Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis

Deirdre K Tobias, Mu Chen, JoAnn E Manson, David S Ludwig, Walter Willett, Frank B Hu

Summary

Background The effectiveness of low-fat diets for long-term weight loss has been debated for decades, with many randomised controlled trials (RCTs) and recent reviews giving mixed results. We aimed to summarise the large body of evidence from RCTs to determine whether low-fat diets contribute to greater weight loss than participants' usual diet, low-carbohydrate diets, and other higher-fat dietary interventions.

Methods We did a systematic review and random effects meta-analysis of RCTs comparing the long-term effect (≥1 year) of low-fat and higher-fat dietary interventions on weight loss by searching MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Cochrane Database of Systematic Reviews to identify eligible trials published from database inception up until July 31, 2014. We excluded trials if one intervention group included a non-dietary weight loss component but the other did not, and trials of dietary supplements or meal replacement drink interventions. Data including the main outcome measure of mean difference in weight change between interventions, and whether interventions were intended to lead to weight loss, weight maintenance, or neither, were extracted from published reports. We estimated the pooled weighted mean difference (WMD) with a DerSimonian and Laird random effects method.

Findings 3517 citations were identified by the search and 53 studies met our inclusion criteria, including 68 128 participants (69 comparisons). In weight loss trials, low-carbohydrate interventions led to significantly greater weight loss than did low-fat interventions (18 comparisons; WMD 1·15 kg [95% CI 0·52 to 1·79]; I^2=10%). Low-fat interventions did not lead to differences in weight change compared with other higher-fat weight loss interventions (19 comparisons; WMD 0·36 kg [–0·66 to 1·37; I^2=82%), and led to a greater weight decrease only when compared with a usual diet (eight comparisons; –5·41 kg [–7·29 to –3·54]; I^2=68%). Similarly, results of non-weight-loss trials and weight maintenance trials, for which no low-carbohydrate comparisons were made, showed that low-fat versus higher-fat interventions have a similar effect on weight loss, and that low-fat interventions led to greater weight loss only when compared with usual diet. In weight loss trials, higher-fat weight loss interventions led to significantly greater weight loss than low-fat interventions when groups differed by more than 5% of calories obtained from fat at follow-up (18 comparisons; WMD 1·04 kg [95% CI 0·06 to 2·03]; I^2=78%), and when the difference in serum triglycerides between the two interventions at follow-up was at least 0·06 mmol/L (17 comparisons; 1·38 kg [0·50 to 2·25]; I^2=62%).

Interpretation These findings suggest that the long-term effect of low-fat diet intervention on bodyweight depends on the intensity of the intervention in the comparison group. When compared with dietary interventions of similar intensity, evidence from RCTs does not support low-fat diets over other dietary interventions for long-term weight loss.

Funding National Institutes of Health and American Diabetes Association.

Lancet Diabetes Endocrinol 2015

Published Online October 30, 2015 http://dx.doi.org/10.1016/S2213-8587(15)00367-8

See Online/Comment http://dx.doi.org/10.1016/S2213-8587(15)00413-1

Division of Preventive Medicine (D K Tobias ScD, Prof J E Manson MD)**, and Channing Division of Network Medicine** (Prof W Willett MD, Prof F B Hu MD), **Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; Department of Nutrition** (D K Tobias, M Chen ScD, Prof D S Ludwig MD, Prof W Willett, Prof F B Hu)**, and Department of Epidemiology** (Prof J E Manson, Prof W Willett, Prof F B Hu), **Harvard T H Chan School of Public Health, Boston, MA, USA; and New Balance Foundation Obesity Prevention Center, Boston Children's Hospital, Boston, MA, USA** (Prof D S Ludwig)

Correspondence to: Dr Deirdre K Tobias, Brigham and Women's Hospital and Harvard Medical School, Division of Preventive Medicine, 900 Commonwealth Avenue, Boston, MA 02215, USA **dtobias@partners.org**

Introduction

Identifying effective strategies for long-term weight control will be crucial to reduce the alarming prevalence of overweight and obesity worldwide. The macronutrient composition of the diet—the proportions of calories contributed by fat, carbohydrate, and protein—has received substantial attention in the past few decades for its potential relevance in weight loss and weight maintenance.[1,2] Many short-term and long-term randomised trials[1,3–5] across various general and clinical populations have attempted to identify the optimum ratio of macronutrients for weight loss. Lowering the proportion of daily calories consumed from total fat has been targeted for many reasons, one of which is that 1 g of fat contains more than twice the calories of 1 g of carbohydrates or protein (9 kcal/g *vs* 4 kcal/g). Thus, a reduction in total fat intake could theoretically lead to an appreciable effect on total calories consumed. However, results of randomised trials[3,6–8] have failed to consistently show that reducing the proportion of energy consumed from total fat leads to long-term weight loss compared with other dietary interventions.

This systematic review and meta-analysis aimed to summarise the large body of evidence from randomised control trials (RCTs) lasting at least 1 year in which weight changes in participants on low-fat diets versus other dietary interventions were compared. Trials were included irrespective of whether weight loss was intended or not, such as studies assessing lipids or cancer endpoints. We aimed to stratify the analysis by characteristics of the interventions that might affect differences in weight loss, including whether the intervention groups received similar attention and intervention intensity, or the composition of the comparison diet. We postulated that low-fat diets would not be associated with greater weight loss than other interventions when differences in these intervention characteristics were taken into account, and that differences in weight loss favouring higher-fat interventions would be larger when adherence was greater.

Methods

Search strategy and inclusion criteria

We predefined our search strategy, study eligibility criteria, and statistical approaches for this systematic review and meta-analysis in an unpublished research protocol, according to PRISMA guidelines. We used MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Cochrane Database of Systematic Reviews to identify eligible trials. The following terms were included in the MEDLINE search, with similar terms used in the other databases: (low fat diet[MeSH] OR "low fat" OR "low-fat" OR "reduced fat" OR "dietary approaches to stop hypertension" OR (DASH AND (diet OR pattern*)) OR (("National Cholesterol Education Program Adult Treatment Panel III" OR "NCEP ATP III" OR "ATP III") AND (diet OR pattern*)) OR "Ornish") AND ("Intervention Studies" [MeSH] OR "intervention"[tiab] OR "clinical trial" OR "controlled trial"[tiab] OR random*[tiab] OR assign*[tiab]). We included trials including non-pregnant adults lasting at least 1 year comparing weight change on a low-fat diet (as defined by the investigators of each trial) with any higher-fat dietary intervention, including participants' usual diet. Trials of shorter duration were excluded because weight-loss trials frequently report an initial maximal weight loss at around 6 months, with subsequent weight regain. We searched for all relevant articles published from inception of each database until July 31, 2014, and we restricted our search to trials published in English. We screened reference lists of eligible studies and reviews published within the previous 2 years to capture additional relevant citations.

The outcome of interest was long-term (≥1 year) change in bodyweight (reported as mean change from baseline, mean difference in change from baseline between intervention groups, or mean bodyweight at end of follow-up). We attempted to contact authors to obtain variance measures if not reported, but ultimately excluded the trial if we could not obtain the data. We excluded trials if one intervention group included a non-dietary weight loss component (eg, exercise regimen, pharmaceutical intervention) while the other did not. We did not make exclusions on the basis of concomitant dietary components (eg, an increase in fruit and vegetable consumption). Non-randomised trials were excluded, as well as trials assessing dietary supplements or meal replacement drink interventions, because these interventions were beyond the scope of our investigation. If trial results were published more than once, we included the report with the most complete follow-up in our main analysis. Two reviewers (DKT, MC) screened abstracts for relevance, and both independently reviewed each eligible full text using an inclusion and exclusion criteria sheet. Conflicts over inclusion were resolved with an in-person discussion and with a third investigator (FBH) if necessary.

