—	163	101
WHT: FSMP, Δ to 18 mo	-488 (NR)	-255 (NR)	—	—	—	—	—	—	—	—	285	194
WINS, 5 yrs	-167 (p value < 0.0001 vs cont)	0	—	—	—	—	—	—	—	—	380	648

est: estimated by review authors from data on g/d and mean energy intakes
Abbreviations: AHA: American Heart Association; CHO: carbohydrates; DBCP: Diet and Breast Cancer Prevention; SD: standard deviation

APPENDICES

Appendix 1. MEDLINE search run to collect adult and child RCTs and cohort studies 15 November 2014

Search adapted from that run in 2010, to search for both adult and child RCTs and cohort studies, but omitting dietary exposures other than dietary fat.

Run 15 November 2014.

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
----
1 exp Weight Gain/ (24259)
2 exp Weight Loss/ (30933)
3 obesity.ab,ti. (152189)
4 obese.ab,ti. (86464)
5 adipos$.ab,ti. (71315)
6 weight gain.ab,ti. (44371)
7 weight loss.ab,ti. (59414)
8 overweight.ab,ti. (42626)
9 over weight.ab,ti. (349)
10 overeat$.ab,ti. (1934)
11 over eat$.ab,ti. (275)
12 weight change$.ab,ti. (8042)
13 ((bmi or body mass index) adj2 (gain or loss or change)).ab,ti. (2786)
14 body fat$.ab,ti. (24784)
15 body composition.ab,ti. (23804)
16 body constitution.ab,ti. (257)
17 exp Dietary Fats/ (73523)
18 exp Diet, Fat-Restricted/ (3040)
19 (fat$ adj2 (total or intake or consum$ or ate or eat or reduce$ or restrict$ or low$ or diet$)).ab,ti. (63037)
20 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (366287)
21 17 or 18 or 19 (114331)
22 20 and 21 (28779)
23 randomized controlled trial.pt. (399992)
24 controlled clinical trial.pt. (90666)
25 Randomized controlled trials/ (99585)
26 random allocation.sh. (84070)
27 double blind method.sh. (132423)
28 single-blind method.sh. (20589)
29 23 or 24 or 25 or 26 or 27 or 28 (658672)
30 (animals not (human and animals)).sh. (5551801)
31 29 not 30 (590901)
32 clinical trial.pt. (501242)
33 exp Clinical trial/ (816129)
34 (clin$ adj25 trial$).ti,ab. (291641)
35 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab. (137043)
36 placebos.sh. (34004)
37 placebo$.ti,ab. (169148)
38 random$.ti,ab. (764596)
39 research design.sh. (82260)
40 comparative study.sh. (1730651)
41 exp Evaluation studies/ (206135)
42 follow up studies.sh. (520109)
43 prospective studies.sh. (390949)
44 (control$ or prospectiv$ or volunteer$).ti,ab. (3243146)
45 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 (5767873)
46 45 not 30 (4293785)
47 31 or 46 (4323589)
48 exp Cohort Studies/ (1438154)
49 (cohort$ or quintile$ or quartile$ or quantile$ or tertile$).mp. (411555)
50 (follow-up$ or followup$).mp,tw. (970994)

51 longitud$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (208935)
52 ((prospectiv$ or observation$) adj5 (research$ or data$ or stud$)).mp. (587538)
53 48 or 49 or 50 or 51 or 52 (2092058)
54 53 not 30 (1996509)
55 47 or 54 (4973664)
56 22 and 55 (9237)
57 limit 56 to (english language and yr="2010 - 2015") (3294)
58 exp Case-Control Studies/ (710182)
59 (case adj3 control$).tw. (93452)
60 (case adj3 series).tw. (42174)
61 case study/ (1736496)
62 letter.pt. (885169)
63 exp Drug Therapy/ (1125358)
64 exp Surgery/ (35422)
65 exp Biochemical Phenomena/ (3179065)
66 exp OBESITY/dt, ec, ra, ri, rt, su, ve [Drug Therapy, Economics, Radiography, Radionuclide Imaging, Radiotherapy, Surgery, Veterinary] (21417)
67 exp HIV/ (89024)
68 exp HIV infections/ (246055)
69 cancer.ti. (653428)
70 (tumour or tumor).ti. (242371)
71 lung.ti. (197074)
72 asthma.ti. (66394)
73 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 (8021499)
74 57 not 73 (1961)

