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Comparison of the Effect of a Low-Carbohydrate Diet with a Low-Fat Diet on Anthropometric Indices and Body Fat Percentage: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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SYSTEMATIC REVIEW and META-ANALYSIS

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ABSTRACT

Background: Although many studies have been conducted to compare the effect of adherence to a low-carbohydrate diet (LCD) with a low-fat diet (LFD) on anthropometric indices and body fat percentage, there is still no definite conclusion in this regard. Therefore, the present study aims to summarize results of studies comparing a LFD and a LCD on weight loss. **Methods:** A systematic search of databases including PubMed, Scopus, and Cochran Library was performed up to November 2020. All randomized controlled trials (RCTs) comparing the effect of adherence to a LCD with a LFD on anthropometric indices and body fat percentage were included. Search results were limited to English-language publications. Sixty-three RCTs, including 7660 participants, were selected for the present study. **Results:** Pooled analysis indicated that adherence to LCD was significantly associated with a greater reduction in BMI (SMD = - 0.07, 95% CI: -0.14,-0.001; P = 0.04), weight (kg) (SMD = - 0.22, 95% CI: - 0.31, - 0.12; $P \leq 0.001$), and percentage of body fat mass (SMD = - 0.28, 95% CI: -0.48, - 0.08; P = 0.006) compared to LFD. However, no significant difference in changes of kilogram of body fat mass and waist circumference was observed between the two diet programs. **Conclusion:** Overall, adhering to LCD was more effective than LFD in losing weight and body fat percentage.

Keywords: *Low-fat; Low-carbohydrate; Weight; Obesity*

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Introduction

Obesity has become one of the most global well-known public health issue, its prevalence has nearly tripled since 1975 (Abarca-Gómez *et al.*, 2017, Zhang *et al.*, 2020). Although several research studies have been conducted to prevent and treat obesity, obesity prevalence is increasing worldwide and it is likely to reach maximum levels between 2026 and 2054 (Janssen *et al.*, 2020).

Lifestyle modification is considered the first line strategy for weight loss and weight maintenance, and diet is the main component of this approach (Wadden *et al.*, 2007, Wadden *et al.*, 2012). Among many diet approaches for weight reduction, diets with altered macronutrient composition such as low-fat diets (LFD) and low-carbohydrate diets (LCD) have been the focus of a large body of evidence. Reduction of dietary fats (low-fat diets were defined to have ≤ 30% total fat content) (Lichtenstein and Van Horn, 1998, Nordmann *et al.*, 2006, van Zuuren *et al.*, 2018) are theoretically reasonable approach for weight loss for several reasons, one them is high calorie density of fats compared with carbohydrates or protein (Buchholz and Schoeller, 2004, Hite *et al.*, 2011, Tobias *et al.*, 2015). Furthermore, studies have examined the association between dietary fat intake and cardiovascular risk and reported that LFD was traditionally applied for weight reduction (Keys *et al.*, 1986, Sackner-Bernstein *et al.*, 2015). However, clinical trials results are inconsistence and evidence does not support LFD superiority to reduce weight and body composition change in comparison to other dietary interventions (Harcombe *et al.*, 2015, Mansoor *et al.*, 2016, Nordmann *et al.*, 2006, Schwingshackl and Hoffmann, 2013, Tobias *et al.*, 2015). On the other hand, LCD characterized by low amounts of carbohydrates and higher quantities of fat and protein is another popular diet for weight loss and control concentrating on macronutrient distribution of the diet (Mansoor *et al.*, 2016). Generally, LCD contains 30-130 g of carbohydrate per day and a very low-carbohydrate ketogenic diet comprises less than 30 g of carbohydrate per day, which usually permit ketosis to occur (Hite *et al.*, 2011). It is hypothesized that sever carbohydrate restriction results in the depletion of glycogen stores and the excretion of bound water (Astrup *et al.*, 2004). In addition, this diet is an appetite suppressing due to its ketogenic nature, increases satiating, and reduces spontaneous food intake due to its high protein-content. Moreover, the restriction of carbohydrates limits food choices and subsequently reduces energy consumption (Astrup *et al.*, 2004). In a recent meta-analysis, it is shown that adherence to LCD was associated with a decrease in body fat. It is hypothesized that low carbohydrate diets contain high amounts of protein, converting to amino acids in the body. Amino acids increase muscle growth, leading to an increase in muscle mass and subsequently decreasing fat mass (FM) (Hashimoto *et al.*, 2016). On the other hand, in a previous trial, it has been shown that an energy-restricted, high-protein, LFD had no significant impact on body fat in comparison to a high-carbohydrate LFD in obese women (Noakes *et al.*, 2005).

For a long time, debates have been existed about the effectiveness of these two kinds of very popular diets in the treatment of obesity and there is still no definite conclusion in this regard particularly in terms of body composition. Therefore, this conclusive systematic review and meta-analysis were undertaken to update previous investigations to assess the effectiveness of LFD interventions in comparison to LCD trials in terms of anthropometry parameters (body mass index (BMI), weight, waist circumference (WC)) as well as body composition (percentage and kilogram of FM).

Materials and Methods

Search strategy: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines (PRISMA) were applied for writing the current study (Moher *et al.*, 2015). Scopus, Google Scholar, PubMed, Web of Science and Cochran Library were searched up to November 2020 without any restrictions to identify eligible trials. The effect of a low carbohydrate diet with LFD on anthropometry parameters (BMI, weight, WC) and

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body composition (percentage and kilogram of FM) were investigated through Medical Subject Heading (MeSH) terms and non-MeSH terms. Moreover, the references list of the included trials was checked for further possible sources as well as to ensure about the comprehensiveness of searches.

Selection criteria: The selected studies had following criteria: (1) randomized controlled trials (RCTs) design (with any duration and any sample size were included without relevance to physical activity or other factorial interventions), (2) investigating the impact of LCD with LFD on anthropometric indices and body composition (percentage and kilogram of FM) (LCD contains 30-130 g of carbohydrate per day and very low-carbohydrate ketogenic diet comprises less than 30 g of carbohydrate per day, which usually permit ketosis to occur) (Chawla *et al.*, 2020) (these limits were chosen upon consulting literature regarding LCD (Diabetes, 2017), and LFD (Lichtenstein and Van Horn, 1998, Nordmann *et al.*, 2006), and consensus was reached between the authors), (3) reporting macronutrients percentage in the diet, (4) encompassing participants aged ≥18 years, and (5) presenting sufficient information linking anthropometric indices and body.

Study selection: Two independent researchers (Darand M and Talebi S) carried out initial screening regarding the articles' titles and abstracts. Then, for selecting RCTs about the effect of a low carbohydrate diet with LFD on anthropometric indices and body fat percentage, full texts of all related articles were assessed by reviewers. Ultimately, any possible disagreement was negotiated and solved via consultation with other researchers (Alizadeh A and Abdollahzad H) (**Figure 1**).

Data extraction: Data extraction was conducted from the selected studies according to criteria including authors' family names, publication year, loss to follow-up, sample size, study duration, diet type, any other intervention, participants' gender, age, and target population, parallel or crossover study design, mean changes and standard deviation (SD) of anthropometric characteristics' levels, as well as mean and SD of anthropometric indices and body fat percentage at the beginning and the end of the trial (**Table 1**).

Quality assessment: The risk of bias in the included trials was evaluated based on the Cochrane criteria (Higgins *et al.*, 2019). Items for assessing the risk of bias in each research are as follows: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective outcome reporting; and (7) other potential sources of bias. According to the Cochrane Handbook recommendations, three scoring items were applied for studies including "yes", "no" and "unclear" which respectively indicating low risk of bias, high risk of bias, and unclear or unknown risk of bias. Moreover, after determining 'key domains', an overall risk of bias was specified for each trial encompassing good (low risk for all items), fair (low risk for more than three items), and poor (low risk for equivalent and less than three items) (Lorzadeh *et al.*, 2019).