Data extraction

Data were extracted and entered into a piloted spreadsheet. Variables captured from the final accepted studies included study-level information (authors, country, centre), study population characteristics, intervention details, including whether interventions were intended to lead to weight loss, weight maintenance, or neither, and the relative intensity of each intervention, as described by the study authors (eg, attention given by study investigators [such as health-care workers, dietitians, physicians, or group counsellors] to the participants, time spent with study clinicians or dietitians, programme materials), and outcomes by treatment group. We also recorded dietary adherence, including change in serum triglyceride concentration and the proportion of calories consumed from fat during follow-up. We analysed the intention-to-treat estimates, when reported.

We assessed the trials' potential for bias using the Cochrane risk of bias assessment tool.[9] DKT and MC both extracted the data from each report separately, and discrepancies were resolved by a third reviewer (FBH), if necessary.

Data analysis

We calculated the mean difference in bodyweight change from baseline by subtracting the mean change of the comparison diet group from the mean change in the low-fat diet group. If the mean change was not reported we compared the groups' final mean bodyweights, under the assumption that randomisation resulted in similar average baseline bodyweights between treatment groups. We estimated the pooled weighted mean difference (WMD) and 95% CI with a DerSimonian and Laird random effects model. We regarded a p value of less than 0·05 as statistically significant.

We assessed heterogeneity from the Mantel-Haenszel model and I^2 values (the percentage of variance in the pooled estimate due to between-study differences), with an I^2 value of greater than 50% suggesting moderate heterogeneity.[10] We did analyses, established a priori, to assess potential heterogeneity according to whether the trial was designed with the intention of causing weight loss, the composition of the comparison higher-fat diet (low-carbohydrate, other moderate fat or healthful diet, or participants' usual diet), the interventions' relative intensity, whether either, neither, or both of the interventions included caloric restriction, and the baseline health status of the participants. Additionally, we stratified by change in triglyceride concentrations and in attained self-reported proportion of calories consumed from fat, with an increase in triglycerides reflecting a relative decrease in fat intake in a given group.[11]

Finally, we did sensitivity analyses to assess the robustness of our findings. We assessed the effect of removing the largest study or studies, based on their percentage weight in the pooled estimates and restricted the analysis to trials with intention-to-treat analyses and with at least 100 participants. We repeated primary analyses using an inverse variance weighted fixed-effect model. We applied Begg's test[12] and Egger's test[13,14] to test for the potential of publication bias by plotting the inverse of the variance against the treatment effect. We did analyses using STATA version 13.1.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

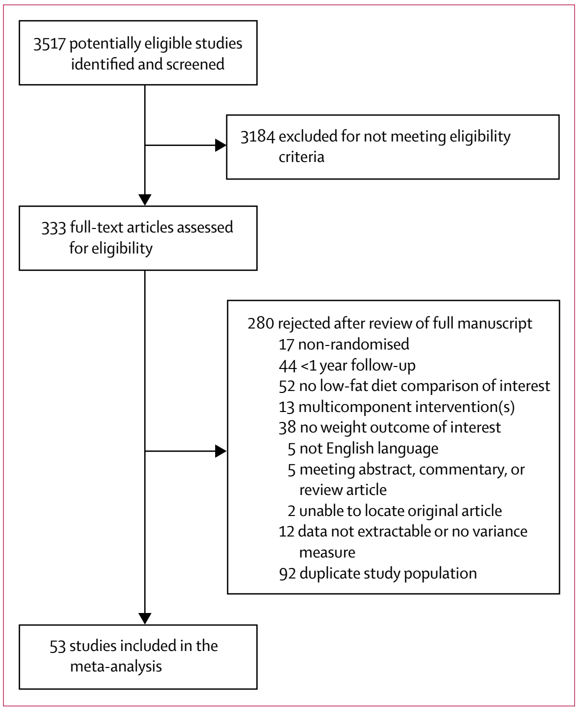

Figure 1: **PRISMA flow diagram**
PRISMA=Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Results

Our search yielded 3517 citations (figure 1), of which 53 RCTs were eligible for inclusion in our analysis (69 comparisons; table 1). Most of the trials were undertaken in North America (n=37) and were 1 year in duration (n=27). 20 trials specifically enrolled participants with prevalent chronic diseases, including breast cancer,[23,60–62] hypercholesterolaemia,[16,29,30] type 2 diabetes,[5,17,22,31,33,34,37,39,55] metabolic syndrome,[41] oesophageal metaplasia,[42] ischaemic heart disease,[47] and colorectal adenoma.[48] In addition to 35 weight loss trials, 13 trials had no intended intervention on weight[8,21,23,29,30,47,48,54,55,59,60–62] and five were weight maintenance trials designed to maintain baseline bodyweight.[6,16,20,27,46]

The low-fat dietary interventions ranged from very low fat (≤10% of calories from fat), to more moderate goals (≤30% of calories from fat). Comparator diets of higher fat intake were diverse, ranging from one baseline interaction with instructions to maintain their usual diet, to various other dietary interventions, including low-carbohydrate and other moderate-to-high-fat diets. The intensity of the interventions varied from pamphlets or instructions given at baseline only, to multicomponent programmes (eg, integrating counselling sessions, regular meetings with dietitians, food diaries, and cooking lessons), to feeding studies, in which participants were given a substantial portion of their food. Caloric restriction was a component of many weight loss interventions, but not all. For example, despite being a weight loss intervention, participants on a low-carbohydrate Atkins-style diet were often told to eat ad libitum (ie, until satiated).

Our primary meta-analysis included 68 128 adults from eligible RCTs, reporting a mean weight loss of 2·71 kg (SD 2·8) in all participants combined, on any diet (including comparators) after a median of 1 year (IQR 1–2) of follow-up; the mean weight loss in trials designed to reduce weight was 3·75 kg (SD 2·7). Figures 2, 3, and 4 present the overall results according to weight loss trial design (weight loss goal, no weight loss goal, or weight maintenance) and composition of comparator intervention (low-carbohydrate intervention, other higher-fat intervention, or usual diet).

We noted no difference between low-fat and higher-fat dietary interventions when all weight loss trials were combined, although there was significant between-study heterogeneity. Low-carbohydrate weight loss interventions led to an average (WMD) 1·15 kg (95% CI 0·52–1·79) greater long-term weight loss than low-fat weight loss interventions, with minimal between-study heterogeneity. We noted no difference, however, between low-fat and other higher-fat dietary interventions (0·36 kg [–0·66 to 1·37]). Compared with groups only following their usual diet, low-fat weight loss interventions led to a 5·41 kg (3·54–7·29) greater weight loss (figure 2).

Non-weight loss trials and weight maintenance trials also found a significant but smaller magnitude of weight loss for low-fat interventions when compared with usual

