Management of Obesity

Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities

M. Hession¹, C. Rolland¹, U. Kulkarni¹, A. Wise² and J. Broom¹

¹Centre for Obesity Research and Epidemiology (CORE), Faculty of Heath and Social Care; ²School of Pharmacy and Life Sciences, Robert Gordon University, Aberdeen, UK

Received 15 April 2008; revised 25 June 2008; accepted 15 July 2008

Address for correspondence: Dr Catherine Rolland, CORE (Centre for Obesity Research and Epidemiology), The Robert Gordon University, Aberdeen AB25 1HG, UK. E-mail: c.rolland@rgu.ac.uk

Summary

There are few studies comparing the effects of low-carbohydrate/high-protein diets with low-fat/high-carbohydrate diets for obesity and cardiovascular disease risk. This systematic review focuses on randomized controlled trials of lowcarbohydrate diets compared with low-fat/low-calorie diets. Studies conducted in adult populations with mean or median body mass index of ≥ 28 kg m⁻² were included. Thirteen electronic databases were searched and randomized controlled trials from January 2000 to March 2007 were evaluated. Trials were included if they lasted at least 6 months and assessed the weight-loss effects of lowcarbohydrate diets against low-fat/low-calorie diets. For each study, data were abstracted and checked by two researchers prior to electronic data entry. The computer program Review Manager 4.2.2 was used for the data analysis. Thirteen articles met the inclusion criteria. There were significant differences between the groups for weight, high-density lipoprotein cholesterol, triacylglycerols and systolic blood pressure, favouring the low-carbohydrate diet. There was a higher attrition rate in the low-fat compared with the low-carbohydrate groups suggesting a patient preference for a low-carbohydrate/high-protein approach as opposed to the Public Health preference of a low-fat/high-carbohydrate diet. Evidence from this systematic review demonstrates that low-carbohydrate/high-protein diets are more effective at 6 months and are as effective, if not more, as low-fat diets in reducing weight and cardiovascular disease risk up to 1 year. More evidence and longer-term studies are needed to assess the long-term cardiovascular benefits from the weight loss achieved using these diets.

Keywords: Cardiovascular risk, low-carbohydrate, meta-analysis, obesity.

obesity reviews (2009) 10, 36-50

Author contributions: Ms Hession, Dr Rolland, Dr Kulkarni, Dr Wise and Professor Broom had full access to all of the data in the study and take responsibility for the integrity of the data analysis: (i) study concept and design: Hession, Rolland, Kulkarni, Wise, Broom; (ii) acquisition of data: Hession, Rolland; (iii) analysis and interpretation of data: Hession, Rolland; (iv) drafting of the manuscript: Hession, Rolland, Kulkarni; (v) critical revision of the manuscript for important intellectual content: Wise, Broom; (vi) statistical analysis: Hession; (vii) administrative, technical or material support: Hession, Rolland, Kulkarni, Wise, Broom and (viii) study supervision: Broom.

Introduction

The prevalence of overweight and obesity is already high and continues to increase in both the developed and developing world (1). Obesity has been implicated as the second most preventable cause of death in the United States. After remaining reasonably constant in the 1960s and 1970s, the prevalence of obesity among adults in the United States increased by around 50% per decade throughout the 1980s and 1990s. Two-thirds of adults in the United States today are obese or overweight. In the United States, 28% of men, 34% of women and nearly 50% of non-Hispanic black women are at present obese (2). At any time, approximately 45% of women and 30% of men in the UK are trying to lose weight (3). Most adults in England are now overweight, and nearly one-quarter are obese (http:// www.foresight.gov.uk/obesity/17.pdf). Obesity has been shown to be associated with increased risk of type 2 diabetes mellitus, hypertension, dyslipidemia and consequent cardiovascular disease. Obesity ranks second only to smoking in the aetiology of cancer and is an important factor in osteoarthritis and obstructive sleep apnoea (4).

Recently, low-carbohydrate/high-protein (LC/HP) diets have become popular as an aid to weight loss. Significant weight loss on a LC/HP diet without significant elevations of serum cholesterol has been reported. Studies comparing the 'Atkins' diet with the classical low-fat (LF) diet have appeared in the literature recently and are the subject of increasing public interest (5) due to the beneficial improvements in cardiovascular risk and weight loss achieved with this type of dietary approach (6,7).

This systematic review focuses on randomized controlled trials (RCTs) of LC/HP diets compared with LF/highcarbohydrate (HC) conventional diets. The systematic review also examines the outcomes of such trials in relation to effects on cardiovascular disease risk. This systematic review focuses on updating the literary evidence from RCTs of LC/HP diets compared with LF/HC diets to assess their impact on weight loss and cardiovascular risk. In addition, it demonstrates lower attrition rates in the LC/HP groups compared with the LF/HC groups suggesting patient preference for the former approach.

Methods

Inclusion criteria

The protocol used for this systematic review follows the methods recommended by the Cochrane Collaboration (8). RCTs were included if they assessed the weight-loss effects of LC/HP diets against LF/HC diets. Only RCTs from January 2000 to March 2007 were evaluated, as this review is intended to assess the current literature in this field and update the National Health Service R&D Health Technology Assessment systematic review of diet and lifestyle on weight loss and cardiovascular risk published by Avenell et al. (8). Only studies conducted in an adult population were included, as defined by minimum age greater than 18 years. RCTs where the participants had a mean or median body mass index (BMI) of $\geq 28 \text{ kg m}^{-2}$ were included. A BMI cut-off of ≥ 28 kg m⁻² was used to allow the inclusion of studies of ethnic groups where the classification of obesity is at a lower BMI cut-off (9). RCTs evaluated in this review had to be of at least 6-month duration, including the period of active intervention and follow-up.

Types of intervention

The focus of this review was to examine LC/HP diets against other types of diets designed to induce weight loss and/or prevent weight gain, and induce changes in cardiovascular risk factors. The types of dietary intervention evaluated were:

• HP 'ketogenic' diet, where the carbohydrate content was less than 40 g d⁻¹, irrespective of calorie content.

• LC diets (carbohydrate $\leq 60 \text{ g d}^{-1}$).

• 'Healthy eating' advice.

• LF (30% or less daily energy from dietary fat) – 600 kcal deficit diet.

Outcome measures

Weight loss or prevention of weight gain was the main outcomes assessed from the RCTs included in the review. With regard to cardiovascular disease risk factors, the following outcomes were also included:

• Serum lipids, including total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triacylglycerols.

- Systolic and diastolic blood pressure.
- Glycemic control.

Attrition rates were also analysed for each study to assess patient acceptability.

Search strategy for the identification of included studies

This systematic review was restricted to RCTs where the full study report was available. A wide search strategy was applied to identify as many RCTs evaluating dietary interventions as possible and which were relevant to the management of obesity and cardiovascular disease risk factors. Thirteen electronic databases were searched including MEDLINE, Commonwealth Agricultural Bureau (CAB) abstracts and the Cochrane Central Register of Controlled Trials. The search strategy incorporated weight loss, cardiovascular disease and obesity-related terms and text terms, specific to each database. Seven obesity and nutrition journals were hand-searched including the *International Journal of Obesity and Obesity Research*. Reference lists of included studies were searched and authors contacted for further details of their trials.

Quality assessment of studies

Full copies of studies were assessed by two researchers for methodological quality using a standard form. The

researchers were not blinded to author, journal or institution. Differences of opinion were resolved by discussion. Trial quality was assessed, including whether or not the analysis was undertaken on an intention to treat basis.

Data abstraction

A data abstraction form was created for this review based on a standard format (8). For each study, data were abstracted and checked by different researchers prior to electronic data entry.

Data analysis

The computer program Review Manager 4.2.2 was used for the analysis of the data from the reviews. If results from studies could be quantitatively combined, a statistical meta-analysis of the data was undertaken to determine the typical effect size of the intervention. For continuous data, a weighted mean difference (WMD) was calculated. The chi-square test was used to test for heterogeneity across the studies. The significance value was set at 0.05.

Handling of missing data

Data processing for this review in Review Manager required the input of the mean and the standard deviation (SD) of the change between two time points. Where weight or risk factors were reported as actual values instead of changes, the differences were calculated by subtracting the end point value from the baseline value. If SD for changes in weight and risk factors were missing, the following assumption was made – a previously published linear regression of the SD of the mean change in weight on the absolute mean change for weight (8), derived from weightloss RCTs, was used to supply missing SD. Similar data were used to infer missing SD for the other variables analysed in this review.

Results

Identified studies

A total of 13 (10–22) out of 123¹ articles met the inclusion criteria and were included in the systematic review. Reasons for which they were not included are summarized in Table 1.

Study characteristics

All the included studies were RCTs ranging from 6- to 36-month duration. Five of the trials were of 6-month

¹A list of papers that were excluded from the systematic review can be obtained from the corresponding author.

 Table 1
 Summary of reasons for which papers were not included in the systematic review

Reasons	Number of studies
	71
Not a randomized controlled trial	71
Study was less than 6-month duration	36
Mean/median body mass index of subjects was less than 28 kg m ⁻²	5
Carbohydrate content of the 'low-carbohydrate' diet was too high	14
Subjects did not receive an appropriate treatment	50
Subjects were not human	5
Subjects were under 18	6

duration and six of 12-month. One trial lasted 17 months and another lasted 36 months. As there was only one study lasting 17 months (11) and one lasting 36 months (12) data reported at that time point in that study were not included in the analysis. All of the studies were designed to reduce or prevent weight gain and also examined cardiovascular disease risk factors.