Appendix 2. EMBASE search run to collect adult and child RCTs and cohort studies 14 November 2014

Search adapted from that run in 2010, to search for both adult and child RCTs and cohort studies, but omitting dietary exposures other than dietary fat.

Run 14 November 2014.

Database: EMBASE <1974 to 2014 November 14>
Search Strategy:
----
1 exp Weight Gain/ (67847)
2 exp weight reduction/ (104267)
3 obesity.ab,ti. (197751)
4 obese.ab,ti. (114407)
5 overweight.ab,ti. (55916)
6 over weight.ab,ti. (671)
7 ((weight or bmi or body mass index) adj2 (gain or loss or change or reduc$)).ab,ti. (154396)
8 exp fat intake/ (42075)
9 exp low fat diet/ (6962)
10 (fat$ adj2 (total or intake or consum$ or ate or eat or reduce$ or restrict$ or low$ or diet$)).ab,ti. (76246)
11 1 or 2 or 3 or 4 or 5 or 6 or 7 (440097)
12 8 or 9 or 10 (102724)
13 11 and 12 (27385)
14 controlled study/ (4458191)
15 randomized controlled trial/ (355956)
16 clinical trial/ (839688)
17 major clinical study/ (2275896)
18 (trial$ or control$).tw. (3805000)
19 (blind$ or placebo).tw. (383515)
20 placebo/ (260940)
21 14 or 15 or 16 or 17 or 18 or 19 or 20 (8434269)
22 exp human/ (15270878)
23 nonhuman/ (4404779)
24 23 not 22 (3499956)
25 21 not 24 (6542287)
26 exp Longitudinal Study/ (70712)

27 exp Prospective Study/ (266457)
28 (cohort$ or quintile$ or quartile$ or tertile$ or quantile$).mp. (498531)
29 (follow-up$ or followup$).mp,tw. (1184342)
30 longitud$.mp. (214152)
31 ((prospectiv$ or observation$) adj5 (research$ or data$ or stud$)).mp. (615851)
32 26 or 27 or 28 or 29 or 30 or 31 (2100044)
33 32 not 24 (2060027)
34 33 or 25 (7492226)
35 13 and 34 (12448)
36 limit 35 to (english language and yr="2010 - 2015") (6329)
37 exp Case-Control Studies/ (90210)
38 (case adj3 control$).tw. (107292)
39 (case adj3 series).tw. (51300)
40 case study/ (28823)
41 letter.pt. (860483)
42 exp Drug Therapy/ (1859698)
43 exp Surgery/ (3481521)
44 exp Biochemical Phenomena/ (81777)
45 exp obesity/cn, di, dr, dt, rt, su [Congenital Disorder, Diagnosis, Drug Resistance, Drug Therapy, Radiotherapy, Surgery] (33545)
46 exp HIV/ (138030)
47 exp HIV infections/ (303673)
48 cancer.ti. (812504)
49 (tumour or tumor).ti. (277200)
50 lung.ti. (240253)
51 asthma.ti. (82529)
52 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 (6915750)
53 36 not 52 (5003)

Appendix 3. CINAHL search run to collect adult and child RCTs and cohort studies 1 December 2014 (Interface EBSCO host Research Databases, Advanced Search, CINAHL Complete)