Data synthesis and analysis: The Difference in mean values was defined as effect size. For computing weighted mean differences (WMDs), the mean value was divided by SD of a difference between two random values taken from each group (Higgins, 2011). If the standard error (SE) were reported in studies, SD was obtained by the following equation: $SD = SE \times \sqrt{n}$ (n=number of participants in each group). The WMDs with 95% confidence intervals (CIs) was calculated using a random-effects model for conducting meta-analysis (Borenstein *et al.*, 2011). Cochran's Q test and I-squared (I^2) statistic was applied to determine heterogeneity of trials which was identified by the following criteria: Q statistic P-value of <0.1; weak heterogeneity: I^2 = 25-50, relatively high heterogeneity: I^2 = 50-75, high heterogeneity: I^2= 75-100 (Higgins and Thompson, 2002). Sub-group analysis was performed to identify possible sources of heterogeneity among the selected trials. As the findings of these trials might be affected by intervention duration, sub-group analysis was

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accomplished according to these variables. Publication bias was also evaluated through assessing funnel plot and asymmetry tests including Egger's regression test and Begg's rank correlation test at P-value of <0.05 (Duval and Tweedie, 2000). Sensitivity analysis was conducted through individual removal of each study and recalculation of pooled estimates, to determine the impact of a specific trial or a particular group of trials. Meta-regression was also carried out to assess the relationship of estimated effect size with trial duration. Stata software, version 11.2 (Stata Corp.) was used for performing statistical analyses. Statistically significant levels were specified at P-value < 0.05.

Data analysis: Sensitivity analysis revealed that the overall effects of a LCD on BMI were significantly affected by removing some studies (Brinkworth *et al.*, 2009, de Luis *et al.*, 2007, Frisch *et al.*, 2009, Gardner *et al.*, 2007, Gardner *et al.*, 2018, Haufe *et al.*, 2011, Jang *et al.*, 2017, Lodi *et al.*, 2020, Perna *et al.*, 2019, Phillips *et al.*, 2008, Rajaie *et al.*, 2013, Vander Wal *et al.*, 2007, Wycherley *et al.*, 2010). However, sensitivity analysis did not represent any change in results for weight change, WC, change in FM percentage, and change in FM (kg).

Meta-regression analysis showed that the effect of the LCD versus the LFD on the study outcomes was not modified by the follow-up duration of studies and age of participants (BMI: slope $_{Duration}$: -0.001; 95 % CI –0.004, 0.001; *P* = 0.21, slope $_{Age}$: -0.004; 95 % CI –0.01, 0.005; *P* = 0.39), (weight: slope $_{Duration}$: 0.001; 95 % CI –0.0004, 0.002; *P* = 0.14, slope $_{Age}$: -0.002; 95 % CI –0.009, 0.003; *P* = 0.38), (Change in percentage of FM: slope $_{Duration}$: 0.006; 95 % CI –0.0005, 0.01; *P* = 0.06, slope $_{Age}$: -0.01; 95 % CI –0.03, 0.009; *P* = 0.28).

Publication bias: Publication bias was not observed based on funnel plots and asymmetry tests (**Table 2, Figure 7**)

Ethical consideration: The present study was approved by the Ethical Committee of Kermanshah University of Medical Sciences

Results

Study characteristics: The initial literature search identified a total of 2514 publications. The flow chart reporting the study selection process is presented in **Figure 1**. A total of 327 duplicate studies were first removed and 2077 unrelated records were excluded based on titles and abstracts. Then, 110 articles underwent full-text screening. For studies that reported results for different groups in stratified analysis, all appropriate data were extracted and compared with the control group. Accordingly, two data sets were extracted for studies conducted by Gardner *et al.* (Gardner *et al.*, 2007), Rock et al. (Rock *et al.*, 2016), Burgess et al. (Burgess *et al.*, 2017), and Petrisko *et al.* (Petrisko *et al.*, 2020). These studies were conducted on two groups of participants with different health status. Finally, 63 relevant RCT studies (67 data sets) , with a total sample size of 7660 participants (4434 for the low-carbohydrate arm and 3266 for the low-fat arm), published between 1995 and 2020, were eligible for this meta-analysis according to the inclusion criteria. The obtained data included 30 studies on BMI, 63 studies with 67 data sets on weight, 21 studies with 22 data sets on WC, 8 studies on the percentage of body FM, and 13 studies with 14 data sets on kilogram of body FM. The sample size of the analyzed studies was between 4 to 648 individuals and the duration of follow-up ranged from 2 to 144 weeks. Of the included studies, 24 data sets were on overweight/obese patients with obesity-related comorbidities and the remaining studies were on apparently healthy overweight/obese individuals. Moreover, 14 studies included only women, 1 study included only men (Sharman and Volek, 2004), and other studies included both genders. The studies quality ranged from poor to high quality. The characteristics of the analyzed studies are reported in **Table 1**.

Overall analysis of pooled data: The overall analysis of the included studies revealed that adherence to LCD was significantly associated with a greater reduction in BMI compared to LFD (SMD = - 0.07, 95% CI: -0.14,-0.001; *P* = 0.04, **Figure 2**),

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weight (SMD = - 0.22, 95% CI: - 0.31, - 0.12; $P \leq$ 0.001, **Figure 3**), and percentage of body FM (SMD = - 0.28, 95% CI: -0.48, - 0.08; P = 0.006, **Figure 4**). However, no significant difference in changes in kilogram of body FM (**Figure 5**) and WC (**Figure 6**) was observed between the two diet programs.

An additional analysis was performed only on parallel studies which showed similar results. (BMI: SMD = - 0.13, 95% CI: -0.21, -0.05; P = 0.002), (weight: SMD = - 0.21, 95% CI: -0.31,-0.11; P = ≤0.001), (WC: SMD = - 0.05, 95% CI: -0.13, 0.02; P = 0.18), and (changes of kilogram of body FM: SMD = - 0.04, 95% CI: -0.22, 0.13; P = 0.61).

Evidence of heterogeneity was found among the studies comparing the effect of a LCD with a LFD on weight and percentage of body FM. However, no significant heterogeneity was observed among the studies which evaluated BMI, WC, and kilogram of body FM (**Table 2**).

The results of the subgroup analysis are presented in **Table 2**. In subgroup analysis by the duration of follow-up, gender, age, carbohydrate percentage, and health status of participants, a significant BMI lowering LCD effect was supported by studies with ≥ 6 months follow-up (SMD = - 0.14, 95% CI: - 0.23 to - 0.04; P = 0.004), age less than 60 years (SMD = - 0.0.8, 95% CI: - 0.16 to - 0.002; P = 0.04), and very low carbohydrate diet (SMD = - 0.19, 95% CI: - 0.31 to - 0.07; P = 0.001). However, for weight, this effect was supported by all subgroups, except for overweight or obese individuals with comorbidities, individuals over the age of 60, and diets with more than 10% carbohydrates. In all subgroups, there was no significant difference in WC, except for overweight or obese individuals without comorbidities (SMD=-0.08, 95% CI: - 0.16 to - 0.03; P = 0.04). Moreover, for body FM percentage, the mentioned decrease was observed in subgroups of overweight/obese subjects without obesity-related comorbidities (SMD = - 0.21, 95% CI: - 0.37 to - 0.05; P = 0.009), after ≥ 6 months follow-up (SMD = - 0.29, 95%CI: - 0.52 to - 0.05; P = 0.01), in studies with less than 10% carbohydrates (SMD = - 0.36, 95%CI: - 0.62 to - 0.10; P = 0.007), and studies on both genders (SMD = - 0.31, 95% CI: - 0.57 to - 0.05; P=0.01). In all subgroup analyses, FM changes (kg) were not significant between the two diet programs (**Table 2**).