Ten of the studies compared LC/HP diets with LF/HC diets and two studies compared medium-protein diets with HP diets. Table 2 gives a summary of the diets and carbo-hydrate content for each of the studies.

Participant characteristics

A total of 1222 volunteers were recruited between the 13 studies. Fig. 1 shows the percentage attrition rates. Out of the 1222 participants assigned to the diets, there were 441 (36%) attritions during the interventions. There was a higher attrition rate in the conventional/LF/medium-protein groups compared with the LC/HP intervention groups. The difference in attrition rates between the two groups was significant (P = 0.001) after performing a chi-squared test.

Quality of trials

For the following variables, the LC/HP refers to the LC/HP intervention groups and the LF/HC refers to the LF/HC comparison/control groups.

Weight

The WMD in weight change was -4.02 kg in favour of the LC/HP group at 6 months (Fig. 2a) (P < 0.00001). At 12 months this difference had fallen to only -1.05 kg (P < 0.05) (Fig. 2b). There were differences (P < 0.0001) among the studies at 6 months, but agreement shown by lack of heterogeneity at 12 months.

Study	Diets compared	Amount of CHO consumed per day for LC/HP	Were the diets energy controlled?
Brehm <i>et al.</i> , 2002 (10)	VLC/HP vs. LF/HC	20 g increased to 40-60 g after 2 weeks	LF – kcal restricted
Brinkworth et al., 2004 (11)	MP vs. SP	40% CHO	Initial 12 weeks energy restriction, followed by 4 weeks energy balance
Cardillo et al., 2006 (12)	LC/HP vs. LF/HC	30 g for 6 months followed by reintroduction of CHO	LF - reduced by 500 kcal d ⁻¹
Dansinger <i>et al.</i> , 2005 (13)	VLC/HP vs. LF/HC	30 g increased to 50 g gradually	LF – kcal restricted
Due <i>et al.</i> , 2004 (14)	MP (12% of energy) vs. HP (25% of energy), both 30% fat	40% CHO	No (<i>ad libitum</i>)
Foster <i>et al.</i> , 2003 (15)	VLC/HP vs. LF/HC	20 g then increased gradually	LF – women: 1200–1500 kcal d ⁻¹ ; men: 1500–1800 kcal d ⁻¹
Gardner <i>et al.</i> , 2007 (16)	VLC/HP vs. LF/HC	20 g increased to 50 g gradually	LF – kcal restricted
Samaha <i>et al.</i> , 2003 (17)	LC/HP vs. LF/HC	30 g	LF – reduced by 500 kcal d ⁻¹
Seshadri <i>et al.</i> , 2004 (18)	LC/HP vs. LF/HC	30 g	LF – reduced by 500 kcal d ⁻¹
Stern et al., 2004 (19)	LC/HP vs. LF/HC	30 g	LF – kcal restricted
Truby et al., 2006 (20)	Atkins vs. LF/HC	20 g increased to 5 g week ⁻¹ when 10 lb away from target weight	LF – kcal restricted
Tsai <i>et al.</i> , 2005 (21)	LC/HP vs. LF/HC	30 g increased to 50 g gradually	LF – kcal restricted
Yancy et al., 2004 (22)	VLC/HP vs. LF/HC	<20 g increased by 5 g d ⁻¹ when reached half of target weight	LF – reduced by 500 kcal d ⁻¹

CHO, Carbohydrate; HC, high-carbohydrate; HP, high-protein; LC, low-carbohydrate; LF, low-fat; MP, moderate protein; SP, standard protein; VLC, very-low-carbohydrate.



Figure 1 Percentage attrition rate in low-carbohydrate (white) and low-fat (black) diets reported in the literature.

Total cholesterol

The WMD in total cholesterol change was 0.19 mmol L⁻¹ at 6 months (P < 0.0001) with the LC/HP group demonstrating the increased cholesterol (Fig. 3a). This was also the case at 12 months, although the difference between the groups was smaller and not significant (0.10 mmol L⁻¹, P = 0.31) (Fig. 3b). There were no differences among the studies at 6 (P = 0.84) and 12 (P = 0.14) months.

Low-density lipoprotein cholesterol

The WMD in LDL cholesterol change was 0.14 mmol L⁻¹ at 6 months (P < 0.00001) with the LC/HP group demonstrating the increased LDL cholesterol (Fig. 4a). The difference between the groups was greater at 12 months (0.37 mmol L⁻¹) (P < 0.00001) with the LC/HP group again demonstrating the increased LDL cholesterol

(Fig. 4b). There were no differences among the studies at 6 months (P = 0.65), but there were differences found between the studies at 12 months (P < 0.00001).

High-density lipoprotein cholesterol

The WMD in HDL cholesterol change was 0.04 mmol L⁻¹ at 6 months (P = 0.03) favouring the LC/HP group (Fig. 5a). There was a slightly greater increase in the WMD in HDL cholesterol at 12 months (0.06 mmol L⁻¹) favouring the LC/HP group (P < 0.05). There were no differences found between the studies at 6 months (P = 0.46) or 12 months (P = 0.49).

Triacylglycerol

The WMD in triacylglycerol was $-0.17 \text{ mmol L}^{-1}$ at 6 months (P = 0.0001) favouring the LC/HP group (Fig. 6a). At 12 months the WMD between the groups was $-0.19 \text{ mmol L}^{-1}$ favouring the LC/HP group (P = 0.04). Again, there was evidence of heterogeneity across the groups (P = 0.01).

Systolic blood pressure

The WMD drop in systolic blood pressure of -1.35 mmHg at 6 months favouring the LC/HP group was not significant (Fig. 7a). At 12 months the WMD between the groups was

or sub category	z	Treatment Mean (SD)	z	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% Cl
Brehm	22	-8.50(1.00)	20	-3.90(1.00)		74.27	-4.60 [-5.21, -3.99]
Brinkworth	21	-8.10(8.20)	22	-8.50(6.10)		1.45	0.40 [-3.94, 4.74]
Dansinger	40	-3.20(4.90)	40	-3.50(5.60)	+	5.12	0.30 [-2.01, 2.61]
Due	23	-9.40(8.50)	23	-5.90(7.50)		1.27	-3.50 [-8.13, 1.13]
Foster	33	-6.90(6.50)	30	-3.10(5.60)	+	3.05	-3.80 [-6.79, -0.81]
Samaha	64	-5.80(8.60)	68	-1.90(4.20)	ł	5.01	-3.90 [-6.23, -1.57]
Seshadri	43	-8.50(9.30)	35	-3.50(4.90)		2.63	-5.00 [-8.22, -1.78]
Truby	40	-6.00(6.40)	47	-6.60(5.40)		4.31	0.60 [-1.91, 3.11]
Yancy	59	-12.00(9.30)	60	-6.50(7.70)	-	2.89	-5.50 [-8.57, -2.43]
	345		345		•	100 00	-4 02 [-4 54 -3 40]
Test for heterogeneity	/: Chi ² = 35.31, df = 8 : Z = 15.08 (<i>P</i> < 0.0000	(<i>P</i> < 0.0001), I ² = 77.3% 01)) 1		•) - - - - - - - - - - - - - - - - - - -	
					-10 -5 0 5	- 0	
					Favours treatment Favours con	itrol	
Review: Sys Comparison: 02 \ Outcome: 01 \	tematic Review April 2 Weight change at 12 π Weight change at 12 π	2008 nonths nonths					
Study or sub category	Z	Treatment Mean (SD)	Z	Control Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
Dansinger	40	-2.10(4.80)	40	-3.00(4.90)		24.02	0.90 [-1.23, 3.03]
Due	23	-6.20(7.60)	18	-4.30(7.10)		5.32	-1.90 [-6.42, 2.62]
Foster	33	-4.20(6.76)	30	-2.45(6.31)	+	10.42	-1.75 [-4.98, 1.48]
Gardner	77	-4.70(7.20)	79	-2.20(6.50)	+	23.38	-2.50 [-4.65, -0.35]
Stern	44	-5.10(8.70)	43	-3.10(8.40)	-	8.40	-2.00 [-5.59, 1.59]
Truby	28	-9.00(4.10)	33	-9.10(6.20)	-	16.00	0.10 [-2.50, 2.70]
Tsai	64	-5.10(8.70)	65	-3.10(8.40)	-	12.45	-2.00 [-4.95, 0.95]
Total (95% CI)	309		308		•	100.00	-1.05 [-2.09, -0.01]
Test for heterogeneity Test for overall effect:	<i>y</i> : Chi ² = 6.71, df = 6 (<i>F</i> : Z = 1.98 (<i>P</i> = 0.05)	⊃ = 0.35), l² = 10.5%			,		
					-10 -5 0 5	10	
					Favours treatment Favours con	itrol	