	N	Population characteristics	Country	Weight loss goal	Low-fat diet(s) intervention	Comparator diet(s) intervention	Follow-up duration, years
A to Z, 2007[15]	311	Overweight, premenopausal women	USA	Yes	LEARN (reduced calorie); Ornish (<10% fat; reduced calorie)	Atkins low-carbohydrate; Zone (30% fat; reduced calorie)	1
Anderson et al, 1992[16]	117	Moderate hypercholesterolaemia	USA	Maintain	American Heart Association Phase II (25% fat)	Usual diet	1
Barnard et al, 2009[17]	99	Type 2 diabetes	USA	Yes	Vegan (10% fat)	American Diabetes Association Diet 2003 (30% fat; reduced calorie)	1·4
Bazzano et al, 2014[18]	148	Obese	USA	Yes	National Cholesterol Education Program (<30% fat)	Low carbohydrate	1
Bertz et al, 2012[19]	68	Breastfeeding mothers	Sweden	Yes	Nordic Nutrition Guidelines (<30% fat; reduced calorie)	Usual diet	1
Boyd et al, 1990[20]	295	Women with high breast cancer risk	Canada	Maintain	15% fat	Canadian Food Guide (no fat intake advice)	1
Breast Cancer Prevention Program, 1997[21]	194	Women with high breast cancer risk	USA	No	15% fat	Usual diet	1
Brehm et al, 2009[22]	124	Overweight or obese with type 2 diabetes	USA	Yes	High carbohydrate (25% fat; reduced calorie)	High monounsaturated fat (40% fat; reduced calorie)	1
BRIDGES, 2001[23]	172	Women with recent breast cancer	USA	No	Nutrition Education Program (20% fat)	Usual diet	1
Brinkworth et al 2009;[24] Tay et al, 2008[25]	118	At risk for metabolic syndrome	Australia	Yes	30% fat (reduced calorie)	Atkins low-carbohydrate (61% fat; reduced calorie)	1
CALERIE phase 1, 2007[26]	34	Overweight	USA	Yes	High glycaemic index, food provided (20% fat; reduced calorie)	Low glycaemic index, food provided (30% fat; reduced calorie)	1
Canadian Diet and Breast Cancer Prevention Study, 2011[27]	4690	Women with high breast cancer risk	Canada	Maintain	15% fat	Canadian Food Guide (no fat intake advice)	10
Dansinger et al, 2005[28]	160	At risk for cardiovascular disease	USA	Yes	Ornish (<10% fat)	Atkins low-carbohydrate; Zone (30% fat); Weight Watchers (reduced calorie)	1
Davis et al, 2009[5]	105	Type 2 diabetes	USA	Yes	Diabetes Prevention Program diet (25% fat)	Atkins low-carbohydrate	1
DEER, 1998[29]	377	Hypercholesterolaemia	USA	No	National Cholesterol Education Program (<30% fat)	Usual diet	1
The Dietary Alternatives Study, 1997[30]	508	Men with hypercholesterolaemia	USA	No	26% fat; 22% fat; 18% fat	30% fat	1
DIRECT, 2008[31]	322	Type 2 diabetes, cardiovascular disease, or obese	Israel	Yes	American Heart Association (30% fat; reduced calorie)	Mediterranean diet (35% fat; reduced calorie); Atkins low-carbohydrate	2
Ebbeling et al, 2007[32]	73	Obese young adults	USA	Yes	20% fat	Low glycaemic-index carbohydrates (35% fat)	1·5
Elhayany et al, 2010[33]	259	Type 2 diabetes	Israel	Yes	American Diabetes Association 2003 (30% fat; reduced calorie); low-fat Mediterranean (30% fat; reduced calorie)	Low-carbohydrate Mediterranean diet (45% fat; reduced calorie)	1
Esposito et al, 2009[34]	215	Type 2 diabetes	Italy	Yes	American Heart Association 2000 (<30% fat; reduced calorie)	Mediterranean diet (>30% fat; reduced calorie)	4
Foster et al, 2003[35]	63	Obese	USA	Yes	25% fat (reduced calorie)	Atkins low carbohydrate	1
Foster et al, 2010[36]	307	Obese	USA	Yes	30% fat (reduced calorie)	Atkins low carbohydrate	2
Guldbrand et al, 2012[37]	61	Type 2 diabetes	Sweden	Yes	<30% fat (reduced calorie)	Low carbohydrate (50% fat; reduced calorie)	2
Harvey-Berino, 1999[38]	80	Overweight or obese	USA	Yes	20% fat	Low calorie	1·5
Iqbal et al, 2010[39]	144	Type 2 diabetes, obese	USA	Yes	<30% fat (reduced calorie)	Low carbohydrate	2
Keogh et al, 2007[40]	44	Overweight/obese	Australia	Yes	20% fat (reduced calorie)	Low carbohydrate (27% fat; reduced calorie)	1
Klemsdal et al, 2010[41]	202	Metabolic syndrome	Norway	Yes	30% fat (reduced calorie)	Low glycaemic load (35-40% fat; reduced calorie)	1
Kristal et al, 2005[42]	93	Overweight/obese with oesophageal metaplasia	USA	Yes	20% fat (reduced calorie)	Usual diet	3
Lapointe et al, 2010[43]	68	Overweight/obese postmenopausal women	Canada	Yes	Reduce fat intake	Increase fruits and vegetables	1·5

(Table 1 continues on next page)

	N	Population characteristics	Country	Weight loss goal	Low-fat diet(s) intervention	Comparator diet(s) intervention	Follow-up duration, years
(Continued from previous page)							
Lim et al, 2010[44]	113	High cardiovascular disease risk	Australia	Yes	Food provided (10% fat; reduced calorie)	Low carbohydrate, food provided (60% fat; reduced calorie); high unsaturated fat, food provided (30% fat; reduced calorie); usual diet	1·25
McAuley et al, 2006[45]	96	Women overweight/obese with insulin resistance	New Zealand	Yes	Diabetes and Nutrition Study Group of the European Association for the Study of Diabetes (<30% fat)	Low carbohydrate Atkins diet; Zone diet (30% fat)	1
McManus et al, 2001[4]	101	Overweight	USA	Yes	20% fat (reduced calorie)	35% fat (reduced calorie)	1·5
Nutrition and Exercise in Women (NEW) Study, 2012[7]	439	Postmenopausal overweight/obese women	USA	Yes	<30% fat (reduced calorie)	Usual diet	1
Nutrition and Breast Health Study, 2002[46]	122	Premenopausal women at risk of breast cancer	USA	Maintain	15% fat; high consumption of fruit and vegetables (15% fat)	Usual diet; high consumption of fruit and vegetables	1
Pilkington et al, 1960[47]	58	Men with ischaemic heart disease	UK	No	20 g fat per day	Increase unsaturated fats	1·5
Polyp Prevention Trial, 2000[48]	2079	Recent colorectal adenoma	USA	No	20% fat	Usual diet	3·1
Pounds Lost Trial, 2009[3]	811	Overweight/obese	USA	Yes	20% fat (reduced calorie); high protein (20% fat; reduced calorie)	40% fat (reduced calorie); high protein (40% fat; reduced calorie)	2
PREDIMED, 2014[8]	7447	High cardiovascular disease risk	Spain	No	Reduce fat intake	Mediterranean diet plus increased extra-virgin olive oil intake or mixed nuts intake	4·8
PREMIER, 2006[49]	810	Prehypertension	USA	Yes	DASH (<25% fat; reduced calorie)	30% fat (reduced calorie)	1·5
Shah et al, 1996[50]	122	Obese women	USA	Yes	20 g fat/day	30% fat (reduced calorie)	1
SMART Study, 2009[51]	200	Overweight/obese	Germany	Yes	German Nutrition Society (30% fat; reduced calorie)	Low-carbohydrate (35% fat; reduced calorie)	1
Stern et al, 2004;[52] Samaha et al, 2003[53]	132	Morbidly obese	USA	Yes	NHLBI (30% fat; reduced calorie)	Low-carbohydrate	1
Swinburn et al, 2001[54]	176	Glucose intolerance	New Zealand	No	Reduce fat	Usual diet	5
Tapsell et al, 2004[55]	63	Type 2 diabetes	Australia	No	27% fat	37% fat	1
Tehran Lipid and Glucose Study, 2007[56]	100	Overweight or obese	Iran	Yes	20% fat (reduced calorie)	30% fat (reduced calorie)	1·2
Turner-McGrievy et al, 2007[57]	64	Overweight or obese postmenopausal women	USA	Yes	Vegan (10% fat)	National Cholesterol Education Program (<30% fat)	2
Viegener et al, 1990[58]	85	Overweight or obese women	USA	Yes	15–25% fat (reduced calorie)	30% fat (reduced calorie)	1
Women's Health Initiative Dietary Modification Trial, 2006[6]	48 835	Postmenopausal women	USA	Maintain	20% fat	Usual diet	7·5
Women's Health Trial Vanguard Study, 1990[59]	303	Women with high breast cancer risk	USA	No	20% fat	Usual diet	2
Women's Healthy Eating and Living (WHEL), 2007[60]	3088	Women with previous breast cancer	USA	No	15–20% fat	USDA guidelines (<30% fat)	7·3
Women's Intervention Nutrition Study (WINS), 2006[61]	2437	Women with breast cancer	USA	No	15% fat	General counselling on nutritional adequacy	5
Women's Intervention Nutrition Study (WINS) Feasibility, 1993[62]	290	Women with postmenopausal breast cancer	USA	No	20% fat	General counselling on nutritional adequacy	1·5
Wood et al, 1991[63]	294	Overweight or obese	USA	Yes	National Cholesterol Education Program (<30% fat; reduced calorie)	Usual diet	1

LEARN=lifestyle, exercise, attitudes, relationships, and nutrition. DASH=Dietary Approaches to Stop Hypertension. NHLBI= National Heart, Lung, and Blood Institute. USDA= US Department of Agriculture.