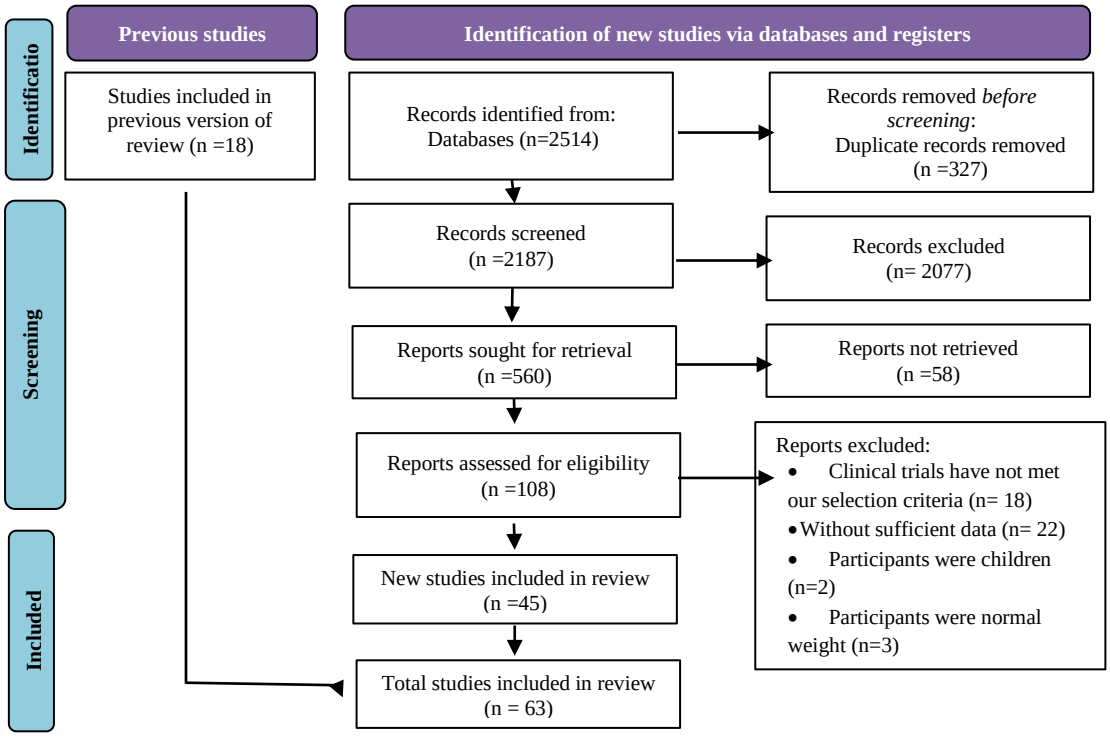

Figure 1. Flow chart of studies selection process.

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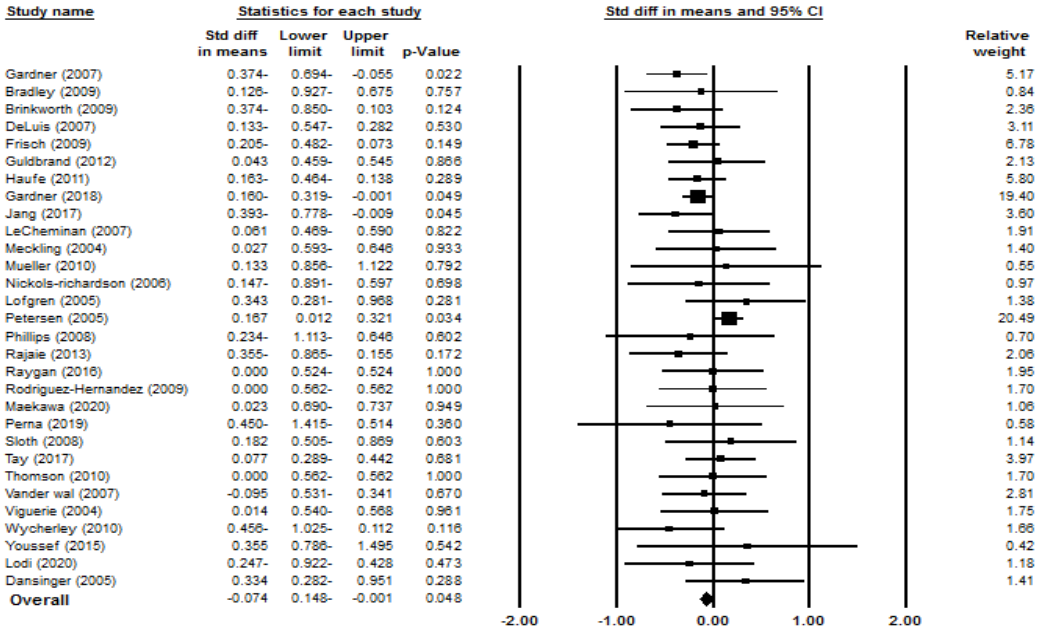

Figure 2. Forest plot illustrating standardized mean difference and 95% confidence intervals for the low-carbohydrate diet versus the low-fat diet on body mass index.

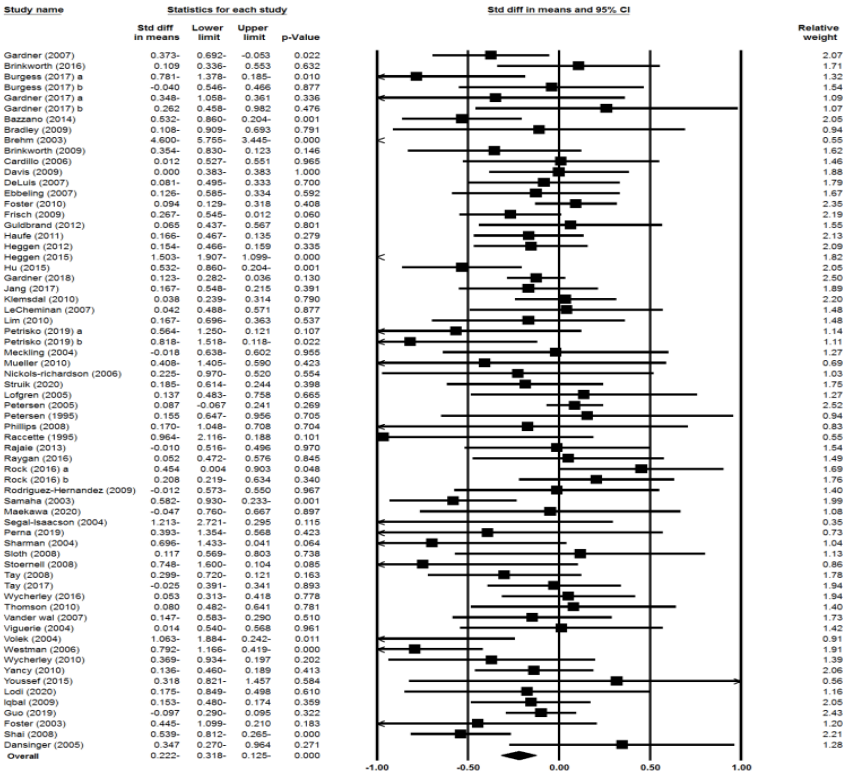

Figure 3. Forest plot illustrating standardized mean difference and 95% confidence intervals for the low-carbohydrate diet versus the low-fat diet on weight.