© 2008 The Authors Journal compilation © 2008 International Association for the Study of Obesity. **obesity** reviews **10**, 36–50

r sub category								
	Z		Mean (SD)	z	Mean (SD)	95% CI	%	95% CI
	2	2	-0.02(1.08)	20	-0.04(1.08)		1.84	0.02 [-0.63, 0.67]
Brinkworth	2	1	0.00(1.08)	22	-0.20(1.08)		1.88	0.20 [-0.45, 0.85]
Dansinger	4	0	-0.02(0.46)	40	-0.20(0.54)	ł	16.25	0.18 [-0.04, 0.40]
Due	2	č	-0.31(1.08)	23	0.03(1.08)		2.02	-0.34 [-0.96, 0.28]
Foster	ε	ć	0.12(0.24)	30	-0.11(0.24)	+	55.76	0.23 [0.11, 0.35]
Samaha	9	4	0.05(1.08)	68	-0.02(1.08)		5.78	0.07 [-0.30, 0.44]
Seshadri	4	c.	0.07(1.00)	35	-0.07(1.10)		3.53	0.14 [-0.33, 0.61]
Truby	4	0	-0.29(0.80)	47	-0.55(0.70)		7.73	0.26 [-0.06, 0.58]
Yancy	5	<u>م</u>	-0.21(1.08)	60	-0.35(1.08)		5.21	0.14 [-0.25, 0.53]
otal (95% CI) est for heterogene	34 ity: Chi ² = 4.17, df =	5 = 8 (P =	0.84), l ² = 0%	345		•	100.00	0.19 [0.10, 0.28]
						-1 -0.5		
eview: Sy omparison: 04 utcome: 01	ystematic Review A 4 Total cholesterol c 1 Total cholesterol c	pril 2008 change a change a	3 at 12 months at 12 months					
tudy r sub category	Z		Freatment Mean (SD)	z	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% CI
Dansinger Due	4 6	0 "	-0.11(0.59)	40 18	-0.21(0.62) 0.68(1.08)		55.78 8.84	0.10 [-0.17, 0.37] -0.58 [-1.25, 0.09]
Foster	I M	i M	0.10(1.08)	30	-0.03(1.08)		13.76	0.13 [-0.40, 0.66]
Stern	4	4	0.16(1.11)	43	-0.21(0.91)		- 21.61	0.37 [-0.06, 0.80]
otal (95% CI) est for heterogenei	14 ity: Chi ² = 5.56, df = ot: 7 - 1 01 / D - 0 3	.0 = 3 (P =	0.14), l ² = 46.0%	131		♦	100.00	0.10 [-0.10, 0.30]
							-	
						Favours treatment Favours contr		

Review:

$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Study	:	Treatment	:	Control	WMD (fixed)	Weight	WMD (fixed)
	or sub category	N	Mean (SD)	Z	Mean (SD)	95% CI	%	95% CI
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Brehm	22	-0.02(0.29)	20	-0.15(0.29)		11.48	0.13 [-0.05, 0.31]
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Brinkworth	21	-0.20(0.29)	22	-0.30(0.29)	+	11.77	0.10 [-0.07, 0.27]
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Dansinger	40	-0.06(0.36)	40	-0.18(0.62)	+	7.17	0.12 [-0.10, 0.34]
Gardner 70 0.04(0.57) 63 -0.04(0.40) 12.83 0.06 10.00 0.21 Semalation 43 0.10(0.53) 58 0.77(0.46) 10.73 0.03 10.13 0.03 Semalation 43 0.13(0.53) 58 0.77(0.46) 10.00 0.14 10.00 0.03 10.13 0.03 Semalation 53 0.04(0.29) 59 0.04(0.29) 50 0.03 10.00 0.14 10.00 0.04 10.00 0.01	Foster	33	0.08(0.33)	30	-0.04(0.40)	+	10.67	0.12 [-0.06, 0.30]
	Gardner	70	0.04(0.57)	63	-0.04(0.40)	+	12.83	0.08 [-0.09, 0.25]
	Samaha	64	0.10(0.59)	68	0.07(0.46)	+	10.78	0.03 [-0.15, 0.21]
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Seshadri	43	0.18(0.98)	35	0.15(0.64)		2.71	0.03 [-0.33, 0.39]
Total (95% CI) 322 Start (P = 0.61), P = 0% 338 100.00 0.14 (0.06, 0.20) 0.14 (0.06, 0.20) Test for neterogeneity: Chi = 5.42, off = 7 (P = 0.61), P = 0% Test for neterogeneity: Chi = 5.42, off = 7 (P = 0.61), P = 0% Test for neterogeneity: Chi = 5.42, off = 7 (P = 0.61), P = 0% Test for overall effect: Z = 4.53 (P < 0.0000)	Yancy	59	0.04(0.29)	60	-0.19(0.29)	+	32.59	0.23 [0.13, 0.33]
Test for heterogeneity: Chi ² = 5.42, df = 7 ($p = 0.61$), $l^2 = 0.61$, Test for heterogeneity: Chi ² = 5.42, df = 7 ($p = 0.61$), $l^2 = 0.61$, Test for verall effect. Z = 4.53 ($p < 0.0001$) Test for overall effect. Z = 4.53 ($p < 0.0001$) Review: Systematic Review April 2008 Comparison: 06 LDL cholesterol change at 12 months Outcome: 01 LDL cholesterol change at 12 months Study NND (fixed) NMD (fixed) %% Cl %% Cl %% Scl %% Cl %% Scl %	Total (95% CI)	352		338		•	100.00	0.14 [0.08, 0.20]
-1 -0.5 0 0.5 1 Review: Systematic Review April 2008 Favours treatment Favours control Favours control Comparison: 06 LDL cholesterol change at 12 months 01 LDL cholesterol change at 12 months MMD (fixed) WMD (fixed) Study 01 LDL cholesterol change at 12 months 01 LDL cholesterol change at 12 months MMD (fixed) WMD (fixed) Study N Treatment N Control 05% Cl % 95% Cl Study N Mean (SD) N Mean (SD) N 95% Cl % 95% Cl Feater 33 0.01(0.42) 53 0.01(0.44) % 95% Cl % 95% Cl Stem 7 0.38(0.02) 63 0.18(0.90) 9.05 0.28 (-0.07) 0.68 Stem 64 -0.10(0.75) 65 0.18(0.90) 9.05 0.28 (-0.07) 0.68 Test for verall effect. Z = 8.44 (P < 0.00001), P = 92.8%	Test for heterog Test for overall	geneity: Chi ² = 5.42, df = 7 (<i>i</i> effect: Z = 4.53 (<i>P</i> < 0.0000	<i>P</i> = 0.61), l ² = 0% 11)					
Review:Favours treatmentFavours controlReview:Systematic Review April 2008Comparision:06 LDL cholesterol change at 12 monthsComparison:06 LDL cholesterol change at 12 monthsOutcome:01 LDL cholesterol change at 12 monthsStudyNTreatmentStudyNTreatmentStudyNMean (SD)StudyNModel (SD)StudyNMean (SD)StudyNMean (SD)StudyNMean (SD)Study0.010 (0.42)30Starther700.58 (0.02)Gardher700.58 (0.02)Stern64-0.10(0.75)Total (95% CI)211Total (95% CI)9.05Total (95% CI)9.05 </th <th></th> <th></th> <th></th> <th></th> <th></th> <th>-1 -0.5 0 0</th> <th>5 1</th> <th></th>						-1 -0.5 0 0	5 1	
Review:Systematic Review April 2008Comparison:06 LDL cholesterol change at 12 monthsOutcomes:01 LDL cholesterol change at 12 monthsOutcomes:01 LDL cholesterol change at 12 monthsStudyNTreatmentNMean (SD)05% CIor sub categoryNMean (SD)95% CIStudy0.01(0.42)Foster33700.58(0.02)630.01(0.75)64-0.10(0.75)650.18(0.90)Total (95% CI)211Total (95% CI)211						Favours treatment Favours	control	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Review: Comparison: Outcome:	Systematic Review April 2 06 LDL cholesterol chang 01 LDL cholesterol chang	2008 ge at 12 months ge at 12 months					
Foster33 $0.01(0.42)$ 30 $-0.09(0.31)$ $-0.09(0.31)$ 22.49 0.10 $[-0.08, 0.28]$ Gardner70 $0.58(0.02)$ 63 $0.01(0.44)$ 62.44 0.57 $[0.46, 0.68]$ Stem 44 $0.18(0.91)$ 43 $-0.10(0.75)$ 65 $0.18(0.90)$ 6.03 0.28 $[-0.77, 0.63]$ Total (95% Cl) 211 211 9.05 $-0.28(1-0.57, 0.01)$ 9.05 $-0.28(1-0.57, 0.01)$ Test for heterogeneity: Chi2 = 41.66, off = 3 ($P < 0.00001$), $P = 92.8\%$ 201 201 $0.37(10.28, 0.46)$ Test for overall effect: Z = 8.44 ($P < 0.00001$) $P = 22.8\%$ 100.00 $0.37(10.28, 0.46)$	Study or sub category	Z	Treatment Mean (SD)	z	Control Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
Gardner 70 0.58(0.02) 63 0.01(0.44) \bullet 62.44 0.57 0.57 0.63 Stern 44 0.18(0.91) 43 -0.10(0.75) 65 0.18(0.90) 6.03 0.28 $= -0.07$, 0.63 Tsai 64 -0.10(0.75) 65 0.18(0.90) \bullet 100.00 0.37 $= 0.28$, 0.63 Total (95% Cl) 211 201 201 201 \bullet 100.00 0.37 $[0.28, 0.46]$ Test for heterogeneity: Chi² = 41.66, of = 3 (P < 0.00001), P = 92.8% 201 \bullet 100.00 0.37 $[0.28, 0.46]$ Test for overall effect: Z = 8.44 (P < 0.00001) P = 92.8% \bullet	Foster	33	0.01(0.42)	30	-0.09(0.31)	+	22.49	0.10 [-0.08, 0.28]
Stem 44 $0.18(0.21)$ 43 $-0.10(0.75)$ 65 $0.18(0.90)$ Tsai 64 $-0.10(0.75)$ 65 $0.18(0.90)$ $=$ 9.05 -0.28 $=$ 0.28 $=$ 0.28 $=$ 0.128 $=$ $0.10(0.75)$ 0.01 Total (95% Cl) 211 9.05 0.28 $=$ 0.28 $=$ 0.28 $=$ 0.28 $=$ 0.28 0.01 Total (95% Cl) 211 2.11 2.01 2.01 2.01 9.05 $=$ 0.28 0.01 Test for heterogeneity: Chi2 = 41.66, off = 3 (P < 0.00001), P = 92.8% 201 201 0.37 $[0.28, 0.46]$ 0.46 100.00 0.37 $[0.28, 0.46]$ 0.46 100.00 0.37 $[0.28, 0.46]$ 100.00 0.37 $[0.28, 0.46]$ 100.00 0.37 $[0.28, 0.46]$ 100.00 0.37 $[0.28, 0.46]$ 100.00 0.37 $[0.28, 0.46]$ 100.00 0.37 $[0.28, 0.46]$ 100.00 0.37 $[0.28, 0.46]$ 100.00 0.37 $[0.28, 0.26]$ </td <td>Gardner</td> <td>70</td> <td>0.58(0.02)</td> <td>63</td> <td>0.01(0.44)</td> <td></td> <td>62.44</td> <td>0.57 [0.46, 0.68]</td>	Gardner	70	0.58(0.02)	63	0.01(0.44)		62.44	0.57 [0.46, 0.68]
Isal 64 $-0.10(0.75)$ 65 $0.118(0.90)$ 9.05 $-0.28(-0.57, 0.01)$ Total (95% Cl) 211 201 201 201 201 9.05 $0.37(0.28, 0.46)$ Test for heterogeneity: $Chi^2 = 41.66$, of $= 3(P < 0.00001)$, $P = 92.8\%$ 201 0.46 100.00 $0.37(0.28, 0.46)$ Test for overall effect: $Z = 8.44$ ($P < 0.00001$) $P = 92.8\%$ 100.00 $0.37(0.28, 0.46)$	Stern	44	(T6.0.8T.0	43	(G/.0)0T.0-			0.28 [-0.07, 0.63]
Total (95% Cl) 211 201 201 Test for heterogeneity: Chi ² = 41.66, df = 3 ($P < 0.00001$), $P = 92.8\%$ 100.00 0.37 $[0.28, 0.46]$ Test for overall effect: Z = 8.44 ($P < 0.00001$) $P = 92.8\%$ 100.00 0.37 $[0.28, 0.46]$	Isai	64	-0.10(0.75)	65	0.18(0.90)		9.05	-0.28 [-0.57, 0.01]
	Total (95% CI) Test for heterog Test for overall	211 geneity: Chi ² = 41.66, df = 3 effect: Z = 8.44 ($P < 0.0000$	(<i>P</i> < 0.00001), I ² = 92.8 11)	201 %		•	100.00	0.37 [0.28, 0.46]
						L		