#	Query	Limiters/Expanders	Results
S1	(MH "weight gain+")	Search modes - Boolean/Phrase	62,681
S2	(MH "weight loss+")	Search modes - Boolean/Phrase	14,411
S3	TI obesity OR AB obesity	Search modes - Boolean/Phrase	32,659
S4	TI obese OR AB obese	Search modes - Boolean/Phrase	15,905
S5	TI adipos* OR AB adipos*	Search modes - Boolean/Phrase	6,462
S6	TI weight gain OR AB weight gain	Search modes - Boolean/Phrase	6,645
S7	TI weight loss OR AB weight loss	Search modes - Boolean/Phrase	11,452
S8	TI overweight OR AB overweight	Search modes - Boolean/Phrase	12,405
S9	TI over weight OR AB over weight	Search modes - Boolean/Phrase	1,157
S10	TI overeat* OR AB overeat*	Search modes - Boolean/Phrase	418
S11	TI over eat* OR AB over eat*	Search modes - Boolean/Phrase	321
S12	TI weight change* OR AB weight change*	Search modes - Boolean/Phrase	3,689

(Continued)

S13	(TI ((bmi or body mass index) N2 (gain or loss or change))) OR (AB ((bmi or body mass index) N2 (gain or loss or change)))	Search modes - Boolean/Phrase	862
S14	TI body fat* OR AB body fat*	Search modes - Boolean/Phrase	5,932
S15	TI body composition OR AB body composition	Search modes - Boolean/Phrase	5,353
S16	TI body constitution OR AB body constitution	Search modes - Boolean/Phrase	26
S17	(MH "Dietary Fats+")	Search modes - Boolean/Phrase	17,455
S18	(MM "Diet, Fat-Restricted")	Search modes - Boolean/Phrase	901
S19	(TI (fat* N2 (total or intake or consum* or ate or eat or reduc* or restrict* or low* or diet*))) OR (AB (fat* N2 (total or intake or consum* or ate or eat or reduc* or restrict* or low* or diet*)))	Search modes - Boolean/Phrase	11,074
S20	(S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16)	Search modes - Boolean/Phrase	99,408
S21	(S17 OR S18 OR S19)	Search modes - Boolean/Phrase	25,122
S22	(S20 AND S21)	Search modes - Boolean/Phrase	6,404
S23	PT randomized controlled trial	Search modes - Boolean/Phrase	45,326
S24	TX "controlled clinical trial"	Search modes - Boolean/Phrase	7,628
S25	MM "Randomized Controlled Trials"	Search modes - Boolean/Phrase	668
S26	MM "Random Assignment"	Search modes - Boolean/Phrase	147
S27	MM "Double-Blind Studies"	Search modes - Boolean/Phrase	76
S28	MM "Single-Blind Studies"	Search modes - Boolean/Phrase	26
S29	S23 OR S24 OR S25 OR S26 OR S27 OR S28	Search modes - Boolean/Phrase	52,650
S30	SU (animals not (human and animals))	Search modes - Boolean/Phrase	53,619
S31	S29 NOT S30	Search modes - Boolean/Phrase	52,575
S32	PT clinical trial	Search modes - Boolean/Phrase	77,533
S33	MH "Clinical Trials+"	Search modes - Boolean/Phrase	184,793
S34	TI (clin* N25 trial*) OR AB (clin* N25 trial*)	Search modes - Boolean/Phrase	53,327
S35	TI ((singl* or doubl* or trebl* or tripl* or quad*) N (blind* or mask*)) OR AB ((singl*	Search modes - Boolean/Phrase	300