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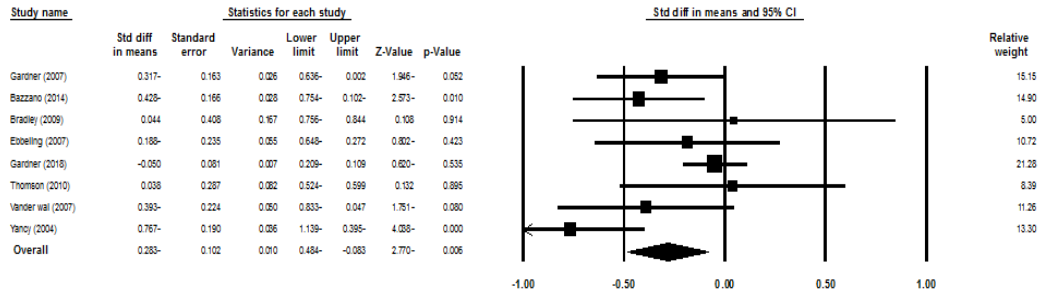

Figure 4. Forest plot illustrating standardized mean difference and 95% confidence intervals for the low-carbohydrate diet versus the low-fat diet on percentage of fat mass.

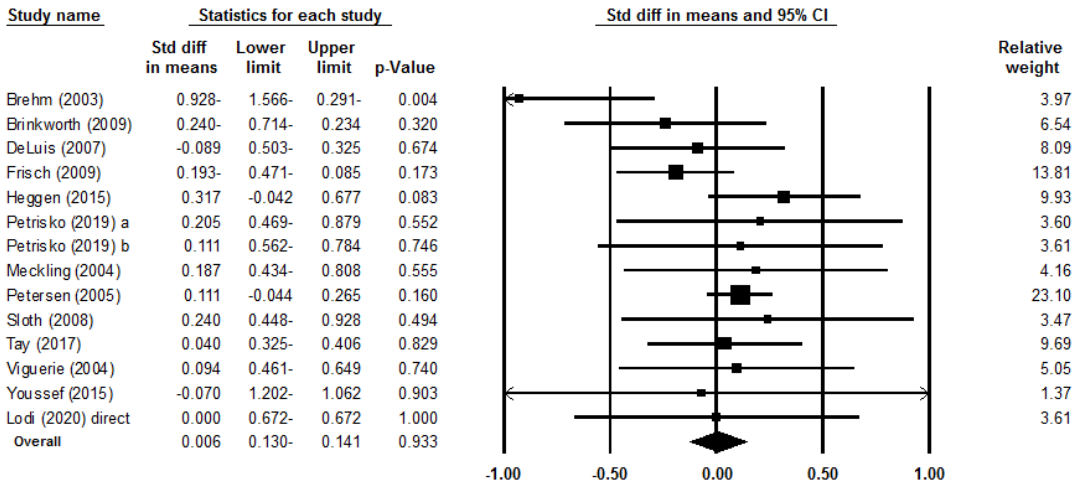

Figure 5. Forest plot illustrating standardized mean difference and 95% confidence intervals for the low-carbohydrate diet versus the low-fat diet on kilogram fat mass.

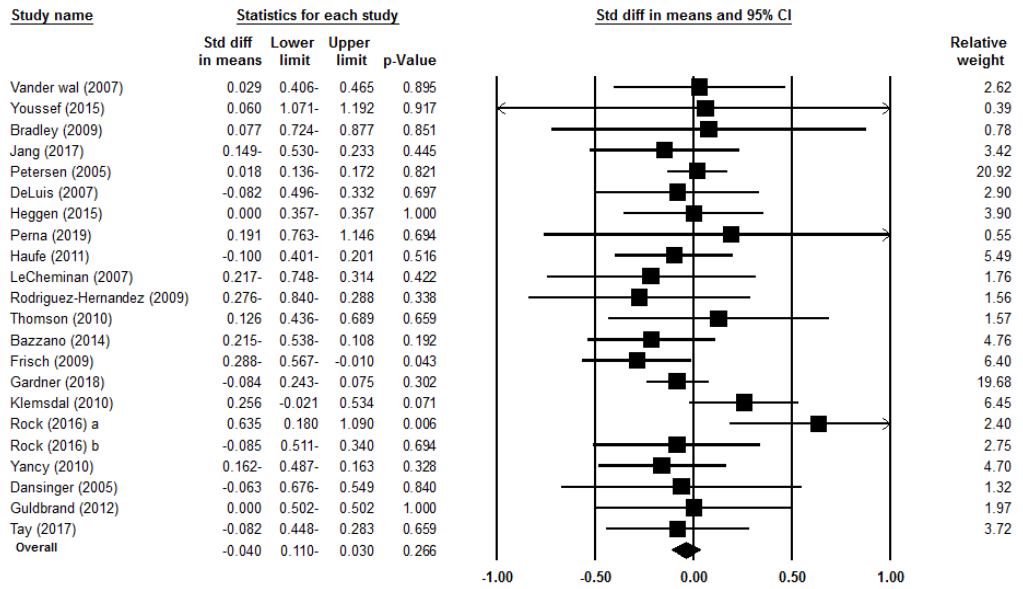

Figure 6. Forest plot illustrating standardized mean difference and 95% confidence intervals for the low-carbohydrate diet versus the low-fat diet on waist circumferences.

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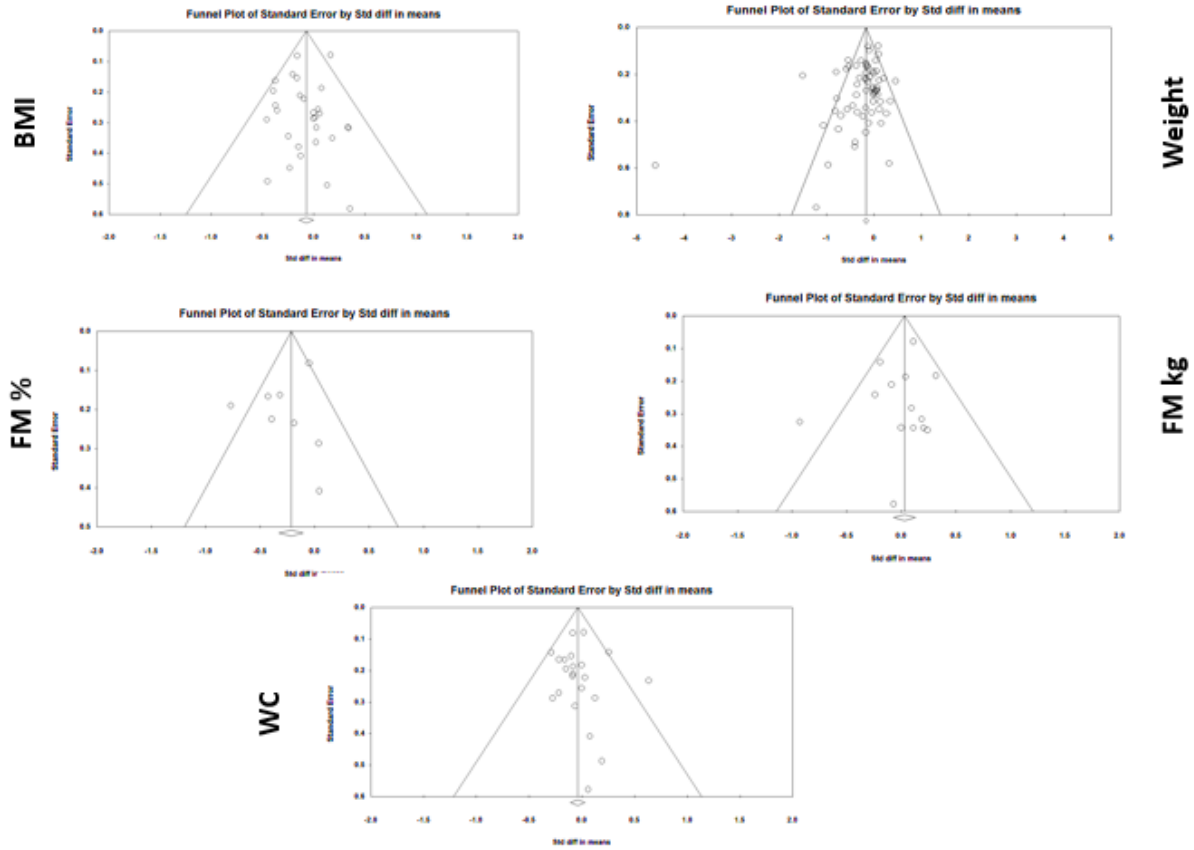

Figure 7. Publication bias for outcomes.