Figure 4 LDL cholesterol at 6 (a) and 12 (b) months. LDL, low-density lipoprotein; SD, standard deviation; WMD, weighted mean difference; Cl, confidence interval; df, degree of freedom.

© 2008 The Authors Journal compilation © 2008 International Association for the Study of Obesity. **obesity** reviews **10**, 36-50

			1007	1			ō		0.010
u sun calegoi	~	z	Mean (SD)	z	Mean (SD)	95%		%	95% CI
Brehm		22	0.18(0.74)	20	0.10(0.74)			0.60	0.08 [-0.37, 0.53]
Brinkworth		21	0.00(0.74)	22	0.04(0.74)			. 0.62	-0.04 [-0.48, 0.40]
Dansinger		40	0.09(0.16)	40	0.06(0.23)	Ŧ	1	16.10	0.03 [-0.06, 0.12]
Due		23	-0.03(0.74)	23	0.23(0.74)	•		0.66	-0.26 [-0.69, 0.17]
Foster		33	0.17(0.53)	30	0.03(0.31)	ł		2.70	0.14 [-0.07, 0.35]
Gardner		70	0.13(0.24)	63	0.05(0.17)		ł	24.65	0.08 [0.01, 0.15]
Samaha		64	0.00(0.12)	68	-0.02(0.18)	T-		45.04	0.02 [-0.03, 0.07]
Seshadri		43	-0.02(0.20)	35	-0.02(0.33)	-	1	7.82	0.00 [-0.12, 0.12]
Yancy		59	0.14(0.74)	66	-0.04(0.74)	1		1.80	0.18 [-0.08, 0.44]
otal (95% CI)		375		367			•	100.00	0.04 [0.00, 0.07]
est for hetero	geneity: Chi ² = 6.28, c effect: Z = 2.20 (<i>P</i> = 0	df = 8 (<i>P</i> = 0.03)	= 0.62), l ² = 0%						
						Favours control	Favours treatm	ent	
teview: comparison:)utcome:	Systematic Review 08 HDL cholestero 01 HDL cholestero	v April 20(I change I change	08 at 12 months at 12 months						
study r sub category	Å	z	Control Mean (SD)	z	Treatment Mean (SD)	WMD (fi 95%	cı Cı	Weight %	WMD (fixed) 95% Cl
Dansinger		40	0.08(0.18)	40	0.08(0.25)			20.65	0.00 [-0.10, 0.10]
Due Fostar		0.4 6	0.12(0./4) 0.13/0 50)	T O C C	-0.09(0./4) 0 00/0 08/			18.4	[/9.0 /67.0-] TZ.0 [/9.0 0 0 0 1 1 1
Gardner		02	0.12(0.23)	63	0.07(0.19)			36.86	0.05 [-0.02. 0.12]
Stern		44	-0.03(0.18)	43	-0.13(0.16)		+	36.78	0.10 [0.03, 0.17]
otal (95% CI) est for hetero	geneity: Chi² = 3.44, c	210 Jf = 4 (<i>P</i> =	: 0.49), l ² = 0%	194			•	100.00	0.06 [0.02, 0.11]
est for overall	effect: Z = 2.82 (<i>P</i> = 1	0.005)							
						-0.5 -0.25 0	0.25	0.5	
						Favours control	Favours treatm	ent	

Review:

Review: Comparison: Outcome:

a)

Study or sub category	z	Treatment Mean (SD)	z	Control Mean (SD)	MW \$	ID (fixed) 95% CI	Weight %	WMD (fixed) 95% Cl
Brehm Brinkworth	22 21	-3.93(0.96) -0.50(0.96)	20 22	0.19(0.96) -0.10(0.96)	•		2.06 2.12	-4.12 [-4.70, -3.54] -0.40 [-0.97, 0.17]
Dansinger	40	-0.11(0.45)	40	-0.11(0.62)		-	12.37	0.00 [-0.24, 0.24] -0.26 [-0.81 0.20]
Foster	0 9 F	2.20(3.30)	30	-1.00(2.10)	1		0.38	3.20 [1.85, 4.55]
Gardner	70	-0.40(0.72)	63	-0.18(0.56)	Ť	Т	14.66	-0.22 [-0.44, 0.00]
Samaha	64	-4.20(9.00)	68	-0.70(6.00)	t		0.10	-3.50 [-6.13, -0.87]
Seshadri	43	-0.01(0.23)	35	0.00(0.25)		•	60.19	-0.01 [-0.12, 0.10]
Yancy	59	-0.84(0.96)	60	-0.31(0.96)			5.86	-0.53 [-0.87, -0.19]
Total (95% Cl) Test for heterogeneity: Ch Test for overall effect: Z =	³⁷⁵ i² = 222.85, df = { 3.76 (<i>P</i> = 0.0002	3 (P < 0.00001), I² = 96.4%)	361		•		100.00	-0.16 [-0.24, -0.08]
					-1 -0.5	0 0.5		
					Favours treatment	Favours control		
Review: Systems	atic Review April 2	2008						



Control is low-fat/high-carbohydrate and treatment is low-carbohydrate/high-protein Figure 6 Triacylglycerols at 6 (a) and 12 (b) months. SD, standard deviation; WMD, weighted mean difference; Cl, confidence interval; df, degree of freedom.