***Table 1*: Randomised controlled trials of low-fat versus other dietary interventions of at least 1 year duration in adults included in the meta-analysis**

diet, and no difference between low-fat and other higher-fat dietary interventions (figures 3, 4). No long-term non-weight loss or weight maintenance trials compared low-fat with low-carbohydrate dietary interventions.

Table 2 presents analyses stratified by additional trial characteristics, limited to trials of similar intensity to minimise bias from one group receiving more attention and higher intervention intensity. Only four of the 17 comparisons among trials without a weight loss goal[30,47,55] and one of the six comparisons among weight maintenance trials[46] remained, limiting our ability to stratify further; thus, table 2 does not report data on

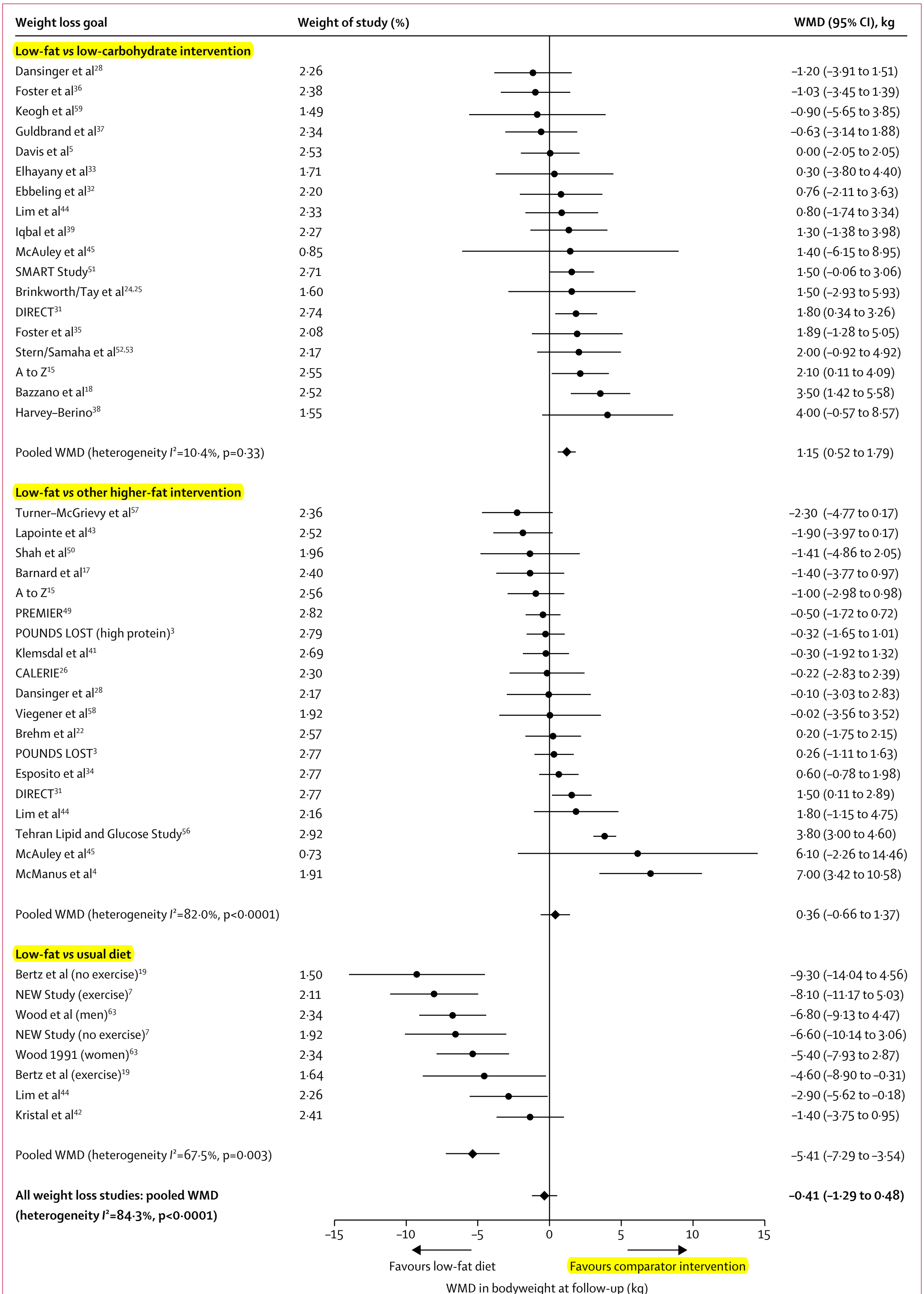

***Figure 2*: Random effects pooled WMD for low-fat *vs* comparator dietary interventions from trials with a weight loss goal**
WMD=DerSimonian and Laird random effects weighted mean difference, in kg.

weight maintenance trials. Analysis suggested that, for similar intervention intensity, weight loss was greater with higher-fat interventions than with low-fat interventions, although this difference did not reach statistical significance. Stratifying by caloric restriction showed no significant difference in weight loss between low-fat and higher-fat dietary weight loss interventions when interventions were concordant for caloric restriction. Calorie-restricted low-fat diets, however, fared significantly worse compared with non-calorie restricted higher-fat interventions. Results were similar for weight loss trials in participants with or without a chronic disease at baseline (table 2). When groups differed by more than 5% calories from fat at follow-up, higher-fat weight loss

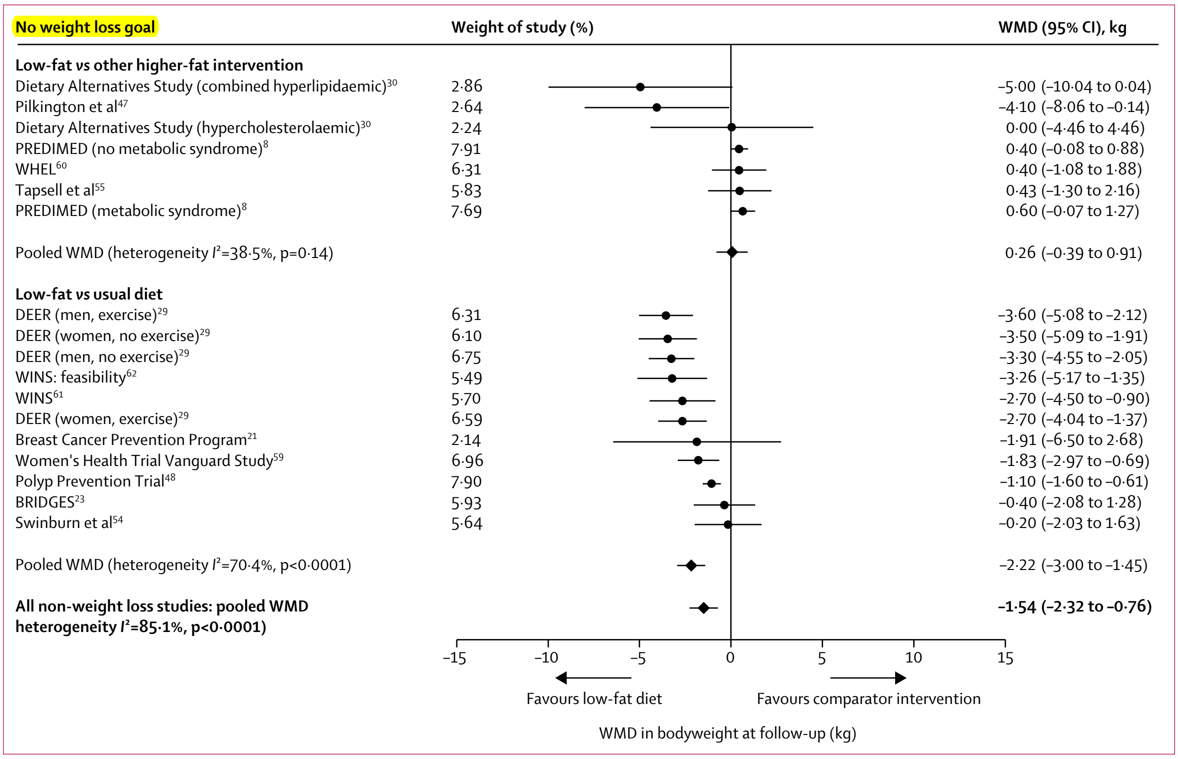

Figure 3: **Random effects pooled WMD for low-fat *vs* comparator dietary interventions from trials with no weight loss goal**
WMD=DerSimonian and Laird random effects weighted mean difference, in kg.