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Table 1. Characteristics of eligible studies.

First author (location; year)	RCT design	Target population	Sex	Mean age (years)		Sample size (low CHO diet / low FAT diet)	Duration (Weeks)	Diet Type		Any other intervention	Outcomes
				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
Struik (Australia; 2020)	Parallel	Obese	Both	59	59	41/43	16	Cho: 14% Pro: 28% Fat: 58% Energy-restricted	Cho: 53% Pro: 17% Fat: 30% Energy-matched	ND	Weight loss
Lodi (Italy; 2020)	Parallel	Overweight	Women	20-35	20-35	17/17	1.5	Ketogenic diets Cho: 7% Pro: 29% Fat: 64%	energy-restricted Mediterranean diet Cho: 60% Pro: 20% Fat: 20%	ND	Weight loss, BMI-change, body fat
Maekawa (Japan; 2020)	Parallel	Obese	Both	45.6	46.5	18/13	48	Cho: <120 g/d low Cho in combination with IGB therapy	Cho: 50-60% Pro: 15-20% Fat: 20-25% calorie-restricted diet in combination with IGB therapy	ND	Weight loss, BMI-change
Petrisko (American; 2020)	Cross-over	Obese	Both	43.2	43.2	17/17	4	Cho: 10% Pro: 30% Fat: 60% Restricted diet included more animal foods	Cho: 61% Pro: 18% Fat: 21%	1600 and 2200 kcal/d	Weight loss, body fat
Petrisko (American; 2020)	Cross-over	Obese	Both	43.2	43.2	17/17	4	Cho: 10% Pro: 40% Fat: 60%	Cho: 61% Pro: 18% Fat: 21%	1600 and 2200 kcal/d	Weight loss, body fat

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
								Restricted diet included more plant foods and mushrooms			
Perna (Bahrain; 2019)	Parallel	T2DM	Both	59.50	67.78	8/9	12	Cho: 27-31% Pro: 22% Fat: 46-50%	Cho: 55-60% Pro: 15-20% Fat: 25-30%	1600-1800 kcal/d	Weight loss, BMI-change, WC change
Guo (American; 2019)	Parallel	Overweight	Both	40.2	39.3	209/205	12/24/48	Cho: 20 g/d	Fat: 20 g/d	-~500–600 kcal/d	Weight loss
Gardner (American; 2018)	Parallel	Overweight	Both	40.2	39.3	305/304	48	Cho: 20 g/d	Fat: 20 g/d	ND	Weight loss, BMI-change, WC change, body fat
Burgess (American; 2017)	Parallel	Non-taster	Women	45.3	48.4	26/31	24	Cho: 50 g/d	Fat: 40 to 50 g/d (1,200 to 1,500 kcal/d)	ND	Weight loss
Burgess (American; 2017)	Parallel	Supertaster	Women	47.8	42.1	31/29	24	Cho: 50 g/d	Fat: 40 to 50 g/d (1,200 to 1,500 kcal/d)	ND	Weight loss
Gardner (American; 2016)	Parallel	Premenopausal with Insulin resistant	Both	42	44	16/15	24	Cho: 21% Pro: 26% Fat: 53%	Cho: 58% Pro: 20% Fat: 22%	ND	Weight loss

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First author (location; year)	RCT design	Target population	Sex	Mean age (years)		Sample size (low CHO diet / low FAT diet)	Duration (Weeks)	Diet Type		Any other intervention	Outcomes
				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
Gardner (American; 2016)	Parallel	Premenopausal with Insulin sensitive	Both	43	41	14/16	24	Cho: 21% Pro: 20-25% Fat: 20-25%	Cho: 58% Pro: 20% Fat: 22%	ND	Weight loss
Jang (Korea; 2018)	Parallel	NAFLD	Both	ND	ND	52/54	8	Cho: 50-60% Pro: 26% Fat: 53%	Cho: 60-70% Pro: 15-20% Fat: 15-20%	25 kcal/kg IBW	Weight loss, BMI-change, WC change
Tay (Australia; 2018)	Parallel	T2DM	Both	58	58	58/57	96	Cho: 14% Pro: 28% Fat: 58% 35% monounsaturated 13% polyunsaturated fat	Cho: 53% Pro: 17% Fat: 30% 15% monounsaturated 9% polyunsaturated fat	Energy-matched, hypocaloric diets and aerobic/resistance exercise	Weight loss, BMI-change, WC change, body fat
Wycherley (Australia; 2016)	Parallel	Obese and T2DM	Both	58.5	58.4	58/57	52	Cho: 14% Pro: 28% Fat: 58% <10% saturated fat	Cho: 53% Pro: 17% Fat: 30% <10% saturated fat	isocaloric, energy reduced diets (~6 - ~7 MJ/ d) and exercise program	Weight loss
Raygan (Iran; 2016)	Parallel	T2DM	Both	61.1	65.2	28/28	8	Cho: 43-49% Pro: 14-18% Fat: 36-40%	Cho: 60-65% Pro: 14-18% Fat: 20-25%	ND	Weight loss, BMI-change

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
Rock (American; 2016)	Parallel	Obese with Insulin Sensitive	Women	50	50	39/39	48	Cho: 45%	Fat: 20%	ND	Weight loss, WC change
Rock (American; 2016)	Parallel	Obese with Insulin Resistant	Women	50	50	42/43	48	Cho: 45%	Fat: 20%	ND	Weight loss, WC change
Heggen (Norwey; 2016)	Parallel	Overweight or obese smokers	Both	49.5	50.8	64/57	4/12	Cho: ≤20% Pro: 25% Fat: 55%	Cho: 50% Pro: 20% Fat: ≤30%	- 500 kcal/d	Weight loss, WC change, body fat
Hu (American; 2015)	Parallel	Obese	Both	45.8	47.8	75/73	12/24/48	Cho: <40 g/d	Fat: <30% < 7 saturated fat	ND	Weight loss
Youssef (Qatar; 2015)	Parallel	Overweight	Women	20-22	20-22	6/6	6	Cho: 30% Pro: 30% Fat: 40%	Cho: 55% Pro: 30% Fat: 15%	Energy-restricted	Weight loss, BMI-change, WC change, body fat
Bazzano (American; 2014)	Parallel	Obese	Both	45.8	47.8	75/73	12/24/36	Cho: <40 g/d	Cho: 55% Pro: ~15 Fat: <30%	ND	Weight loss, WC change, body fat
Rajaie (Iran; 2013)	Cross-over	Metabolic Syndrome	Both	42.4	42.4	30/30	6	Cho: 43-47% Pro: 15-17% Fat: 36-40%	Cho: 60-65% Pro: 15-17% Fat: 20-25%	ND	Weight loss, BMI-change
Guldbrand (Sweden; 2012)	Parallel	T2DM	Both	61.2	62.7	30/31	24/48/96	Cho: 20% Pro: 30%	Cho: 55-60% Pro: 10-15%	ND	Weight loss, BMI-