Favours control 0.5

Favours treatment -0.5

0

7

$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		z	Mean (SD)	z	Mean (SD)	95%	G	%	95% CI
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Brehm	22	4.00(12.70)	20	2.00(12.70)			- 6.12 2.22	2.00 [-5.69, 9.69]
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Brinkworth	12	-4.90(12.70)	27	-3.60(12.70)			6.28	-1.30 [-8.89, 6.29]
Feature 33 -2.70(1.1/70) 30 -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.20) -1.30(12.30) -1.30(Dansinger	40	-0.70(10.00)	40	-4.80(14.00)	I		- 12.73	4.10 [-1.23, 9.43]
Cardner 77 $-6.40(9.50)$ 79 $-4.30(17.60)$ -47 $-4.10(1170)$ $-47.20(11.60)$ $-47.20(11.60)$ $-47.20(11.60)$ $-47.20(11.60)$ $-47.20(11.60)$ $-47.20(11.60)$ -1.35 -2.10 $-4.30(1.20)$ Test (br/sch) 233 238 $-7.20(11.60)$ 47 $-4.10(1.70)$ -1.35 $-2.30(1.60)$ -1.35 -1	Foster	33	-2.70(11.70)	30	1.20(12.20)			10.34	-3.90 [-9.82, 2.02]
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Gardner	77	-6.40(9.50)	79	-4.30(7.60)		-1	49.51	-2.10 [-4.80, 0.60]
Total (95% cl) 233 Total (95% cl) 233 Total (95% cl) 233 Test for overall effect, Z = 1,3) (P = 0.17) Test for overall effect, Z = 1,3) (P = 0.17) Test for overall effect, Z = 1,3) (P = 0.17) 100.00 -1.135 [-3.25, 0.56] Test for overall effect, Z = 1,3) (P = 0.17) Test for overall effect, Z = 1,3) (P = 0.17) Test for overall effect, Z = 1,3) (P = 0.17) 100.00 -1.135 [-3.25, 0.56] Review: Systematic Review April 2008 Testment Favours control Model (SD) %	Truby	40	-7.20(11.60)	47	-4.10(11.70)			15.01	-3.10 [-8.01, 1.81]
Tast for heterogeneity: Chi ⁺ = 5.24, df = 5 (P = 0.28), l ⁺ = 19.9% Test for neterogeneity: Chi ⁺ = 6.24, df = 5 (P = 0.28), l ⁺ = 19.9% Test for overall effect: Z = 1.39 (P = 0,17) Test for overall effect: Z = 1.39 (P = 0,17) Test for overall effect: Z = 1.39 (P = 0,17) Fevours treatment Review: Systematic Review April 2008 Comparison: 12 System blood pressure change at 12 months Outcome: 01 System blood pressure change at 12 months Outcome: 01 System blood pressure change at 12 months Study Nean (SD) NMD (fixed) Study Nean (SD) NMD (fixed) Study Nean (SD) 95% Cl Study Nean (SD) 95% Cl Densingler 7 -7.60(11.00) Start 7 -7.60(11.00) Start 33 -0.22(19.40) Start 33 -0.22(10.40) Start 44 1.00(19.00) Start 5 2.00(15.00) Start 5 2.00(15.00) Start 5 2.00(15.00) Sta	Total (95% CI)	233		238				100.00	-1.35 [-3.25, 0.56]
Fevours treatment 5 10 5 10 Review: Systematic Review April 2008 Fevours treatment Favours control Comparison: 12 Systematic Review April 2008 Study N Mean (SD) Study N Mean (SD) Study N Mean (SD) Dansinger 40 0.20(13.00) State 33 -0.21(9.40) State 33 -0.21(9.30) State 44 1.00(19.00) State 44 1.00(19.00) State 53 -4.50 State 53 -4.50 State 53 -4.50 State 53 -4.50 State 53 -3.20 State	Test for heteroge Test for overall e	neity: Chi ² = 6.24, df = 5 (ffect: Z = 1.39 (<i>P</i> = 0.17)	(<i>P</i> = 0.28), l ² = 19.9%						
Review:Favours controlReview:Systematic Review April 2008Comparision:12 Systelic blood pressure change at 12 monthsComparision:12 Systelic blood pressure change at 12 monthsStudyNTreatmentStudyNTreatmentStudyNMean (SD)StudyNMean (SD)Study33-0.21(9,40)State33-0.21(9,40)State33-0.21(9,40)State441.00(19,00)State452.00(15,00)State452.00(15,00)State557, df = 4(P = 0.23), P = 28.2%Test for neurogeneity: Chira = 557, df = 4(P = 0.23), P = 28.2%-0State for overall effect: Z = 1.99 (P = 0.05)50Test for overall effect: Z = 1.99 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51State for overall effect: Z = 1.90 (P = 0.05)51						-10 -5 0	5	10	
Review:Systematic Review April 2008Comparision:12 Systolic blood pressure change at 12 monthsOutcome:12 Systolic blood pressure change at 12 monthsOutcome:12 Systolic blood pressure change at 12 monthsOutcome:01 Systolic blood pressure change at 12 monthsStudyNTreatmentStudyNMean (SD)NMean (SD)NMean (SD)NMean (SD)Dansinger400.20(19.00)Foster33-0.20(19.00)Carloter77-7.60(19.00)Stern441.00(19.00)Stern441.00(19.00)Stern441.00(19.00)Stern2572.00(15.00)Stern2582.00(15.00)Total (35% CI)2582.55, df = 4, 2.51, df = 4, 4.51, 4.91]Total (35% CI)2582.56Total (35% CI)2582.56Test for neterogeneity: Chi* 5.57, df = 4 (P = 0.23), P = 28.2%-100.00Test for overall effect: Z = 1.39 (P = 0.05)-1.00Test for overall effect: Z = 1.39 (P = 0.05)-1.00Test for overall effect: Z = 1.39 (P = 0.05)-1.00Test for overall effect: Z = 1.39 (P = 0.05)-1.00Test for overall effect: Z = 1.39 (P = 0.05)-1.00 </td <td></td> <td></td> <td></td> <td></td> <td></td> <td>Favours treatment</td> <td>Favours control</td> <td></td> <td></td>						Favours treatment	Favours control		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Review: Comparison: Outcome:	Systematic Review April 12 Systolic blood pressur 01 Systolic blood pressur	2008 re change at 12 months re change at 12 months						
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Study or sub category	Z	Treatment Mean (SD)	Z	Control Mean (SD)	WMD (95%	fixed) CI	Weight %	WMD (fixed) 95% CI
Gardner77-7.60(11.00)79-3.10(9.30)-4.50(-7.70)-1.30]Stern441.00(19.00)432.00(15.00)9.03-1.00[-8.18]6.18]Taai641.00(19.00)652.00(15.00)9.03-1.00[-8.18]6.18]Taai641.00(19.00)652.00(15.00)9.03-1.00[-8.18]6.18]Taai641.00(19.00)652.00(15.00)9.03-1.00[-8.18]6.18]Taai651.00(19.00)652.00(15.00)9.03-1.00[-8.18]6.18]Taai651.00(19.00)652.00(15.00)9.03-1.00[-8.18]6.18]Taai65C)25825541.00(19.00)-2.19[-4.35, -0.03]Test for overall effect: Z = 1.99 (P = 0.05)-1.09 (D = 0.05)-1.00-2.19[-4.35, -0.03]Test for overall effect: Z = 1.99 (P = 0.05)-1.0950510	Dansinger Foster	40 33	0.20(12.00) -0.21(9.40)	40 30	-2.70(13.00) 2.00(11.80)			15.51 16.59	2.90 [-2.58, 8.38] -2.21 [-7.51, 3.09]
Stem 44 1.00(19.00) 43 2.00(15.00) 43 2.00(15.00) 9.03 -1.00 [-8.18], 6.18] 6.18] Tasi 64 1.00(19.00) 65 2.00(15.00) 65 2.00(15.00) 9.03 -1.00 [-8.18], 6.18] 6.18] Total (95% Cl) 258 2.57 257 257 9.03 100.00 -2.19 [-4.35, -0.03] Test for heterogeneity: Chi2 = 5.57, df = 4 (P = 0.23), l^2 = 28.2% 257 -10 5 0 5 10 Test for overall effect: Z = 1.99 (P = 0.05) -10 5 0 5 10	Gardner	27	-7.60(11.00)	67	-3.10(9.30)			45.53	-4.50 [-7.701.30]
Total 64 1.00(19.00) 65 2.00(15.00) 65 $2.00(15.00)$ 13.34 -1.00 <td>Starn</td> <td></td> <td>1 00(19 00)</td> <td></td> <td>0 00/1E 00)</td> <td></td> <td></td> <td>00.01</td> <td></td>	Starn		1 00(19 00)		0 00/1E 00)			00.01	
Tsai 64 1.00(19.00) 65 2.00(15.00) 13.34 -1.00 -6.91, 4.91 Total (95% Cl) 258 2.37 257 257 -2.19 $-4.35, -0.03$ Test for overall effect: Z = 1.99 (P = 0.05) -2.19 $-4.35, -0.03$ $-10, -5, 0, 5, 0, 5, 10$ -2.19 $-4.35, -0.03$	OIEIII	44	(00.61)00.1	0.42	(00.CT) 00.Z			00.2	[0T'0 '0T'0_] NN'T-
Total (95% CI) 258 257 $4f = 4 (P = 0.23)$, $l^2 = 28.2\%$ Test for heterogeneity: Chi ² = 5.57, df = 4 (P = 0.23), l^2 = 28.2\% Test for overall effect: Z = 1.99 (P = 0.05) -2.19 [-4.35, -0.03] -10 5 0 5 10	Tsai	64	1.00(19.00)	65	2.00(15.00)			13.34	-1.00 [-6.91, 4.91]
Test for overall effect: Z = 1.99 (P = 0.05) -10 -5 0 5 10	Total (95% CI) Test for heteroge	258 neity: Chi ² = 5.57, df = 4 ((<i>P</i> = 0.23), I ² = 28.2%	257		•		100.00	-2.19 [-4.35, -0.03]
-10 -5 10	l est for overall e	TTECT: Z = 1.99 (P = 0.05)							
						-10 -5	2	10	

Review:

Figure 7 Systolic blood pressure at 6 (a) and 12 (b) months. SD, standard deviation; WMD, weighted mean difference; CI, confidence interval; df, degree of freedom.

a decrease of 2.19 mmHg favouring the LC/HP group (P = 0.05) (Fig. 7b). There was no difference between the studies at either time.