(Continued)

	or doubl* or trebl* or tripl* or quad*) N (blind* or mask*))		
S36	MM "Placebos"	Search modes - Boolean/Phrase	828
S37	TI placebo* OR AB placebo*	Search modes - Boolean/Phrase	27,852
S38	TI random* OR AB random*	Search modes - Boolean/Phrase	144,733
S39	MM "study design"	Search modes - Boolean/Phrase	5,275
S40	MM "comparative studies"	Search modes - Boolean/Phrase	283
S41	MH "Evaluation Research+"	Search modes - Boolean/Phrase	20,984
S42	MM "prospective studies"	Search modes - Boolean/Phrase	800
S43	TI (control* or prospectiv* or volunteer*) OR AB (control* or prospectiv* or volunteer*)	Search modes - Boolean/Phrase	357,450
S44	S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43	Search modes - Boolean/Phrase	542,974
S45	S44 NOT S30	Search modes - Boolean/Phrase	535,502
S46	S31 OR S45	Search modes - Boolean/Phrase	541,731
S47	MH "prospective studies+"	Search modes - Boolean/Phrase	254,176
S48	TX cohort* or quintile* or quartile* or quantile* or tertile*	Search modes - Boolean/Phrase	152,914
S49	TX follow-up* or followup*	Search modes - Boolean/Phrase	249,854
S50	TX longitud*	Search modes - Boolean/Phrase	103,954
S51	TX ((prospectiv* or observation*) N5 (research* or data* or stud*))	Search modes - Boolean/Phrase	382,309
S52	S47 OR S48 OR S49 OR S50 OR S51	Search modes - Boolean/Phrase	613,040
S53	S52 NOT S30	Search modes - Boolean/Phrase	610,840
S54	S46 OR S53	Search modes - Boolean/Phrase	963,714
S55	S22 AND S54	Search modes - Boolean/Phrase	3,017
S56	S22 AND S54	Limiters - Published Date: 20100101-20151231; English Language Search modes - Boolean/Phrase	1,236
S57	MH "Case Control Studies+"	Limiters - Published Date: 20100101-20151231; English Language Search modes - Boolean/Phrase	23,820

(Continued)

S58	TX case N3 control*	Limiters - Published Date: 20100101-20151231; English Language Search modes - Boolean/Phrase	35,592
S59	TX case N3 series	Limiters - Published Date: 20100101-20151231; English Language Search modes - Boolean/Phrase	10,407
S60	MM "Case Studies"	Search modes - Boolean/Phrase	623
S61	PT letter	Search modes - Boolean/Phrase	198,888
S62	MH "Drug Therapy+"	Search modes - Boolean/Phrase	109,541
S63	MH "Surgery, Operative+"	Search modes - Boolean/Phrase	385,583
S64	MH "Biochemical Phenomena+"	Search modes - Boolean/Phrase	29,949
S65	MH "Obesity+/DT/EC/RA/RT/SU"	Search modes - Boolean/Phrase	5,470
S66	MH "Human Immunodeficiency Virus+"	Search modes - Boolean/Phrase	5,947
S67	MH "HIV Infections+"	Search modes - Boolean/Phrase	62,282
S68	TI cancer	Search modes - Boolean/Phrase	137,532
S69	TI tumor OR tumour	Search modes - Boolean/Phrase	21,392
S70	TI lung	Search modes - Boolean/Phrase	24,925
S71	TI asthma	Search modes - Boolean/Phrase	15,732
S72	S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71	Search modes - Boolean/Phrase	913,702
S73	S56 NOT S72	Search modes - Boolean/Phrase	765

Appendix 4. CENTRAL search run as part of the update in March 2014

#1 lipid near (low* or reduc* or modifi*)

#2 cholesterol* near (low* or modifi* or reduc*)

#3 (#1 or #2)

#4 MeSH descriptor: [Nutrition Therapy] explode all trees

#5 diet* or food* or nutrition*

#6 (#4 or #5)

#7 (#3 and #6)

#8 fat* near (low* or reduc* or modifi* or animal* or saturat* or unsaturat*)

#9 MeSH descriptor: [Diet, Atherogenic] explode all trees

#10 MeSH descriptor: [Diet Therapy] explode all trees

#11 (#7 or #8 or #9 or #10)