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
								Fat: 50%	Fat: 30% < 10% saturated fat		change, WC change
Heggen (Norwey; 2012)	Parallel	Obesity with at least one additional metabolic syndrome risk factor	Both	50.3	49.8	78/80	12	Low–Glycemic Load Diet Cho: 30-35% Pro: 25-30% Fat: 35-40%	Cho: 55-60% Pro: 10-15% Fat: <30%	Hypocaloric diets (- 500 kcal/d)	Weight loss
Haufe (Germany; 2011)	Parallel	Obese	Both	43.5	45	84/86	24	Cho: <90 g/d	Cho: <30%	-30% of energy intake before diet	Weight loss, BMI-change, WC change
Foster (American; 2010)	Parallel	Obese	Both	46.2	44.9	153/154	12/24/48/96	Cho: 20 g/d	Cho: 55% Pro: 15% Fat: 30% 1200 to 1800 kcal/d	ND	Weight loss
Klemsdal (Norwey; 2010)	Parallel	least one criterion of metabolic syndrome	Both	50.1	49.9	100/102	12/24/48	Cho: 30-35% Pro: 25-30% Fat: 35-40%	Cho: 55-60% Pro: 15% Fat: <30%	ND	Weight loss, WC change
Lim (Australia; 2010)	Parallel	one additional cardiovascular risk factor	Both	48.3	48.6	27/28	12/60	Cho: 4% Pro: 35% Fat: 60% 20% saturated fat	Cho: 70% Pro: 20% Fat: 10% 3% saturated fat	6500 KJ	Weight loss

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
Mueller (American; 2010)	Parallel	Obese	Both	49	46	9/7	10/20	Cho: 30% Pro: 20% Fat: 50%	Cho: 50% Pro: 20% Fat: 30%	-500 to -750 calorie/d	Weight loss, BMI-change
Thomson (American; 2010)	Parallel	Overweight breast cancer survivors	Women	57.8	57.8	21/19	6/12/18/24	Cho: 35% Pro: 25-30% Fat: 35-40%	Cho: 55-60% Pro: 15-20% Fat: 25%	ND	Weight loss, BMI-change, WC change, body fat
Wycherley (Australia; 2010)	Parallel	Overweight/ Obese	Both	49.9	50.2	26/23	52	Cho: 4% Pro: 35% Fat: 61% 20% saturated fat	Cho: 46% Pro: 24% Fat: 30% <8% saturated fat	isocaloric with moderate energy restriction (~6000 to ~7000 Kj/d)	Weight loss, BMI-change
Yancy (American; 2010)	Parallel	Overweight/ Obese	Both	52.9	52	72/74	48	ketogenic diet Cho: <20 g/d	Fat: <30% <10% saturated fat and <300 mg cholesterol + Orlistat therapy	-500 to 1000	Weight loss, WC change
Bradley (American; 2009)	Parallel	Obese	Both	37.1	40.5	12/12	8	Cho: 20% Pro: 20% Fat: 60%	Cho: 60% Pro: 20% Fat: 20%	ND	Weight loss, BMI-change, WC change, body fat
Frisch (American; 2009)	Parallel	Obese	Both	47	47	100/100	24/48	Cho: <40% Pro: 25% Fat: 35%	Cho: >55% Pro: 15% Fat: 30%	energy-restricted diets	Weight loss, BMI-change,

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
											WC change, body fat
Brinkworth (Australian; 2009)	Parallel	Obesity with at least one additional metabolic syndrome risk factor	Both	51.5	51.4	33/36	8/52	Cho: 4% Pro: 35% Fat: 61%	Cho: 46% Pro: 24% Fat: 30%	isocaloric with moderate energy restriction	Weight loss, BMI-change, body fat
Davis (American; 2009)	Parallel	T2DM	Both	54	53	55/50	12/24/48	Cho: 20-25 g/d	Fat: 25%	ND	Weight loss
Rodriguez-Hernandez (Germany; 2009)	Parallel	Obese	Women	45.3	45.4	21/29	24	Cho: 45% Pro: 27% Fat: 28%	Cho: 54% Pro: 25% Fat: 21% 10% saturated fat	ND	Weight loss, BMI-change, WC change
Iqbal (American; 2010)	Parallel	Obese, Diabetic	Both	60	60	70/74	24/48/96	Cho: 30%	Fat: ≤30% -500 kcal/d	ND	Weight loss
Phillips (American; 2008)	Parallel	Obese	Both	33	38	10/10	4/6	Atkins diet Cho: 20 g/d	Fat: 30%	ND	Weight loss, BMI-change
Stoernell (American; 2008)	Parallel	Hypertriglyceridemic/ Obese	Both	57	48.4	10/13	8	Atkins diet Cho: 15% Pro: 20-30% Fat: 55-65% <10% saturated fat	Cho: 50-60% Pro: 15% Fat: 30% <10% saturated fat	ND	Weight loss

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
Sloth (Denmark; 2009)	Parallel	Overweight	Both	30	28	15/18	24	Fat: 35-45% high in MUFA, 20%	Fat: 20-30%	ND	Weight loss, BMI-change, body fat
Tay (Australia; 2008)	Parallel	Obese	Both	50.3	51	45/43	24	Cho: 4% Pro: 35% Fat: 61% 20% saturated fat	Cho: 46% Pro: 24% Fat: 30% <8% saturated fat	Isocaloric, (restriction of ~6,000 ~7,000 kJ)	Weight loss
Gardner (American; 2007)	Parallel	Overweight Premenopausal	Women	42	42	77/76	8/24/48	Atkins diet Cho: 20 g/d	Ornish diet Fat: 10%	ND	Weight loss, BMI-change, body fat
DeLuis (Spanish; 2007)	Parallel	Obese	Both	43	42.1	43/47	12	Cho: 38% Pro: 26% Fat: 36%	Cho: 52% Pro: 20% Fat: 27%	1500 kcal/day	Weight loss, BMI-change, WC change, body fat
Ebbeling (American; 2007)	Parallel	Obese	Both	28.2	26.9	36/37	24/72	Low–Glycemic Load Diet Cho: 40% Pro: 25% Fat: 35%	Cho: 55% Pro: 25% Fat: 20%	ND	Weight loss, body fat
LeCheminan (American; 2007)	Parallel	Overweight/ Obese	Both	47.9	45.7	29/26	12/24	Cho: 20%	Fat: 30%	ND	WC change

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
Vanderwal (American; 2007)	Parallel	Overweight	Both	50.46	49.58	41/40	4	Cho: 17 g/d Fat: 18 g/d	Cho: 22 g/d Fat: 3 g/d	ND	Weight loss, BMI-change, WC change, body fat
Cardillo (American; 2006)	Parallel	Obese	Both	54	55	27/26	144	Cho: <30 g/d	Fat: <30% - 500 calories	ND	Weight loss
Westman (American; 2006)	Parallel	Obese with LDL-C >130 mg/dl or triglyceride >200 mg/dl	Both	44.2	45.6	59/60	24	ketogenic diets with fish, borage and flaxseed oil supplementation Cho: <20 g/d	Fat:? reduced-calorie diet	ND	Weight loss
Nickols-richardson (American; 2005)	Parallel	Overweight Premenopausal	Women	38.8	40.1	13/15	6	Atkins Cho: ≤20 to 40 1500-1700 kcal/d	Cho: 60% Pro: 15% Fat: 25%	ND	Weight loss, BMI-change
Löfgren (Sweden; 2005)	Parallel	Obese	Women	35.7	36.1	20/20	10	Cho: 40-45% Pro: 15-20% Fat: 40-45%	Cho: 60-65% Pro: 15-20% Fat: 20-25%	- 600 kcal/day	Weight loss, BMI-change
Petersen (Germany; 2006)	Parallel	Obese	Both	37.5	37.5	312/336	10	Cho: 40-45% Pro: 15% Fat: 40-45%	Cho: 60-65% Pro: 15% Fat: 20-25%	- 600 kcal/day	Weight loss, BMI-change, WC change, body fat