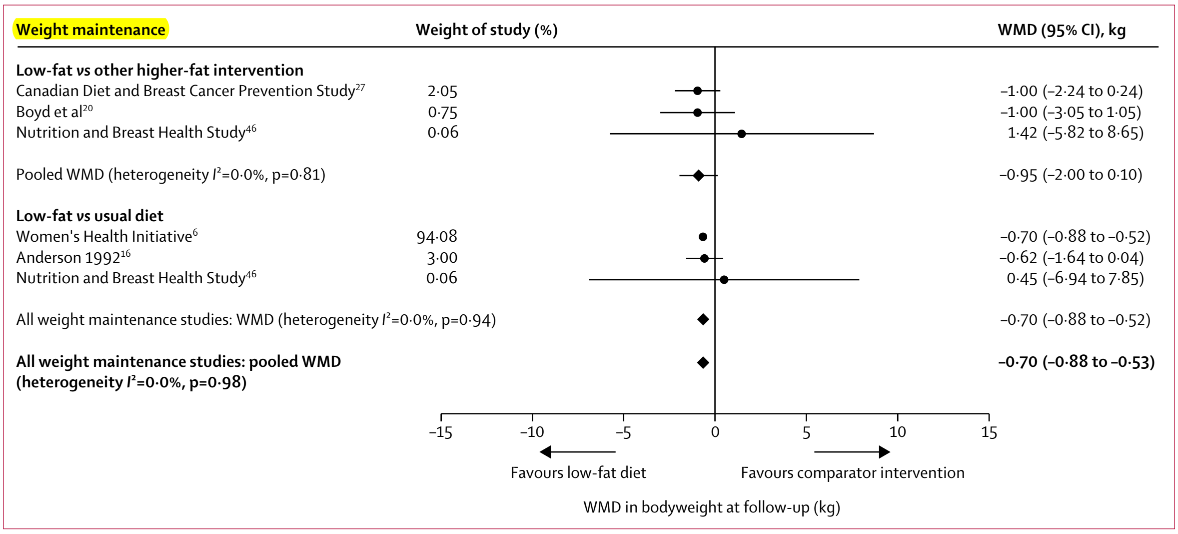

Figure 4: **Random effects pooled WMD for low-fat *vs* comparator dietary interventions from trials with a weight maintenance goal**
WMD=DerSimonian and Laird random effects weighted mean difference, in kg.

interventions led to significantly greater weight loss than low-fat interventions. Similarly, weight loss trials with at least a 0·06 mmol/L greater change in triglycerides for low-fat versus higher-fat interventions led to significantly greater weight loss for the higher-fat intervention groups.

In a sensitivity analysis excluding the Women's Health Initiative trial[6] (94·08% of weight) from weight maintenance trials, the findings were not affected (n=5; WMD −0·77 kg [95% CI −1·50 to −0·04], p=0·039; I^2=0·0%, $p_{heterogeneity}$=0·95). Results were similar when restricted to studies with intention-to-treat analyses and when excluding smaller trials of fewer than 100 participants, although few non-weight loss or weight maintenance trials remained eligible according to these

	Comparisons*, n	WMD (95% CI), kg	p value	I^2 ($p_{heterogeneity}$ value)
Interventions with weight loss goal				
Similar intervention intensity	33	0·62 (−0·08 to 1·32)	0·084	71·6% (p<0·0001)
Comparator diet				
Low carbohydrate	18	1·15 (0·52 to 1·79)	<0·0001	10·4% (p=0·33)
Other higher-fat intervention	19	0·36 (−0·66 to 1·37)	0·49	82·0% (p<0·0001)
Usual diet	0	NA	NA	NA
Caloric restriction				
Both interventions	18	0·74 (−0·19 to 1·68)	0·12	78·4% (p<0·0001)
Neither intervention	8	0·33 (−1·18 to 1·83)	0·67	65·1% (p=0·005)
Low-fat diet only	6	1·49 (0·53 to 2·45)	0·002	7·7% (p=0·37)
Comparator diet only	5	−0·62 (−1·95 to 0·72)	0·37	15·5% (p=0·32)
Chronic disease population				
No	25	0·77 (−0·15 to 1·69)	0·10	76·1% (p<0·0001)
Yes	8	0·37 (−0·33 to 1·07)	0·30	10·3% (p=0·35)
Difference in fat intake at follow-up (% calories)				
<5% difference in fat intake	8	0·14 (−0·80 to 1·09)	0·77	30·1% (p=0·19)
≥5% difference in fat intake	18	1·04 (0·06 to 2·03)	0·038	77·7% (p<0·0001)
Difference in triglycerides at follow-up (mmol/L change)				
<0·06 mmol/L change difference	8	−0·21 (−0·86 to 0·43)	0·52	0·0% (p=0·92)
≥0·06 mmol/L greater change in low-fat group	17	1·38 (0·50 to 2·25)	0·002	62·3% (p<0·0001)
Interventions with no weight loss goal				
Similar intervention intensity	4	−1·71 (−4·52 to 1·10)	0·23	59·3% (p=0·061)
Comparator diet				
Low carbohydrate	0	NA	NA	NA
Other higher fat intervention	4	−1·71 (−4·52 to 1·10)	0·23	59·3% (p=0·061)
Usual diet	0	NA		NA
Caloric restriction				
Both interventions	0	NA		NA
Neither intervention	2	−1·47 (−5·85 to 2·91)	0·51	76·3% (p=0·04)
Low-fat diet only	0	NA		NA
Comparator diet only	0	NA		NA
Chronic disease population				
No	0	NA		NA
Yes	4	−1·71 (−4·52 to 1·10)	0·23	59·3% (p=0·061)
Difference in fat intake at follow-up (% calories)				
<5% difference in fat intake	1	NA	NA	NA
≥5% difference in fat intake	2	−2·18 (−6·19 to 1·83)	0·29	45·0% (p=0·18)
Difference in triglycerides at follow-up (mmol/L change)				
<0·06 mmol/L change difference	1	NA	NA	NA
≥0·06 mmol/L greater change in low-fat group	1	NA	NA	NA

Negative values favour the low-fat dietary intervention; positive values favour the comparator dietary intervention. WMD=DerSimonian and Laird random effects weighted mean difference, in kg. NA=not applicable. *The number of comparisons might exceed the number of total trials because some trials contributed more than one comparison of unique intervention groups (eg, estimates for men and women separately).

Table 2: **Random effects pooled WMD for low-fat versus comparator dietary interventions from 35 weight loss trials and 13 trials without a weight loss goal with ≥1 year of follow-up, stratified by trial characteristics**

criteria (appendix pp 2–3). The fixed effect meta-analysis, which gives less weight to smaller trials with greater variance, estimated a 0·44 kg (95% CI 0·12–0·77) greater weight loss for the comparator versus low-fat interventions among the weight loss trials. Fixed effect analyses stratified by comparator group also suggested that participants achieved greater weight loss with other higher-fat interventions than with low-fat interventions in trials with and without a weight loss goal, which showed no difference in the random effects analysis (appendix pp 4–5).