#12 MeSH descriptor: [Cardiovascular Diseases] this term only

#13 MeSH descriptor: [Heart Diseases] explode all trees

#14 MeSH descriptor: [Vascular Diseases] explode all trees

#15 MeSH descriptor: [Cerebrovascular Disorders] this term only

#16 MeSH descriptor: [Brain Ischemia] explode all trees

#17 MeSH descriptor: [Carotid Artery Diseases] explode all trees

#18 MeSH descriptor: [Dementia, Vascular] explode all trees

#19 MeSH descriptor: [Intracranial Arterial Diseases] explode all trees

#20 MeSH descriptor: [Intracranial Embolism and Thrombosis] explode all trees

#21 MeSH descriptor: [Intracranial Hemorrhages] explode all trees

#22 MeSH descriptor: [Stroke] explode all trees

#23 coronar* near (bypas* or graft* or disease* or event*)

#24 cerebrovasc* or cardiovasc* or mortal* or angina* or stroke or strokes or tia or ischaem* or ischem*

#25 myocardi* near (infarct* or revascular* or ischaem* or ischem*)

#26 morbid* near (heart* or coronar* or ischaem* or ischem* or myocard*)

#27 vascular* near (peripheral* or disease* or complication*)

#28 heart* near (disease* or attack* or bypas*)

#29 (#12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28)

#30 (#11 and #29)

FEEDBACK

Tobias 2016, 7 July 2016

Summary

In their systematic review and meta-analysis of 32 randomized controlled trials, representing 54,000 participants, Hooper et al. reported that a lower proportion of energy intake from total fat was associated with a small reduction in body weight (difference = 1.5 kg).[1] The authors' conclusion, however, was contradicted by findings from their parallel meta-analysis of 25 observational cohort studies. The erroneous conclusion from the review of trials is a consequence of biased study selection criteria, inclusion of short-term follow-up (<12 months), and other methodologic flaws.

First, their criteria explicitly included only trials in which weight loss was not an objective of the intervention. This led to the exclusion of several long-term, rigorously conducted RCTs designed specifically to test the hypothesis that the fat composition of the diet affects weight change. The criteria used by Hooper et al. resulted in a heterogeneous subset of the of low-fat dietary intervention RCTs, which included trials conducted to test the effects of low-fat diets on endpoints such as cancer incidence or lipids in higher risk study populations. In fact, only three trials in their meta-analysis were among healthy participants, not recruited on the basis of risk factors or disease. The authors' contend that including only studies not intending to alter weight would reduce potential publication bias. On the contrary, we believe this would increase the likelihood of publication bias, since investigators of diet trials not explicitly conducted for weight loss would not be motivated to publish null or contrary results. Since the point of this work is to advise generally healthy individuals as to how to maintain or lose weight, it is bizarre to specifically exclude trials designed to answer that question.

Second, the authors' included short-term trials (of as little as 6 months duration). Six months is typically when the effect of dietary interventions on body weight wane and weight regain commences; thus short-term results do not reflect sustained effects at 1 year or longer, which is of primary interest.[2]

Third, most of the studies included by Hooper et al. were seriously confounded by factors other than the fat content of the diet. Some of the trials coupled a low-fat intervention with other advice, such as eating more fruits and vegetables, which obscures the interpretation of the findings. The other key characteristic is the differences in intensity or attention between intervention groups (e.g., fewer or no in-person visits, dietary counseling meetings, etc), because the control group was often simply assigned to maintain their usual diet. Aspects related to the intensity of a dietary intervention, such as behavioral support, are modest predictors of weight loss success;[3] thus, most RCT's designed to assess the effects of diet composition on weight intentionally balanced the intensity of interventions, but these were the studies explicitly excluded by Hooper it al. In our previous meta-analysis of RCTs comparing low-fat vs. higher fat dietary interventions, we conducted stratified analyses by these key trial characteristics.[4] We observed that significant long-term weight loss favoring low-fat interventions was observed only for trials in which the comparator group was "usual diet" or received less attention during the intervention from study investigators. This was true regardless of whether the RCTs had a weight loss focus or not. Comparisons between low-fat and higher fat interventions of similar intensity demonstrated no benefit of low-fat over higher fat diets, regardless of weight loss goal. Indeed, the overall results of these trials favored a small but statistically significant greater weight loss with higher fat diets. Our findings clearly demonstrated the biased impact of differential attention across treatment groups.