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
Meckling (Canada; 2004)	Parallel	Obese	Both	41.2	43.2	20/20	10	Cho: 15.4%	Fat: 17.8%	Females: 5020–6690 and males 5860–9200 kJ/d	Weight loss, BMI-change, body fat
Segal-Isaacson (American; 2004)	Cross-over	Overweight /Obese Premenopausal	Women	52.3	52.3	4/4	12	Cho: 5% Pro: 30% Fat: 65%	Cho: 50% Pro: 30% Fat: 20%	- 200 kcal/d	Weight loss
Sharman (American; 2004)	Cross-over	Overweight	Male	33.2	33.2	15/15	6	Atkins Cho: 10% Pro: 30% Fat: 60%	Cho: 55% Pro: 20% Fat: 25% <10% saturated fat and 300 mg cholesterol	ND	Weight loss
Viguerie (American; 2005)	Parallel	Obese	Both	21-49	21-49	25/25	10	Cho: 45-50% Pro: 15% Fat: 40-45%	Cho: 60-65% Pro: 15% Fat: 20-25%	Energy-restricted diets	Weight loss, BMI-change, body fat
Yancy (American; 2004)	Parallel	Overweight, Hyperlipidemic	Both	44.2	45.6	59/60	24	Cho: <20 g/d	Fat: <30% <10% saturated fat and <300 mg cholesterol -500 to 1000 kcal	ND	Weight loss, body fat
Volek (American; 2004)	Parallel	Overweight	Women	34	34	13/13	4	Cho: 10% Pro: 30% Fat: 60%	Cho: 55% Pro: 20% Fat: 25%	-500 kcal/d	Weight loss, body fat mass

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
									<10% saturated fat and <300 mg cholesterol		
Brehm (American; 2003)	Parallel	Obese	Women	44.22	43.10	22/20	12/24	Cho: 20 g/d (After 2wk of dieting, increase intake of Cho to 40–60 g)	Cho: 55% Pro: 15% Fat: 20%	ND	Weight loss, body fat
Samaha (American; 2003)	Parallel	Obese	Both	53	54	64/68	24	Cho: <30 g/d	Fat: <30% - 500 calories	ND	Weight loss
Petersen (American; 1995)	Crossover	Obese	Women	38.3	38.3	12/12	6	Cho:40%	Cho:55%	ND	Weight loss
Raccette (American; 1995)	Parallel	Obese	Women	41	37	6/7	12	Cho:25% Pro: 25% Fat: 50%	Cho: 60% Pro: 25% Fat: 15%	-5.00 ± 0.56 MJ/d	Weight loss
Foster GD (American; 2003)	Parallel	Obese	Both	44	44.2	20/17	48	Cho: 20 g/d (After 2wk of dieting, increase intake of Cho)	Cho: 60% Pro: 25% Fat: 15%	ND	Weight loss
Shai I (Israel; 2008)	Parallel	Obese	Both	52	51	109/104	96	Cho: 20 g/d (After 2-month of dieting, increase intake of Cho to 120g/d)	Fat: 30%	Mediterranean diet	Weight loss
Dansinger ML	Parallel	Obese or	Both	47	49	21/20	48	Atkins diet	Ornish diet	Weight	Weight

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				low CHO diet	low FAT diet			Percentage of macronutrients in low CHO diet	Percentage of macronutrients in low FAT diet		
(American;2007)		overweight						Cho: 20 g/d	Fat: 10%	Watchers, and Zone Diets	loss, BMI-change, WC change

CHO, carbohydrate; PRO, protein; FAT, lipid; T2DM, type 2 diabetes mellitus; NAFLD, nonalcoholic fatty liver disease; IGB, Intragastric balloon; IBW, ideal body weight; BMI, body mass index; WC, waist circumference; ND, non-defined; gr; gram, mg; milligram, d; day.

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Table 2. Main analyses and prespecified subgroup analyses for effect of low-carbohydrate diet compared with low-fat diet on changes in obesity measures.

Parameters of obesity	Subgroup		Number of datasets	Test of association			Test of heterogeneity		Publication bias	
				SMD	95%CI	P	I^2 (%)	P	Begg test	Egger test
Change in BMI (kg/m2)	Overall		30	-0.07	-0.14,-0.001	0.04	1.53	0.44	0.17	0.65
	Follow-up Duration	< 6 months	16	0.01	-0.09, 0.12	0.78	0.0	0.5		
		≥ 6 months	14	-0.14	-0.23,- 0.04	0.004	0.0	0.63		
	Health status	Overweight/obesity without comorbidities	22	-0.06	-0.14, 0.02	0.17	5.63	0.38		
		Overweight/obesity with comorbidities	8	-0.15	-0.32, 0.01	0.07	0.0	0.53		
	Sex	Female	7	-0.16	-0.37, 0.03	0.11	3.86	0.39		
		Both	23	-0.05	-0.13, 0.02	0.15	0.19	0.45		
	% Carbohydrates	LCD > 50gr/d or 10%	21	-.001	-0.09,0.08	0.98	0.00	0.65		
		VLCD ≤ 50gr/d or 10%	9	-0.19	-0.31, -0.07	0.001	0.00	0.66		
	Age	<60 years	27	-0.08	-.16, -0.002	0.04	9.02	0.33		
		≥60years	3	-0.03	-0.37-0.30	0.83	0.00	0.66		
Change in weight (kg)	Overall		67	-0.22	-0.31, - 0.12	<0.001	67.85	<0.001	0.11	0.05
	Follow-up Duration	< 6 months	27	-0.28	-0.46, - 0.10	0.002	64.69	<0.001		
		≥ 6 months	40	-0.19	-0.30, - 0.07	0.001	70.43	<0.001		
	Health status	Overweight/obesity without comorbidities	43	-0.30	-0.44, - 0.17	<0.001	74.36	<0.001		
		Overweight/obesity with comorbidities	24	-0.08	-0.20, 0.02	0.13	34.53	0.05		
	Sex	Male	1	-0.69	-1.43, 0.04	0.06	0.00	0.1		
		Female	16	-0.36	-0.73, - 0.002	0.04	82.28	<0.001		
		Both	50	-0.20	-0.29, - 0.11	<0.001	58.46	<0.001		
	% Carbohydrates	LCD > 50gr/d or 10%	39	-0.12	-0.24,0.001	0.05	55.49	<0.001		

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Parameters of obesity	Subgroup		Number of datasets	Test of association			Test of heterogeneity		Publication bias	
				SMD	95%CI	P	I^2 (%)	P	Begg test	Egger test
		VLCD ≤ 50gr/d or 10%	28	-0.034	-0.5, -0.17	0.00	76.81	<0.001		
	Age	<60 years	63	-0.22	-0.33,-0.12	<0.001	69.87	<0.001		
		≥60years	4	-0.07	-0.31,0.15	0.51	0.00	0.76		
Change in WC (cm)	Overall		22	- 0.04	-0.11, 0.03	0.26	0.00	0.46	0.18	0.74
	Follow-up Duration	< 6 months	8	-0.003	-0.12, 0.11	0.95	0.0	0.99		
		≥ 6 months	14	-0.05	-0.16, 0.06	0.38	32.84	0.11		
	Health status	Overweight/obesity without comorbidities	14	- 0.08	-0.16, -.003	0.04	0.00	0.94		
		Overweight/obesity with comorbidities	8	0.10	-0.08, 0.28	0.27	30.25	0.18		
	Sex	Female	5	0.11	-0.23, 0.46	0.53	48.20	0.1		
		Both	17	-0.05	-0.12, 0.01	0.13	0.0	0.79		
	% Carbohydrates	LCD > 50gr/d or 10%	17	-0.01	-0.13,0.10	0.77	17.54	0.25		
		VLCD ≤ 50gr/d or 10%	5	-0.10	-0.22,0,01	0.09	0.00	0.9		
	Age	<60 years	20	-0.05	-0.14,0.03	0.21	9.75	0.33		
		≥60years	2	0.04	-0.4,0.48	0.85	0.00	0.72		
Change in fat mass (%)	Overall		8	- 0.28	-0.48, - 0.08	0.006	57.38	0.02	0.62	0.36
	Follow-up Duration	< 6 months	2	-0.29	-0.67, 0.09	0.13	0.0	0.34		
		≥ 6 months	6	-0.29	-0.52, - 0.05	0.01	67.49	0.009		
	Health status	Overweight/obesity without comorbidities	6	-0.21	-0.37, - 0.05	0.009	25.03	0.24		
		Overweight/obesity with comorbidities	2	-0.39	-1.18, 0.39	0.32	81.75	0.01		