Results from the Cochrane risk of bias assessment tool were variable and assessment was limited for many studies by a lack of reporting (appendix pp 6–7). Incomplete outcome data was a high potential source of bias for 39 trials because of drop-out and loss-to-follow-up rates exceeding 5%. Differential intervention intensity was deemed a source of bias for 20 trials. Both the Begg's and Egger's tests for small-study effects did not suggest publication bias (p=0·83 and p=0·85, respectively). Visual inspection of the funnel plot showed a roughly symmetrical distribution of the inverse variances, which is consistent with these findings (appendix p 8).

Discussion

Results from this comprehensive meta-analysis of RCTs with at least 1 year of follow-up suggest that low-fat dietary interventions do not lead to greater weight loss than do low-carbohydrate and other higher-fat dietary interventions of a similar intensity, irrespective of the weight loss intention of the trial. In fact, in the setting of weight loss trials, higher-fat, low-carbohydrate dietary interventions led to a slight but significant, greater long-term weight loss than did low-fat interventions. Other higher-fat dietary interventions led to similar weight loss as the low-fat groups, irrespective of whether the trial had a weight loss goal or not. Low-fat interventions were favoured only in comparison with interventions of lesser intensity, particularly those in which controls were only asked to maintain their usual diet. Furthermore, trials achieving greater differences in dietary fat intake and serum triglyceride concentrations resulted in greater weight loss in participants on the higher-fat interventions than in those on the low-fat diet. Although these measures of dietary fat intake are not perfect, in view of the potential for measurement error in self-reported diets and confounding by weight loss for triglycerides as a marker of fat intake, results were consistent between these two methods.

This systematic literature review and meta-analysis highlights several important points. First, of the 53 eligible RCTs, 19 included participants on higher-fat comparator groups who maintained their usual intake, whereas the low-fat groups underwent interventions with more frequent or more intense interaction with research staff. Such comparisons do not provide evidence to support the effect of the low-fat diets themselves, since the effect of lowering total fat intake cannot be distinguished from the other components of the intervention. Stratification by this type of comparator group (figure 2) shows that a reduction in fat intake was not an independent contributor to weight loss. Second, despite concerted efforts among motivated clinical trial participants and staff, the average weight loss in all groups after a median 1 year of follow-up was just 2·7 kg, and 3·8 kg when calculated from only trials in which the intention was weight loss.

See Online for appendix

Our findings contrast with the findings of a previous systematic review and meta-analysis by Hooper and colleagues,[1] which concluded that reduction in total fat intake leads to clinically meaningful weight loss, reporting 1·57 kg (95% CI 1·16–1·97) greater weight loss for low-fat versus other diet interventions. The main differences between their study selection criteria and ours were their inclusion of trials with less than 1 year of follow-up and their deliberate exclusion of trials with any weight loss intention. Trials of short duration (eg, 6 months) are unlikely to show effects that are representative of long-term effects of diet on weight. Additionally, assessment of low-fat diets for weight loss exclusively among trials without a weight loss goal excluded a substantial proportion of the available scientific literature, giving a pooled estimate that was over-weighted by trials comparing low-fat diets with usual diet, as well as trials in populations at high risk for specific non-bodyweight-related endpoints of interest (eg, cholesterol lowering, breast cancer prevention). In our meta-analysis of trials without a weight loss goal and at least 1 year duration, we noted that after removing comparisons between low-fat and usual diets, low-fat interventions did not lead to more weight loss than higher-fat interventions (n=7; WMD 0·26 kg [95% CI –0·39 to 0·91]). In fact, of the 33 trials included in Hooper and colleagues' overall analysis, only eight comparisons were done between trials giving similar attention to the low-fat and comparator treatment groups, and only one of these lasted at least 1 year. Furthermore, only three were among healthy participants. Therefore, generalisability of their findings to overall populations intending to lose weight is highly questionable, and their estimated effects of reducing fat intake are likely to be seriously confounded by differences in comparator group intensity, which was shown to be a major source of heterogeneity in our analysis.

Johnston and colleagues[2] did a network meta-analysis of trials comparing named popular diet programmes. Pooling both direct comparisons (ie, head-to-head comparison of two interventions within one RCT) and indirect comparisons (ie, non-randomised comparisons of two intervention effects derived from separate trials) produced estimates similar to ours, suggesting significant weight loss at 12 months for low-fat interventions compared with a usual diet, and no significant benefit when compared with other dietary interventions of similar intensity. Limitations of indirect comparisons, however, include the inability to control for between-study and between-participant differences that might confound the pooled estimates. Another meta-analysis by Bueno and colleagues[64] assessed 13 trials of low-fat versus very low-carbohydrate diet interventions with at least 12 months of follow-up. Their pooled estimate indicated a 0·91 kg (95% CI 0·17–1·65) greater weight loss for very low-carbohydrate diets compared with low-fat diet interventions, consistent with our pooled estimate of 1·15 kg greater weight loss for low-carbohydrate versus low-fat weight loss interventions.

A limitation of our meta-analysis is the substantial heterogeneity within several strata, suggesting inconsistent effects across studies. Some degree of heterogeneity was expected in view of the various intervention designs, baseline characteristics of the participants, and comparator diets. Stratified analyses reduced heterogeneity in many cases. Additionally, our study did not have a prepublished protocol, and our search was limited to English language publications and did not include all potential databases or a search of grey literature, and so might have missed trials. Finally, most of the RCTs of at least 1 year duration were not feeding trials, since large-scale long-term trials of this nature can be costly; therefore, our analysis addresses the effectiveness of dietary interventions, and not necessarily the diets themselves.

The strength of evidence of the scientific literature included in this systematic review is variable with a high concern for attrition bias from significant drop-out and loss to follow-up in most of the trials. Retaining participants for long-term lifestyle interventions can be difficult and bias is a concern when attrition is related to intervention assignment. Other bias measures were difficult to assess as a whole, without details of methods for randomisation and allocation concealment, and whether staff members measuring outcomes were masked.

Findings from our systematic literature review and meta-analysis of RCTs do not support the efficacy of low-fat diet interventions over higher-fat diet interventions of similar intensity for significant, long-term, clinically meaningful weight control. Previous trials comparing low-fat diet interventions with participants' usual diets or minimal intensity control groups have misled perceptions of the efficacy of reductions in fat intake as a strategy for long-term weight loss. In fact, comparisons of similar intervention intensity conclude that dietary interventions that aim to reduce total fat intake lead to significantly less weight loss compared with higher-fat, low-carbohydrate diets. Health and nutrition guidelines should cease recommending low-fat diets for weight loss in view of the clear absence of long-term efficacy when compared with other similar intensity dietary interventions. Additional research is needed to identify optimum intervention strategies for long-term weight loss and weight maintenance, including the need to look beyond variations in macronutrient composition.

Contributors
DKT developed the study protocol, did the scientific literature search, extracted, analysed, and interpreted the data, and drafted the report. MC did the scientific literature search and extracted the data. JEM, DSL, WW, and FBH contributed to the study protocol, interpreted key data, and reviewed the report.

Declaration of interests
DSL received royalties for books on nutrition and obesity. FBH has received research support from California Walnut Commission and Metagenics. All other authors declare no competing interests.

Acknowledgments
This study was supported by grants from the National Institutes of Health (DK082730, HL34594, HL60712, CA176726, DK58845, DK46200, DK103720, and CA155626). DKT was supported by a fellowship from the American Diabetes Association (7-12-MN-34). The funding sources did not participate in the design or conduct of the study; collection, management, analysis or interpretation of the data; or preparation, review, or approval of the manuscript.