Diastolic blood pressure

The WMD decrease in diastolic blood pressure of 0.49 mmHg at 6 months favouring the LC/HP group was not significant (Fig. 8a). At 12 months, the WMD between the two groups of 0.81 mmHg lowering favouring the LC/HP group was greater, but was also not significant (Fig. 8b). There was no evidence of statistical heterogeneity across the studies at either time.

Fasting plasma glucose

The WMD between the groups in fasting plasma glucose was not significant and there was no evidence of statistical heterogeneity at either time (Fig. 9).

Discussion

The results of the present review show that weight loss was significantly greater in the LC/HP (treatment) group after 6 and 12 months compared with the LF/HC group. The difference was greater at 6 months and at that time there was significant heterogeneity among the studies, probably due to the different study designs, but at 12 months the heterogeneity was no longer significant. The 36-month follow-up by Cardillo *et al.* (12) reported that mean weight change between baseline and 36 months was not different between the LC/HP and the LF/HC group. However, they do report that between 6 and 36 months weight was unchanged for the LF/HC group but that subjects on the LC/HP approach regained weight, but this change was not significant.

Avenell *et al.* (23) examined the effects of a protein sparing modified fast (PSMF) compared with a low-calorie diet and a very low-calorie diet. A PSMF is a LC diet, which allows a maximum of 40 g of carbohydrate per day. The review examined weight loss comparing the PSMF with low-calorie diets after 12, 18, 24, 36 and 60 months. There was a greater weight loss favouring the PSMF group compared with the control after 12, 24 and 36 months, but only seven RCTs were included in this analysis, which included a total of 480 participants (23). These results are consistent with the results of the present systematic review.

A review by Nordmann *et al.* (24) comparing LC diets with LF diets showed significant weight loss with the LC group at 6 months, but not at 12 months. The metaregression by Krieger *et al.* (25) also reports a greater weight loss in addition to a greater body fat and percentage body fat loss in studies lasting more than 3 months. Bravata *et al.* (26), however, showed no significant differences in weight loss for both groups at either 6 or 12 months, but this review included studies with dietary approaches that are not considered LC, which may have affected their outcomes.

The present review showed that there was a significant improvement in HDL cholesterol and triacylglycerols at 6 and 12 months favouring the LC/HP group, but this was not significant at 17 months. The lack of significance at 17 months may be caused by the reintroduction of carbohydrates in the LC/HP group. There was heterogeneity between the studies for triacylglycerols, but this may have been due to differences in study design.

Low HDL cholesterol and raised triacylglycerol levels are risk factors for cardiovascular disease and impact on the atherogenicity of the LDL particle and these results indicate that a LC/HP diet may be a better approach to weight loss and lowering the risk of cardiovascular disease. These results are consistent with the review carried out by Nordmann *et al.* (24). However, Bravata *et al.* (26) did not show any significant improvement in these parameters, which again may have been affected by their choice of studies.

The present review showed a significant improvement in total cholesterol and LDL cholesterol favouring the LF/HC group at 6 months, at which point total cholesterol and LDL cholesterol increased more in the LC/HP group but not at 12 months or 17 months. Nordmann et al. (24) in a meta-analysis of LC vs. LF diets found reports on four groups of patients demonstrating an improvement in total and LDL cholesterol favouring LF diets rather than LC diets. This finding is consistent with the studies included in the present review. An elevated total cholesterol could in part be explained by an increase in HDL cholesterol observed in the LC/HP group. Also, although an elevated LDL cholesterol increases the risk of acute cardiovascular events, we have just shown evidence that LC/HP diets increase HDL and decrease triacylglycerol which impacts on the atherogenicity of the LDL particle. These studies failed to investigate changes in LDL particle size. Furthermore, evidence from Sharman et al. (27) suggests that on a LC/HP LDL particle sizes change from small to large and therefore resulting in a less atherogenic profile.

There was a trend towards improvement in diastolic and systolic blood pressure at 6, 12 and 17 months favouring the LC/HP group. The difference was significant at 12 months favouring the LC/HP group for systolic blood pressure. Bravata *et al.* (26) reported no change in systolic blood pressure after the low- and very-low-carbohydrate diets (26). Nordmann *et al.* (24) showed no significant difference in blood pressure at any time point.

At 6 months there was a trend towards improvement in fasting plasma glucose only slightly favouring the LF/HC group in which there was a greater decrease in fasting plasma glucose in the LF/HC group. This was surprising