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				SMD	95%CI	P	I^2 (%)	P	Begg test	Egger test
	Sex	Female	2	-0.21	-0.52, 0.09	0.17	13.53	0.28		
		Both	6	-0.31	-0.57, - 0.05	0.01	67.22	0.009		
	% Carbohydrates	LCD > 50gr/d or 10%	3	-0.07	-0.39,0.25	0.65	0.00	0.79		
		VLCD ≤ 50gr/d or 10%	8	-0.36	-0.62, -0.1	0.007	73.56	0.004		
Change in fat mass (kg)	Overall		14	0.006	-0.13, 0.14	0.93	24.66	0.18	0.78	0.44
	Follow-up Duration	< 6 months	9	0.11	-0.004, 0.23	0.05	0.00	0.96		
		≥ 6 months	5	-0.19	-0.48, 0.09	0.19	51.14	0.08		
	Health status	Overweight/obesity without comorbidities	12	0.01	-0.14, 0.17	0.82	31.01	0.14		
		Overweight/obesity with comorbidities	2	-0.06	-0.35, 0.22	0.66	0.0	0.35		
	Sex	Female	3	-0.38	-1.04, 0.27	0.25	53.59	0.11		
		Both	11	0.05	-0.04, 0.16	0.28	0.00	0.60		
	% Carbohydrates	LCD > 50gr/d or 10%	9	0.02	-0.13,0.17	0.76	0.00	0.54		
		VLCD ≤ 50gr/d or 10%	5	-0.38	-0.88,0.12	0.13	54.54	0.11		

Discussion

This is a meta-analysis of RCTs investigating the effect of LCD compared to LFD on anthropometric characteristics. Treatment strategies are important in improving anthropometric indices. Abnormalities of anthropometric characteristics were strongly associated with diseases such as diabetes, hypertension, and cardiovascular disease (Furtado *et al.*, 2018, Hadaegh *et al.*, 2009, Khader *et al.*, 2019). Studies have reported that different diets could affect anthropometric indices. The present meta-analysis study showed that adherence to LCD compared to LFD significantly reduced BMI in studies with ≥ 6 months follow-up, very low carbohydrate diet, and age less than 60 years. The protective effect of LCD on weight was observed except for overweight or obese individuals with comorbidities, individuals over the age of 60 and with diets more than 10% carbohydrates.

A possible reason was that older people generally had less physical activity compared to young people, so that activity-related energy expenditure was also lower. This can lead to increased BMI and weight (Elmadfa and Meyer, 2008). Also, adherence to LCD can reduce FM percentage compared to LFD, but body FM (kg) and WC did not change.

A meta-analysis was similar to the present study published in 2020, investigating the effect of LFD and LCD on weight and lipid profile. In this study, only 38 trials were included and other anthropometric indices were not investigated (Chawla *et al.*, 2020). Previous meta-analysis studies have reported the protective effect of LCD. Another meta-analysis study was conducted on RCTs. It was reported that LCD (50 g carbohydrate or 10% calorie from carbohydrates) can reduce body weight (BW) and FM compared to LCD (about 40% calorie from carbohydrate) (Hashimoto *et al.*, 2016). Another meta-analysis investigated the effect of very-low-carbohydrate ketogenic diets (VLCKD) compared to LFD. Results of this study showed that VLCKD decreased BW, triglyceride and diastolic blood pressure while increased high-density lipoprotein (HDL-C) and low-density lipoproteins (LDL-C) compared to LCD (Bueno *et al.*, 2013). Results of another meta-analysis study showed that LCD-C reduced triglycerides concentration and increased HDL cholesterol concentration (Meng *et al.*, 2017). A meta-analysis study showed that LCD can significantly decrease BMI and serum levels of total cholesterol and LDL-C in polycystic ovary syndrome (PCOS) women (Zhang *et al.*, 2019). Some reports have shown that LCD cannot have a protective effect (Foster *et al.*, 2003, Yancy Jr *et al.*, 2004). Results of a study have indicated that LCD can affect weight loss more than the conventional diet in the first six months, but the differences were not significant during a year in another study (Foster *et al.*, 2003). It was also shown that changes in LDL-C levels did not differ statistically with the LCD and LFD (Yancy Jr *et al.*, 2004).

The low percentage of carbohydrate intake from energy will be compensated with high fat and protein intake (Farabi and Hernandez, 2019, Frigolet *et al.*, 2011). Protein consists of amino acids. Amino acids are necessary for preserving lean body mass and muscle growth (Coker *et al.*, 2012, Simonson *et al.*, 2020), also intake of protein is positively associated with lean mass (Houston *et al.*, 2008). Ebbeling *et al.* reported that to decrease an individual's BMR (basal metabolic rate) LCD is effective compared to LFD. LCD may result in the modulation of resting energy expenditure (Ebbeling *et al.*, 2012). LCD decreases supply of glucose to the liver, muscles and brain, thereby inactivating gluconeogenesis. The main source of gluconeogenesis is glycerol (Brouns, 2018). It is caused by triglycerides breakdown (Chourpiliadis and Mohiuddin, 2020). The Decomposition of triglycerides is associated with reduced FM. The current study results showed that LCD significantly reduced body FM percentage; however, no significant difference in body FM changes was observed. In fact, LCD can change the body composition.

This study had several strengths. RCTs with less bias were included in comparison to observational studies. A large number of included studies lets us assess publication bias. This meta-analysis due to

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the large sample size could recognize statistically significant mean differences in outcomes. Further subgroup analyses based on the duration of follow-up, gender, and health status would provide beneficial insights into these diets.

This study had some limitations. Given that one of the inclusion criteria was English language publications, some studies might have been missed. Most studies did not prepare food for the duration of the trial, which may reduce adherence to diet protocols. Some studies did not also report any data about participant's physical activity. Crossover trials in this study only reported overall results for low-carb and low-fat arm; so, these measures were used in the present analysis. Furthermore, diets did not account for the quality of the food consumed. The type of intake carbohydrates was not clear. Refine cereals or whole grains have different effects on the risk of disease. Other limitations of the study were heterogeneity during follow-up and the amount of carbohydrates in both the interventional and comparative diets.

Conclusion

Dietary intake is the main cause of abnormal anthropometric characteristics, and diet changes are suggested to improve this condition. Generally, LCD compared to LFD had an effect in losing BMI, weight and body fat percentage, but did not affect body FM and WC. In the future, more interventions with a specific carbohydrate dose are needed to reach a definitive conclusion.

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Conflict of interest

The authors declare that they have no conflict of interest.

Authors' contributions

Darand M designed the research; Darand M and Alizadeh S conducted the research; Hassanizadeh S analyzed the data; Darand M, Talebi S and Darand Z extracted the data, Darabi Z, Yaghoubi F, Bagherniya M and Azamian Y wrote the paper, Abdollahzad H finalized the paper. All authors read and approved the final manuscript.

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