References
1 Hooper L, Abdelhamid A, Moore HJ, Douthwaite W, Skeaff CM, Summerbell CD. Effect of reducing total fat intake on body weight: systematic review and meta-analysis of randomised controlled trials and cohort studies. *BMJ* 2012; **345:** e7666.
2 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* 2014; **312:** 923–33.
3 Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med* 2009; **360:** 859–73.
4 McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low fat, low-energy diet for weight loss in overweight adults. *Int J Obes Relat Metab Disord* 2001; **25:** 1503–11.
5 Davis NJ, Tomuta N, Schechter C, et al. Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. *Diabetes Care* 2009; **32:** 1147–52.
6 Howard BV, Manson JE, Stefanick ML, et al. Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. *JAMA* 2006; **295:** 39–49.
7 Foster-Schubert KE, Alfano CM, Duggan CR, et al. Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. *Obesity (Silver Spring)* 2012; **20:** 1628–38.
8 Babio N, Toledo E, Estruch R, et al. Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. *CMAJ* 2014; **186:** E649–57.
9 Higgins JPT, Altman DG, Sterne JAC, eds. Chapter 8: assessing risk of bias in included studies. In: Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions, version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011.
10 Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327:** 557–60.
11 Willett W, Stampfer M, Chu NF, Spiegelman D, Holmes M, Rimm E. Assessment of questionnaire validity for measuring total fat intake using plasma lipid levels as criteria. *Am J Epidemiol* 2001; **154:** 1107–12.
12 Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994; **50:** 1088–101.
13 Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; **315:** 629–34.
14 Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Comparison of two methods to detect publication bias in meta-analysis. *JAMA* 2006; **295:** 676–80.
15 Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. *JAMA* 2007; **297:** 969–77.

16 Anderson JW, Garrity TF, Wood CL, Whitis SE, Smith BM, Oeltgen PR. Prospective, randomized, controlled comparison of the effects of low-fat and low-fat plus high-fiber diets on serum lipid concentrations. *Am J Clin Nutr* 1992; **56:** 887–94.

17 Barnard ND, Cohen J, Jenkins DJ, et al. A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. *Am J Clin Nutr* 2009; **89:** 1588S–96S.

18 Bazzano LA, Hu T, Reynolds K, et al. Effects of low-carbohydrate and low-fat diets: a randomized trial. *Ann Intern Med* 2014; **161:** 309–18.

19 Bertz F, Brekke HK, Ellegard L, Rasmussen KM, Wennergren M, Winkvist A. Diet and exercise weight-loss trial in lactating overweight and obese women. *Am J Clin Nutr* 2012; **96:** 698–705.

20 Boyd NF, Cousins M, Beaton M, Kriukov V, Lockwood G, Tritchler D. Quantitative changes in dietary fat intake and serum cholesterol in women: results from a randomized, controlled trial. *Am J Clin Nutr* 1990; **52:** 470–76.

21 Simon MS, Heilbrun LK, Boomer A, et al. A randomized trial of a low-fat dietary intervention in women at high risk for breast cancer. *Nutr Cancer* 1997; **27:** 136–42.

22 Brehm BJ, Lattin BL, Summer SS, et al. One-year comparison of a high-monounsaturated fat diet with a high-carbohydrate diet in type 2 diabetes. *Diabetes Care* 2009; **32:** 215–20.

23 Hebert JR, Ebbeling CB, Olendzki BC, et al. Change in women's diet and body mass following intensive intervention for early-stage breast cancer. *J Am Diet Assoc* 2001; **101:** 421–31.

24 Brinkworth GD, Noakes M, Buckley JD, Keogh JB, Clifton PM. Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. *Am J Clin Nutr* 2009; **90:** 23–32.

25 Tay J, Brinkworth GD, Noakes M, Keogh J, Clifton PM. Metabolic effects of weight loss on a very-low-carbohydrate diet compared with an isocaloric high-carbohydrate diet in abdominally obese subjects. *J Am Coll Cardiol* 2008; **51:** 59–67.

26 Das SK, Gilhooly CH, Golden JK, et al. Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: a 1-y randomized controlled trial. *Am J Clin Nutr* 2007; **85:** 1023–30.

27 Martin LJ, Li Q, Melnichouk O, et al. A randomized trial of dietary intervention for breast cancer prevention. *Cancer Res* 2011; **71:** 123–33.

28 Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 2005; **293:** 43–53.

29 Stefanick ML, Mackey S, Sheehan M, Ellsworth N, Haskell WL, Wood PD. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. *N Engl J Med* 1998; **339:** 12–20.

30 Knopp RH, Walden CE, Retzlaff BM, et al. Long-term cholesterol-lowering effects of 4 fat-restricted diets in hypercholesterolemic and combined hyperlipidemic men. The Dietary Alternatives Study. *JAMA* 1997; **278:** 1509–15.

31 Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med* 2008; **359:** 229–41.

32 Ebbeling CB, Leidig MM, Feldman HA, Lovesky MM, Ludwig DS. Effects of a low-glycemic load vs low-fat diet in obese young adults: a randomized trial. *JAMA* 2007; **297:** 2092–102.

33 Elhayany A, Lustman A, Abel R, Attal-Singer J, Vinker S. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: a 1-year prospective randomized intervention study. *Diabetes Obes Metab* 2010; **12:** 204–09.

34 Esposito K, Maiorino MI, Ciotola M, et al. Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. *Ann Intern Med* 2009; **151:** 306–14.

35 Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 2003; **348:** 2082–90.

36 Foster GD, Wyatt HR, Hill JO, et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. *Ann Intern Med* 2010; **153:** 147–57.

37 Guldbrand H, Dizdar B, Bunjaku B, et al. In type 2 diabetes, randomisation to advice to follow a low-carbohydrate diet transiently improves glycaemic control compared with advice to follow a low-fat diet producing a similar weight loss. *Diabetologia* 2012; **55:** 2118–27.

38 Harvey-Berino J. Calorie restriction is more effective for obesity treatment than dietary fat restriction. *Ann Behav Med* 1999; **21:** 35–39.

39 Iqbal N, Vetter ML, Moore RH, et al. Effects of a low-intensity intervention that prescribed a low-carbohydrate vs. a low-fat diet in obese, diabetic participants. *Obesity (Silver Spring)* 2010; **18:** 1733–38.

40 Keogh JB, Brinkworth GD, Clifton PM. Effects of weight loss on a low-carbohydrate diet on flow-mediated dilatation, adhesion molecules and adiponectin. *Br J Nutr* 2007; **98:** 852–59.

41 Klemsdal TO, Holme I, Nerland H, Pedersen TR, Tonstad S. Effects of a low glycemic load diet versus a low-fat diet in subjects with and without the metabolic syndrome. *Nutr Metab Cardiovasc Dis* 2010; **20:** 195–201.

42 Kristal AR, Blount PL, Schenk JM, et al. Low-fat, high fruit and vegetable diets and weight loss do not affect biomarkers of cellular proliferation in Barrett esophagus. *Cancer Epidemiol Biomarkers Prev* 2005; **14:** 2377–83.

43 Lapointe A, Weisnagel SJ, Provencher V, et al. Comparison of a dietary intervention promoting high intakes of fruits and vegetables with a low-fat approach: long-term effects on dietary intakes, eating behaviours and body weight in postmenopausal women. *Br J Nutr* 2010; **104:** 1080–90.

44 Lim SS, Noakes M, Keogh JB, Clifton PM. Long-term effects of a low carbohydrate, low fat or high unsaturated fat diet compared to a no-intervention control. *Nutr Metab Cardiovasc Dis* 2010; **20:** 599–607.

45 McAuley KA, Smith KJ, Taylor RW, McLay RT, Williams SM, Mann JI. Long-term effects of popular dietary approaches on weight loss and features of insulin resistance. *Int J Obes (Lond)* 2006; **30:** 342–49.

46 Djuric Z, Poore KM, Depper JB, et al. Methods to increase fruit and vegetable intake with and without a decrease in fat intake: compliance and effects on body weight in the nutrition and breast health study. *Nutr Cancer* 2002; **43:** 141–51.

47 Pilkington TR, Stafford JL, Hankin VS, Simmonds FM, Koerselman HB. Practical diets for lowering serum lipids. *BMJ* 1960; **1:** 23–25.

48 Schatzkin A, Lanza E, Corle D, et al. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. *N Engl J Med* 2000; **342:** 1149–55.

49 Elmer PJ, Obarzanek E, Vollmer WM, et al. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. *Ann Intern Med* 2006; **144:** 485–95.