$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Study		Treatment		Control	WMD (fixed)	Weight	WMD (fixed)
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	or sub category	Z	Mean (SD)	Z	Mean (SD)	95% CI	%	95% CI
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Brehm	22	5.00(8.30)	20	1.00(8.30)		7.24	4.00 [-1.03, 9.03]
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Brinkworth	21	-1.70(8.30)	22	-1.60(8.30)		- 7.43	-0.10 [-5.06, 4.86]
	Dansinger	40	-4.00(6.50)	40	-1.80(6.90)	+	21.19	-2.20 [-5.14, 0.74]
Gardner 77 -3.30 (6.00) 79 -3.50 (5.00) -0.80 (-3.06, 3.00) -0.50 (-4.06, 3.00) -0.50 (-5.00)	Foster	33	2.00(12.70)	30	-1.10(14.20)		4.10	3.10 [-3.58, 9.78]
Tuby do -4.90(8.30) 27 -4.40(8.60) 14.45 -0.50 (-4.06, 3.06) Total (95% C1) 233 233 233 100.00 -0.49 [-11.85, 0.86] Test for inheirogenehy: Chi' = 5.83, di = 5 (P = 0.35), Pi = 10.6% 233 100.00 -0.49 [-11.85, 0.86] Test for inheirogenehy: Chi' = 5.83, di = 5 (P = 0.35), Pi = 10.6% Provenal effect Z = 0.72 (P = 0.47) 100.00 -0.49 [-11.85, 0.86] Test for overall effect Z = 0.72 (P = 0.47) Provenall effect Z = 0.72 (P = 0.47) Prove Provenall effect Z = 0.72 (P = 0.47) Provenall effect Z = 0.72 (P = 0.47) Prove Prove Provenall effect Z = 0.72 (P = 0.47) Prove Prove Prove Prove Prove Prove Prove Prove Prove ProveProve Prove	Gardner	LL	-3.30(6.90)	79	-2.50(5.80)	Ŧ	45.60	-0.80 [-2.80, 1.20]
Total (95% C) 233 100.00 -0.49 [-1.65, 0.86] Test for neural effect. Z = 0.72 ($\mu = 0.37$), $\mu = 10.6\%$ -0.49 [-1.65, 0.86] Test for neural effect. Z = 0.72 ($\mu = 0.37$) -0.49 [-1.65, 0.86] Test for neural effect. Z = 0.72 ($\mu = 0.37$) -0.49 [-1.65, 0.86] Test for neural effect. Z = 0.72 ($\mu = 0.37$) -0.49 [-1.65, 0.86] Review: Systematic Review April 2008	Truby	40	-4.90(8.30)	47	-4.40(8.60)	-	14.45	-0.50 [-4.06, 3.06]
Review. :10 :5 10 :5 10 Review. Systematic Review April 2008 Favours treatment Favours control Favours control Comperison. 14 Diastolic blood pressure change at 12 months Control WMD (fixed) Weight WMD (fixed) Station control 11 Diastolic blood pressure change at 12 months No Mean (SD) No MMD (fixed) Second Study N Treatment Control No Mean (SD) No MMD (fixed) Second	Total (95% CI) Test for heteroge Test for overall e	233 eneity: Chi ² = 5.59, df = 5 (sffect: Z = 0.72 (<i>P</i> = 0.47)	(<i>P</i> = 0.35), l ² = 10.6%	238		•	100.00	-0.49 [-1.85, 0.86]
Review: Review: Systematic Review April 2008 Comparison: 14 Diastolic blood pressure change at 12 months Outcome:Favours treatment Favours control MeightFavours control MolightComparison: Outcome:10 liastolic blood pressure change at 12 months Outcome:Vield Moli (Rised)Weight Moli (Rised)Weight 						-10 -10	5 10	
Review:Systematic Review April 2008Comparison:14 Diastolic blood pressure change at 12 monthsComparison:14 Diastolic blood pressure change at 12 monthsOutcome:10 Ilastolic blood pressure change at 12 monthsStudyNTreatmentNStudyNStudyNStudyNStudyNStudyNStudyNStudyNStudyNStudyVMUD (fixed)StudyVMD (fixed)Study40-1.40(7.50)40-1.20(7.50)30-2.20(6.70)30Gardner77-4.43.00(15.00)Stem48.74-1.0-5Stem-1.10(0.00)Stem-1.00(10.00)Stem-1.00(10.00)Stem-1.00(10.00)Stem-1.00(10.00)Stem-1.00						Favours treatment Favours	control	
Review: Systematic Review April 2008Number Statematic Review April 2008Comparison: Outcome:14 Disstolic blood pressure change at 12 months 								
Study to sub category or sub categoryTreatment Mean (SD)Control Mean (SD)WMD (fixed) 95% CIWMD (fixed) %WMD (fixed) %WMD (fixed) %SG% CI %MMD (fixed) %SG% CI %MMD (fixed) %MMD (fixed) % <td>Review: Comparison: Outcome:</td> <td>Systematic Review April . 14 Diastolic blood pressu 01 Diastolic blood pressu</td> <td>2008 ire change at 12 moi ire change at 12 mo</td> <td>nths inths</td> <td></td> <td></td> <td></td> <td></td>	Review: Comparison: Outcome:	Systematic Review April . 14 Diastolic blood pressu 01 Diastolic blood pressu	2008 ire change at 12 moi ire change at 12 mo	nths inths				
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Study or sub category	z	Treatment Mean (SD)	Z	Control Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% Cl
Total (35% Cl) 79 $-2.00(15.00)$ 79 $-2.20(6.70)$ 43 $1.00(10.00)$ 9.73 $-2.20(-4.59, 0.19)$ 44 $3.00(15.00)$ 43 $1.00(10.00)$ 9.73 $2.00(-3.35, 7.35)$ 7.35 Total (35% Cl) 194 $3.00(15.00)$ 43 $1.00(10.00)$ 9.73 $2.00(-2.43, 0.90)$ Total (35% Cl) 194 $3.00(15.00)$ 192 $100(10.00)$ $-0.76(-2.43, 0.90)$ Total (35% Cl) 194 100.00 $-0.76(-2.43, 0.90)$ Total (35% Cl) 100.00 $-0.76(-2.43, 0.90)$ -0.90	Dansinger	40	-1.40(7.50)	40	-1.70(6.40)		29.78	0.30 [-2.76, 3.36] 0.20 [-4.66 E.06]
Stem 44 $3.00(15.00)$ 43 $1.00(10.00)$ 9.73 $2.00(-3.35, 7.35)$ Total (95% Cl) 194 192 192 $0.076(-2.43, 0.90)$ Test for heterogeneity: Chi ² = 3.03, df = 3 (P = 0.39), P = 1.1% 192 100.00 $-0.76(-2.43, 0.90)$ Test for overall effect: Z = 0.90 (P = 0.37) 192 100.00 $-0.76(-2.43, 0.90)$ Fest for overall effect: Z = 0.90 (P = 0.37) 192 100.00 $-0.76(-2.43, 0.90)$ Fest for overall effect: Z = 0.90 (P = 0.37) $120(-5, 0, 5, 0, 5, 10)$ 100.00 $-0.76(-2.43, 0.90)$	Gardner	50 12	-4.40(8.40)	62	-2.20(6.70)		48.74	-2.20 [-4.59, 0.19]
Total (95% Cl) 194 192 192 100.00 -0.76 $[-2.43, 0.90]$ Test for heterogeneity: Chi ² = 3.03, df = 3 (P = 0.39), l ² = 1.1% Test for overall effect: $Z = 0.30$ ($P = 0.37$) -0.76 $[-2.43, 0.90]$ Test for overall effect: $Z = 0.30$ ($P = 0.37$) $P = 0.39$, $P = 0.39$, $P = 0.39$, $P = 0.39$, $P = 0.37$ $P = 0.37$ $P = 0.37$ Test for overall effect: $Z = 0.30$ ($P = 0.37$) $P = 0.37$ $P = 0.37$ $P = 0.37$	Stern	44	3.00(15.00)	43	1.00(10.00)		9.73	2.00 [-3.35, 7.35]
Test for heterogeneity: Chi ² = 3.03, df = 3 (P = 0.39), P = 1.1% Test for overall effect: Z = 0.90 (P = 0.37) Test for overall effect: Z = 0.90 (P = 0.37) Favours treatment Favours control	Total (95% CI)	194		192		•	100.00	-0.76 [-2.43, 0.90]
-10 -5 0 5 10 Favours treatment Favours control	Test for heteroge Test for overall e	eneity: Chi ² = 3.03, df = 3 (sffect: Z = 0.90 (<i>P</i> = 0.37)	(<i>P</i> = 0.39), l ² = 1.1%)		
Favours treatment Favours control						-10 -5-	5 10	
						Favours treatment Favours	s control	

Review:

Systematic Review April 2008	15 Fasting plasma glucose change	01 Fasting plasma glucose change	
	son:		



lo L	lo m	
9	9	
at	at	
change	change	
glucose	glucose	
plasma	plasma	
Fasting	Fasting	
	0	

(a)	Review: Comparison: Outcome:	Systematic Revi 15 Fasting plasm 01 Fasting plasm	ew April 2(าล glucose าล glucose	008 • change at 6 months • change at 6 months						
	Study or sub categor	~	z	Treatment Mean (SD)	z	Control Mean (SD)	WMD (fixed) 95% Cl	Weight %	WMD (fixed) 95% CI	
	Brehm		22	0.50(1.35)	20	-0.19(1.35)		3.00	0.69 [-0.13, 1.51]	
	Brinkworth		21	0.10(1.35)	22	-0.10(1.35)		^{3.08}	0.20 [-0.61, 1.01]	
	Dansinger		40	-0.43(1.40)	40	-0.21(1.20)		6.14	-0.22 [-0.79, 0.35]	
	Due		23	0.00(1.35)	18	0.00(1.35)	-81-	- 2.89	0.00 [-0.83, 0.83]	
	Gardner		7 0	0.01(0.42)	63	-0.04(0.54)		73.06	0.05 [-0.12, 0.22]	
	Samaha		64	-0.61(1.30)	68	-0.11(1.10)	-	11.82	-0.50 [-0.91, -0.09]	
	Total (95% CI) Test for hetero. Test for overall	geneity: Chi ² = 9.53 ' effect: Z = 0.13 (<i>P</i>	240 i, df = 5 (<i>P</i> = 0.90)	·= 0.09), I ² = 47.5%	231		•	100.00	-0.01 [-0.15, 0.13]	
							-1 -0.5 0 0.5			
							Favours treatment Favours contro	0		
(q)	Review: Comparison: Outcome:	Systematic Revii 16 Fasting plasm 01 Fasting plasm	ew April 2(าa glucose าa glucose	008 • change at 12 months • change at 12 months						
	Study or sub category	λ	z	Treatment Mean (SD)	z	Control Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI	
	Dansinger		40	0.07(1.66)	40	-0.26(1.05)		6.80	0.33 [-0.28, 0.94]	
	Gardner		70	(55.1)01.0 -0.09(0.74)	18 63	0.02(0.51)0.00		3.63 54.87	-0.20 [-1.03, 0.63] -0.11 [-0.32, 0.10]	
	Stern		44	0.17(0.61)	43	0.17(0.67)	-#-	34.70	0.00 [-0.27, 0.27]	





0.11]

[-0.20,

-0.05

100.00

0.5

0

-0.5

7

164

Total (95% Cl) 177Test for heterogeneity: Chi² = 2.05, df = 3 (P = 0.56), l² = 0% Test for overall effect: Z = 0.56 (P = 0.58)

when compared with the review by Layman *et al.* where there is clear evidence of improvements in fasting glucose, postprandial glucose and insulin responses and glycosylated haemoglobin (HbA_{1c}) for individuals on an LC/HP diet (6). At 12 months, the opposite occurred in which there was a greater decrease in fasting plasma glucose, favouring the LC/HP group. The difference was not significant at 6, 12 and 17 months. Bravata *et al.* (26) reported no change in fasting serum glucose among recipients of the low- and very-low-carbohydrate diets. Nordmann *et al.* (24) showed a greater improvement in fasting plasma glucose favouring the LC group at 6 months, but this was no longer significant at 12 months.

Furthermore, fasting glucose provides a limited assessment of overall glycaemic status; therefore, future studies should use HbA1c values or more direct measurements of insulin sensitivity.

There was a higher attrition rate in the LF/HC compared with the LC/HP groups (Fig. 1). Reasons for attrition included difficulty in complying with the diet or disliking the diet, difficulty in maintaining the scheduled visits and significant events such as pregnancy and surgery.