Only 4 RCTs in Hooper's meta-analysis (419 total participants) remained after exclusion of trials in which control groups were asked simply to maintain usual diet or received differentially less attention than the low-fat intervention arms. Three were 6 month trials, and the fourth was published in 1960 among men with recent myocardial infarction to examine lipid changes after a 1 year intervention with either a low-fat or a "unsaturated-fat" diet.[5] These 4 RCTs also were judged by Hooper et al. to have relatively high "risk of bias" according to authors' methodological quality criteria.

In summary, the results from the most recent Hooper et al. meta-analysis provide no convincing evidence for recommending a low-fat diet for the prevention of weight gain and obesity in the general population. In fact, their strict exclusion criteria restricting the analysis only to trials in which weight-loss was not intended led to biased results. Although the authors' felt that limiting their analysis to non-weight loss trials would enhance validity, this selectively excluded trials designed to avoid confounding by intensity of intervention and other factors. Analysis of trials that include those specifically testing interventions for weight control, that exclude short-term trials, and account for key trial characteristics yield consistent results that are consonant with observational studies. Would we derive recommendations for statin use in the primary prevention of coronary heart disease solely from trials with a completely different disease endpoint? Promoting low fat diets for weight control can lead to increased consumption of refined carbohydrates, causing increased weight gain,4 an array of adverse metabolic effects,[6] and premature death.[7] The overall body of scientific evidence clearly demonstrates that dietary recommendations should focus not on lowering the total fat content of the diet but rather on specific types of fats and carbohydrates and, more importantly, on specific foods and overall dietary patterns.[8]

References

1. Hooper L, Abdelhamid A, Bunn D, Brown T, Summerbell CD, Skeaff CM. Effects of total fat intake on body weight. The Cochrane database of systematic reviews. 2015(8):CD011834.
2. Willett WC. Dietary fat plays a major role in obesity: no. Obesity reviews : an official journal of the International Association for the Study of Obesity. May 2002;3(2):59-68.
3. Johnston BC, Kanters S, Bandayrel K, et al. Comparison of weight loss among named diet programs in overweight and obese adults: a meta-analysis. Jama. Sep 3 2014;312(9):923-933.
4. Tobias DK, Chen M, Manson JE, Ludwig DS, Willett W, Hu FB. Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis. The lancet. Diabetes & endocrinology. Dec 2015;3(12):968-979.
5. Pilkington TR, Stafford JL, Hankin VS, Simmonds FM, Koerselman HB. Practical Diets for Lowering Serum Lipids. British medical journal. Jan 2 1960;1(5165):23-25.
6. Appel LJ, Sacks FM, Carey VJ, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. Jama. Nov 16 2005;294(19):2455-2464.
7. Wang DD, Li Y, Chiuve SE, et al. Association of Specific Dietary Fats With Total and Cause-Specific Mortality. JAMA internal medicine. Jul 5 2016.
8. U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015 – 2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at http://health.gov/dietaryguidelines/2015/guidelines/

I do not have any affiliation with or involvement in any organisation with a financial interest in the subject matter of my comment

Reply

Thank you for your interest in our systematic review (1). You are incorrect, we did not state anywhere in the review that "a lower proportion of energy intake from total fat was associated with a small reduction in body weight (difference = 1.5 kg)". We were not interested in associations, we were interested in causality, so we included RCTs that reduced total fat in one randomised arm and not in the other. In the abstract we stated "There is consistent evidence from RCTs in adults of a small weight-reducing effect of eating a smaller proportion of energy from fat; this was seen in almost all included studies and was highly resistant to sensitivity analyses. The effect of eating less fat (compared with usual diet) is a mean weight reduction of 1.5 kg (95% confidence interval (CI) -2.0 to -1.1 kg), but greater weight loss results from greater fat reductions."