50 Shah M, Baxter JE, McGovern PG, Garg A. Nutrient and food intake in obese women on a low-fat or low-calorie diet. *Am J Health Promot* 1996; **10:** 179–82.

51 Frisch S, Zittermann A, Berthold HK, et al. A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program. *Cardiovasc Diabetol* 2009; **8:** 36.

52 Stern L, Iqbal N, Seshadri P, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med* 2004; **140:** 778–85.

53 Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. *N Engl J Med* 2003; **348:** 2074–81.

54 Swinburn BA, Metcalf PA, Ley SJ. Long-term (5-year) effects of a reduced-fat diet intervention in individuals with glucose intolerance. *Diabetes Care* 2001; **24:** 619–24.

55 Tapsell LC, Hokman A, Sebastiao A, et al. The impact of usual dietary patterns, selection of significant foods and cuisine choices on changing dietary fat under 'free living' conditions. *Asia Pac J Clin Nutr* 2004; **13:** 86–91.

56 Azadbakht L, Mirmiran P, Esmaillzadeh A, Azizi F. Better dietary adherence and weight maintenance achieved by a long-term moderate-fat diet. *Br J Nutr* 2007; **97:** 399–404.

57 Turner-McGrievy GM, Barnard ND, Scialli AR. A two-year randomized weight loss trial comparing a vegan diet to a more moderate low-fat diet. *Obesity (Silver Spring)* 2007; **15:** 2276–81.

58 Viegener BJ, Perri MG, Nezu AM, Renjilian DA, McKelvey WF, Schein RL. Effects of an intermittent, low-fat, low-calorie diet in the behavioral treatment of obesity. *Behav Ther* 1990; **21:** 499–509.

59 Henderson MM, Kushi LH, Thompson DJ, et al. Feasibility of a randomized trial of a low-fat diet for the prevention of breast cancer: dietary compliance in the Women's Health Trial Vanguard Study. *Prev Med* 1990; **19:** 115–33.

60 Pierce JP, Natarajan L, Caan BJ, et al. Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: the Women's Healthy Eating and Living (WHEL) randomized trial. *JAMA* 2007; **298:** 289–98.

61 Chlebowski RT, Blackburn GL, Thomson CA, et al. Dietary fat reduction and breast cancer outcome: interim efficacy results from the Women's Intervention Nutrition Study. *J Natl Cancer Inst* 2006; **98:** 1767–76.

62 Chlebowski RT, Blackburn GL, Buzzard IM, et al. Adherence to a dietary fat intake reduction program in postmenopausal women receiving therapy for early breast cancer. The Women's Intervention Nutrition Study. *J Clin Oncol* 1993; **11:** 2072–80.

63 Wood PD, Stefanick ML, Williams PT, Haskell WL. The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. *N Engl J Med* 1991; **325:** 461–66.

64 Bueno NB, de Melo IS, de Oliveira SL, da Rocha Ataide T. Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. *Br J Nutr* 2013; **110:** 1178–87.

Prescribing low-fat diets: useless for long-term weight loss?

What diet is best for weight loss? This question has been hotly debated for decades, and answering it correctly is becoming increasingly important in view of the rising prevalence of obesity worldwide.[1] Previous recommendations to consume low-fat diets might have been ill advised, especially if dietary fat is replaced by refined carbohydrates. In *The Lancet Diabetes & Endocrinology*, Deirdre Tobias and colleagues[2] add to this message by presenting results of a systematic review and meta-analysis of randomised controlled trials comparing low-fat diets to other diets in their ability to generate long-term (ie, ≥1 year) weight loss. Their main conclusion is that there is no good evidence for recommending low-fat diets: when low-fat weight loss interventions were compared with various other higher-fat weight loss interventions, the weighted mean difference (WMD) in weight loss was just 0·36 kg (95% CI –0·66 to 1·37), and was not statistically significant. In fact, low-carbohydrate, higher-fat weight loss diets led to significantly greater weight loss than did low-fat interventions (WMD 1·15 kg [0·52 to 1·79]).

However, before proclaiming the superiority of low-carbohydrate diets for the treatment of obesity, consider the magnitude of the benefit: participants prescribed low-carbohydrate diets lost only about 1 kg of additional weight after 1 year compared with those advised to consume low-fat diets. Although statistically significant, such a miniscule difference in weight loss is clinically meaningless. Furthermore, irrespective of the diet prescription, the overall average weight loss in trials testing interventions designed to reduce bodyweight was unimpressive (3·75 kg [SD 2·7]).

Why was long-term weight loss so poor, regardless of the type of diet prescribed? One key reason is that adherence to the diets probably lapsed long before the 1 year mark. Outpatient weight-loss studies ubiquitously achieve a maximum weight loss after about 6–8 months, followed by weight regain.[3] Energy balance calculations suggest that at the point of maximum weight loss, diet adherence has already substantially waned.[4–6] Confirming these calculations, one diet study[7] used expensive biomarker methods to measure energy intake and reported that adherence was poor even when participants were provided with all their food for the first 6 months, and adherence fell further after food provision was stopped. Tobias and colleagues only included diet studies lasting at least 1 year, so any reported differences in weight loss were probably due to diet differences that had long since dissipated.

Investment in outpatient randomised controlled weight-loss trials comparing diet advice has been enormous, but very little evidence has been amassed about the effects of actually eating the prescribed diets over the long term. A major problem is that accurate assessment of diet adherence in outpatient studies is severely limited,[8,9] although promising new methods are being developed.[6] Much more research is needed to determine the factors that affect diet adherence and thereby help maintain weight loss over the long term.[10] What seems to be clear is that long-term diet adherence is abysmal, irrespective of whether low-fat or other diets, such as low-carbohydrate diets, are prescribed.

Ashley Cooper/Science Photo Library

Lancet Diabetes Endocrinol 2015
Published Online October 30, 2015
http://dx.doi.org/10.1016/S2213-8587(15)00413-1
See Online/Articles
http://dx.doi.org/10.1016/S2213-8587(15)00367-8

Kevin D Hall
National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD 20892, USA
kevinh@niddk.nih.gov

I am supported by the Intramural Research Program of the National Institutes of Health (NIH), National Institute of Diabetes and Digestive and Kidney Diseases. I have a patent pending on a method of personalised dynamic feedback control of bodyweight (US Patent Application No. 13/754,058; assigned to the NIH) and I have received funding from the Nutrition Science Initiative to investigate the effects of ketogenic diets on human energy expenditure.

1. Swinburn BA, Sacks G, Hall KD, et al. The global obesity pandemic: shaped by global drivers and local environments. *Lancet* 2011; **378:** 804–14.
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. *Lancet Diabetes Endocrinol* 2015; published online Oct 30. http://dx.doi.org/10.1016/S2213-8587(15)00367-8.
3. Franz MJ, VanWormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc* 2007; **107:** 1755–67.
4. Hall KD. Predicting metabolic adaptation, body weight change, and energy intake in humans. *Am J Physiol Endocrinol Metab* 2010; **298:** E449–66.
5. Hall KD, Sacks G, Chandramohan D, et al. Quantification of the effect of energy imbalance on bodyweight. *Lancet* 2011; **378:** 826–37.
6. Sanghvi A, Redman LA, Martin CK, Ravussin E, Hall KD. Validation of an inexpensive and accurate mathematical method to measure long-term changes in free-living energy intake. *Am J Clin Nutr* 2015; **102:** 353–58.
7. Das SK, Gilhooly CH, Golden JK, et al. Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: a 1-y randomized controlled trial. *Am J Clin Nutr* 2007; **85:** 1023–30.
8. Schoeller DA. How accurate is self-reported dietary energy intake? *Nutr Rev* 1990; **48:** 373–79.
9. Winkler JT. The fundamental flaw in obesity research. *Obes Rev* 2005; **6:** 199–202.
10. MacLean PS, Wing RR, Davidson T, et al. NIH working group report: innovative research to improve maintenance of weight loss. *Obesity (Silver Spring)* 2015; **23:** 7–15.