Limitations

It is important to take account of attrition rates in the interpretation of outcomes as high attrition rates lead to a smaller statistical power. An intention to treat approach is commonly used to overcome attrition rates and possible bias in the outcomes. There are, however, limitations when using this approach in lifestyle trials as the intention to treat approach has been derived from drug trials and may not yield robust outcomes. This results in the need for higher retention rates to assess for real changes in response to the dietary interventions.

In addition, the use of a RCT design in dietary interventions may not be appropriate. In general, any weight-loss strategy has a maximum weight loss at 6 months followed by a return to initial weight. It is clear that patients are changing their treatment by their own accord, perhaps subconsciously or perhaps due to a metabolic response of the body aiming to return to its initial weight. The current thinking within the field of obesity suggests that the use of continuous improvement methodology may be more appropriate for weight-loss management (28).

Also there was some evidence of heterogeneity between the studies included in this analysis. This calls for the use of more consistent and robust study designs for which we have to establish a clear definition of a LC/HP diet.

Conclusion

This systematic review included all known RCTs of LC diets vs. the LF/HC diet from 2000 to 2007. Factors

including weight, cholesterol, blood pressure and glycemic control were evaluated, as these are important in weight loss and cardiovascular disease risk.

Evidence from this systematic review demonstrates that LC/HP diets are more effective at 6 months and are as effective, if not more, as LF diets in reducing weight and cardiovascular disease risk up to 1 year. As there were only 13 studies included and several of them allowed the reintroduction of carbohydrates in the LC/HP diet, the evidence of the long-term efficacy of these diets is not complete. Certainly at 6 months, the evidence is in favour of the use of LC/HP diet. It may not be appropriate to return to a HC intake for weight maintenance (29,30). A gradual reintroduction while still limiting the intake of carbohydrate may be more appropriate.

With the prevalence of obesity increasing there is a need for larger and long-term RCTs of low- or very-lowcarbohydrate diets compared with the LF/HC diets to be carried out. The influence of behavioural therapy and exercise interventions needs to be evaluated, as well as lifestyle, appetite and mood questionnaires.

It is not known with certainty which aspect of LC diets causes the weight loss and cardiovascular disease risk factor changes. Whether it is the LC, the HP or calorie restriction needs to be examined. In addition, there is a need to assess if the greater weight loss achieved at 6 months on a LC/HP diet results in more important longterm improvements of cardiovascular disease.

There is a need for trials to include a follow-up period, to examine adherence to the LC diets and whether participants maintain their weight loss and CVD risk factor change when there is minimum contact with the study investigators. Finally, taking account of high attrition rates when using RCTs for dietary and lifestyle interventions, perhaps we will witness a move towards a continuous improvement methodology in the future.

Conflict of Interest Statement

No conflict of interest was declared.

Acknowledgement

MH was supported by a commercial grant from LighterLife.

References

1. Caballero B. The global epidemic of obesity: an overview. *Epidemiol Rev* 2007; **29**: 1–5.

2. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brody J, Hayflick L, Butler RN, Allison DB, Ludwig DS. A potential decline in life expectancy in the U.S. in the 21st century. *N Engl J Med* 2005; **352**: 1138–1145.

3. Ware JH. Interpreting incomplete data in studies of diet and weight loss. *N Engl J Med* 2003; 348: 21.

4. Wilding J. Science medicine and the future. *BMJ* 1997; 315: 997–1000.

5. Veech LR. The therapeutic implications of ketene bodies in pathological conditions: ketosis, ketogenic diet, redox states, insulin resistance, and mitochondrial metabolism. *Prostaglandins Leukot Essent Fatty Acids* 2004; **70**: 309–319.

6. Layman DK, Clifton P, Gannon MC, Krauss RM, Nuttall FQ. Protein in optimal health: heart disease and type 2 diabetes. *Am J Clin Nutr* 2008; 87: 1571S–1575S.

7. Volek JS, Fernandez ML, Feinman RD, Phinney SD. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. *Prog Lipid Res* 2008; **47**: 307–318.

8. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, Smith WCS, Jung RT, Campbell LK, Grant AM. Systematic review of the long term effects and economic consequences of treatments for obesity and implications for health improvement. *HTA* 2004; 8: 1–458.

9. Caterson I, Broom J. 2. Definition, assessment and epidemiology. *Obesity*. Mosby International Ltd.: London, 2001, pp. 10–19. 10. Brehm BJ, Seeley R, Daniels SR, D'Alessio DA. A randomized control trial comparing a very low carbohydrate diet and a calorie restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *J Clin Endocrinol Metab* 2002; 88: 1617–1623.

11. Brinkworth GD, Noakes M, Keogh JB, Luscombe ND, Wittert GA, Clifton PM. Long term effects of a high protein, low carbohydrate diet in weight control and cardiovascular risk factors in obese, hyperinsulinemic subjects. *Int J Obes* 2004; **28**: 661–670. 12. Cardillo S, Seshadri P, Iqbal N. The effects of a lowcarbohydrate versus low-fat diet on adipocytokines in severely obese adults: 3-year follow-up of a randomized trial. *Eur Rev Med Pharmacol Sci* 2006; **10**: 99–106.

13. Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, WeightWatchers, and Zone Diets for weight loss and heart disease risk reduction. *JAMA* 2005; **293**: 43–53.

14. Due A, Toubro S, Skov AR, Astrup A. Effects of normal fat diets, either medium or high in protein, on body weight in overweight subjects: a randomized control 1-year trial. *Int J Obes* 2004; 28: 1283–1290.

15. Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammad BS, Szapary PO, Rader DJ, Edman JS, Klein S. A randomized control trial of a low carbohydrate diet for obesity. *N Engl J Med* 2003; **348**: 2082–2090.

16. Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS, Balise RR. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women. *JAMA* 2007; **297**: 969–977.

17. Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams T, Williams M, Gracely EJ, Stern L. A low carbohydrate diet as compared with a low fat diet in severe obesity. N Engl J Med 2003; 348: 2074–2081.

18. Seshadri P, Iqbal N, Stern L, Williams M, Chicano KL, Daily DA, McGrory J, Gracely EJ, Rader EJ, Samaha FF. A randomized study comparing the effects of a low CHO diet and a conventional diet on lipoprotein subfractions and C-reactive protein levels in patients with severe obesity. *Am J Med* 2004; **117**: 398–405.

19. Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams M, Gracely EJ, Samaha FF. The effects of a low carbohydrate diet versus conventional weight loss diets in severely obese adults: a 1-year follow-up of a randomized trial. *Ann Intern Med* 2004; **140**: 778–785.

20. Truby H, Baic S, deLooy A, Fox K, Livingstone MBE, Logan LM, MacDonald IA, Morgan LM, Taylor MA, Millward DJ. Randomized controlled trial of four commercial weight loss programmes in the UK: initial findings from the BBC diet trials. *BMJ* 2006; **332**: 1309–1314.

21. Tsai AG, Glick HA, Shera D, Stern L, Samaha FF. Costeffectiveness of a low-carbohydrate diet and a standard diet in severe obesity. *Obes Res* 2005; 13: 1834–1840.

22. Yancy SW, Olsen MK, Guyton JR, Bakst RP, Westman EC. A low carbohydrate ketogenic diet versus a low fat diet to treat obesity and hyperlipidemia. *Ann Intern Med* 2004; **140**: 769–777. 23. Avenell A, Brown TJ, McGee MA, Campbell MK, Grant MK, Broom J, Jung RT, Smith WCS. What are the long term benefits of weight reducing diets in adults? A systematic review of randomized control trials. *J Hum Nutr Diet* 2004; **17**: 317–335.

24. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS, Brehm BJ, Bucher HC. Effects of low-carbohydrate vs. low-fat diets on weight loss and cardiovascular risk factors. A metaanalysis of randomized controlled trials. *Arch Intern Med* 2006; **166**: 285–293.

25. Krieger JW, Sitren HS, Daniels MJ, Langkamp-Henken B. Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: a meta-regression. *Am J Clin Nutr* 2006; 83: 260–274.

26. Bravata DM, Sanders L, Huang J, Krumholz HM, Olkin I, Gardner D. Efficacy and safety of low carbohydrate diets – a systematic review. *JAMA* 2003; **289**: 1837–1850.

27. Sharman MJ, Kraemar WJ, Love DM, Avery NG, Gomez AL, Scheett TP, Volek JS. A ketogenic diet favourably affects serum biomarkers for cardiovascular disease in normal weight men. *J Nutr* 2002; **132**: 1879–1885.

28. McQuigg M, Broom J, Laws RA, Reckless JPD, Noble PA, Kumar S, McCombie EL, Lean MEJ, Lyons GF, Frost GS, Quinn MF, Barth JH, Haynes SM, Finer N, Haslam DW, Ross HM. Tricks and tools for the primary care provider. The Counterweight Programme: a continuous improvement methodology model of weight management in UK primary care. *Int J Obesity* 2008; **32**: S6.

29. Mazlan N. Effects of fat and carbohydrate on energy intake and macronutrient selection in humans. 2001. PhD thesis, Aberdeen University, Aberdeen, Scotland.

30. Stubbs RJ, Johnstome AM, Harbron CG, Reid C. Covert manipulation of energy density of high carbohydrate diets in 'pseudo free-living' humans. *Int J Obes Relat Metb Disord* 1998; 22: 885–892.