Yes, we only included studies where weight loss was NOT a goal (where fat reduction was assessed for its effect on cardiovascular disease, cancer risk or other health issues). The reason for this was that we were interested not in weight reducing diets for overweight people, but in usual diets eaten day to day by generally healthy people all over the world. This issue was discussed in great detail by the World Health Organization NUGAG committee before the review was commissioned and the committee was very clear that their instructions were in setting goals for generally healthy populations and not therapeutic diets for those who were already overweight or obese. Therapeutic weight reducing diets are very different and, whatever their macronutrient or food composition, cannot be disentangled from the overriding and conscious requirement to eat less food (i.e. reduce energy intake). Indeed, and importantly, the participants in the studies we reviewed were not recruited to studies that aimed to promote weight loss in participants, or where participants were aware that one of the aims of the study was to promote a loss in their weight to achieve a healthy weight. This also meant that we did not include studies where low fat diets were compared to other therapeutic diets (such as very low carbohydrate diets).

Our review assesses the effects on weight of encouraging normal populations to reduce their total fat intake over the long term. The studies included durations of 6 months up to over 8 years. The effect in studies of between 6 and 12 months duration was a reduction of 1.74kg in the low fat group compared to control (95% CI -2.34 to -1.13), similar to that at 12 to 24 months (-2.00kg, 95% CI -2.51 to -1.48) and at 24 to 60 months (-1.18kg, 95% CI -1.65 to -0.70). The effect over more than 5 years was smaller (-0.68kg, 95% CI -1.66 to 0.29) but two of the four large RCTs still showed statistically significantly lower weight in the intervention groups (perhaps reflecting differences in the intensity of the intervention delivery and support this far into the trials), and meta-regression did not suggest a significant effect of duration on the extent of weight reduction in the low fat group compared to control. Dr Tobias' own systematic review also clearly shows that in studies where there was no intention to reduce weight "that low-fat interventions led to greater weight loss" compared to usual diets (abstract of (2)).

Strategies to help obese adults and children to lose weight are also clearly very important – but how to lose weight is a different question from how populations should eat day to day, year to year (there are a set of specific systematic reviews about weight reduction strategies in different populations on the Cochrane Library).

We used sensitivity analysis to assess the effect of "attention bias" (see Analysis 3.1). We removed studies where there appeared to have been more attention and/or time spent on the intervention group than the control group. Five studies provided data for this meta-analysis, finding that there was still a statistically significantly reduced weight in the low fat group (-1.25kg, 95% CI -2.09 to -0.41). Three further trials did not provide variance data so could not be included in the meta-analysis, but they all clearly showed greater weight reduction in the low fat compared to usual fat arms, on average (though their statistical significance cannot be assessed). This is a very consistent effect, is not dependent on short duration, and does not rely on increased attention or behavioural strategies in the low fat arms.

We reiterate, "Trials where participants were randomised to a lower fat intake versus usual or moderate fat intake, but with no intention to reduce weight, showed a consistent, stable but small effect of low fat intake on body fatness: slightly lower weight, BMI and waist circumference compared with controls. Greater fat reduction and lower baseline fat intake were both associated with greater reductions in weight."

References

1. Hooper L, Abdelhamid A, Bunn DK, Brown T, Summerbell CD, Skeaff CM. Effects of total fat intake on body weight. Cochrane Database Syst Rev 2015;8:Art. No.: CD011834.doi: 10.1002/14651858.CD011834
2. Tobias DK, Chen M, Manson JE, Ludwig DS, Willett W, Hu FB. Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis. The Lancet Diabetes & Endocrinology 2015;3:968-79.

Contributors

Julia Lowe, feedback editor for Cochrane Heart

WHAT'S NEW

Date	Event	Description
19 August 2016	Feedback has been incorporated	Comment and authors' response added.
2 March 2016	Amended	The description of data included in the main analysis for the WHI study was incorrect, so the entry for the "Characteristics of Included Studies" table now reflects that the weight, BMI and waist circumference data used in the main analyses were 7.5 year follow up data (as is appropriate). The data in the forest plots were already correct. Additionally the main reference for WHI is now indicated as the paper that provides this 7.5 year follow up data.

Date	Event	Description
		The first paragraph of the text on "Associations between total dietary fat in youth and measures of body fatness in children, young people and adults (as seen in cohorts)" was unclear, so we have tried to clarify these results. Table 2 is helpful to read in understanding this section.

HISTORY

Protocol first published: Issue 2, 1999
Review first published: Issue 8, 2015

Date	Event	Description
21 July 2015	New search has been performed	The searches were run on 12 November 2014.
11 July 2015	New citation required and conclusions have changed	We split a previously published review (Reduced and modified dietary fat for preventing cardiovascular disease, DOI: 10.1002/14651858.CD002137.pub3) into six smaller review updates. The conclusions are therefore now focused on the effects of total fat intake on body weight instead of the effects of reducing or modifying fat intake overall on cardiovascular disease risk. At the request of the World Health Organization (WHO) Nutrition Guidance Expert Advisory Group (NUGAG) group we extended this review to include cohort studies, and studies in children and young people. This split review update includes 32 randomised controlled trials and also 30 sets of analyses of 25 cohorts.
11 June 2010	New citation required and conclusions have changed	—
9 September 2008	Amended	—
1 February 2000	New citation required and conclusions have changed	Substantive amendment.

CONTRIBUTIONS OF AUTHORS

The WHO NUGAG subgroup on diet and health (which included LH, MS and CDS) discussed and developed the question for this review. The protocol was drafted by LH and approved by the NUGAG subgroup on diet and health. LH, WD, and HJM carried out the searches for the first version of the review, AA and LH carried out searches for the update. LH, AA, WD, HJM and CSE assessed the eligibility of the studies for inclusion of the first review, extracted data and assessed trial validity, while AA, DKB, TB and LH carried this out for the update. LH carried out the first GRADE assessment, which was refined by the NUGAG subgroup on diet and health, LH carried out the GRADE assessment for this update. LH wrote the first drafts of the original paper and this update. All authors contributed to the analysis, as did the NUGAG subgroup on diet and health in response to the first draft of the review. All authors agreed on the final draft of this review. LH is the guarantor.

DECLARATIONS OF INTEREST

AA: none known.

TB: none known.

DB: none known.

LH: the World Health Organization (WHO) provided funding to the University of East Anglia towards the cost of carrying out the update of this systematic review. LH is a member of the WHO NUGAG subgroup on diet and health and received funding from WHO to cover expenses associated with attendance at meetings of the NUGAG subgroup on diet and health.

CMS: none known

CDS: none known.

SOURCES OF SUPPORT

Internal sources

- University of East Anglia, UK.

  For the original version of this systematic review: help with acquiring papers for the review, time for Lee Hooper to work on the review.

External sources

- The World Health Organization (WHO) provided funding to Durham University towards the cost of carrying out the original version of this systematic review, Not specified.

  No funding was received for the searching, analysis, or writing up of the data from randomised controlled trials in adults for the first version of the review. The funders did not have any vested interests in the findings of this research
- WHO provided funding to the University of East Anglia (PI Lee Hooper) for the update of this systematic review and translation into a Cochrane review, Not specified.

INDEX TERMS

Medical Subject Headings (MeSH)

*Energy Intake; *Portion Size; *Waist Circumference; *Weight Loss; Age Factors; Body Mass Index; Body Weight; Dietary Fats [*administration & dosage]; Obesity [diet therapy]; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Adult; Child; Female; Humans; Male; Middle Aged; Young Adult