

Effect of Different Dietary Approaches in Comparison with High/Low-Carbohydrate Diets on Systolic and Diastolic Blood Pressure in Type 2 Diabetic Patients: A Systematic Review and Meta-Analysis

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ABSTRACT: Dietary modification is an effective method for preventing and managing hypertension. Therefore, we conducted a systematic review and meta-analysis to assess the effects of different dietary approaches for comparing high- and low-carbohydrate diets on systolic and diastolic blood pressure (SBP and DBP, respectively) in patients with type 2 diabetes mellitus (T2DM). We carried out a comprehensive literature search using PubMed, the Cochrane Library, Web of Science, and Scopus without any language and time restrictions until April, 2019. We carried out a meta-analysis using both fixed and random effects models where appropriate and used the I^2 index to evaluate heterogeneity. We identified 16 eligible studies, with a total of 1,610 participants. The overall pooled net effect of different dietary approaches on SBP and DBP were -2.29 mmHg [95% confidence interval (CI): -3.49 to -1.1] and -1.03 mmHg (95% CI: -1.77 to -0.29), respectively, compared with high-carbohydrate diets. Indeed, diets high in monounsaturated fatty acids more effective in reducing both SBP and DBP than high-carbohydrate diets, whereas high-protein diets were not effective. Furthermore, we found that different dietary approaches, such as low-fat diets, did not reduce SBP or DBP to a greater extent than low-carbohydrate diets. Overall, the results of our meta-analysis show that diets high in monounsaturated fatty acids are more effective in reducing both SBP and DBP than diets high in carbohydrate, whereas other dietary approaches were not effective.

Keywords: blood pressure, different dietary approaches, high monounsaturated diet, meta-analysis, type 2 diabetes mellitus

INTRODUCTION

The global prevalence of type 2 diabetes mellitus (T2DM) is increasing. It is estimated that by 2030 the global prevalence of diabetes will be approximately 400 million (Wild et al., 2004). Diabetes is associated with several complications, such as cardiovascular disease (CVD) and stroke (Woodward et al., 2003), and is a major cause of blindness and kidney disease in developed countries (Ciulla et al., 2003; Jha et al., 2013). Moreover, patients with diabetes generally have higher blood pressure than healthy individuals (Hypertension in Diabetes Study,

1993). Hypertension is a common manifestation of diabetes and is one of the main causes of CVD in patients with diabetes (Cryer et al., 2016). Several mechanisms have been proposed for this increase in blood pressure, including involvement of the adrenergic system (Santulli et al., 2012). Due to the high prevalence of hypertension, several studies have examined the clinical management and treatment of hypertension in patients with T2DM.

Management of T2DM includes achieving healthy body weight and increasing physical activity to control blood glucose levels and decrease cardiovascular risk factors (Wing et al., 2011; Soare et al., 2014; Alipour et al., 2018).

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Evidence suggests that dietary modifications improve glycemic control and cardiometabolic health in overweight and obese people with diabetes (Wing et al., 2011; Soare et al., 2014). Consuming a healthy diet is one of the most important aspects of managing diabetes, and studies have shown that different dietary approaches have different effects on glycemic control in diabetic patients (Evert et al., 2014). Furthermore, it is well known that dietary intervention is effective for preventing and managing hypertension. According to the latest American Heart Association guidelines, hypertensive and pre-hypertensive patients should follow dietary recommendations to control hypertension (Eckel et al., 2014). Low-carbohydrate and low-fat diets are commonly used for managing disease in diabetic patients (Evert et al., 2014). It has been well documented that replacing a high-carbohydrate diet with other dietary approaches, such as a diet high in unsaturated fat, improves hemoglobin A1c and blood lipid profiles, and reduces diabetes medication requirements (Tay et al., 2014). Diets rich in monounsaturated fats (MUFA) lower fasting triacylglycerol and cholesterol concentrations to a greater extent than diets rich in carbohydrates in both individuals with and without diabetes (Garg, 1998). However, studies comparing the high-carbohydrate diet with other dietary approaches for their ability to improve blood pressure report contradictory results (Mensink et al., 1988; Shah et al., 2005). Moreover, the metabolic effects of diets low in carbohydrates may be particularly beneficial for patients with T2DM. In previous studies, low-carbohydrate diets have been shown to be beneficial for improving glycemic control in patients with T2DM (Nielsen and Joensson, 2008). However, the beneficial effect of low-carbohydrate diet compared with other dietary approaches, such as low-fat diets, on blood pressure in T2DM is not well understood (Davis et al., 2009). The lack of sufficient evidence has prevented health authorities from making conclusive recommendations on the use of low-carbohydrate diets for managing T2DM (Evert et al., 2014). Considering the high prevalence of hypertension in patients with diabetes and the importance of dietary modifications in managing diabetes, it is important to determine which diets are most effective in controlling hypertension. Therefore, we conducted a systematic review and meta-analysis to compare the results of high- and low-carbohydrate diets with other dietary approaches on systolic and diastolic blood pressure (SBP and DBP, respectively) in patients with T2DM.

MATERIALS AND METHODS

This systematic review and meta-analysis was performed according to the guidelines of the 2009 preferred reporting items for systematic reviews and meta-analysis

(PRISMA) statement (Moher et al., 2009).

Data sources and search strategies

A comprehensive literature search of four databases, including PubMed, the Cochrane Library, Web of Science, and Scopus were conducted using the merge of medical subject headings (MeSH) and non-MeSH terms: “Diabetes Mellitus”, “Noninsulin-Dependent Diabetes Mellitus”, or “Type 2 Diabetes Mellitus” in combination with the keywords “Carbohydrate Restricted Diet”, “High Carbohydrate Diet”, “Low Carbohydrate Diet”, “Mediterranean Diet”, “Fat Restricted Diet”, “Low Fat Diet”, “Fat Free Diet”, “Vegetarian Diet”, “Ketogenic Diet”, “Protein Restricted Diet”, “Low Protein Diet”, “Protein Free Diet”, or “Diabetic Diet”, and “Blood Pressure”, “Diastolic Pressure”, “Pulse Pressure”, or “Systolic Pressure”, for studies in all languages published until April 2019.

Study selection

Two investigators (FF and PK) reviewed all the potentially relevant studies obtained from the databases. The titles and abstracts of the publications were initially screened for potentially eligible studies, which were subsequently evaluated by full-text review. The inclusion criteria for study selection were: 1) studies that included adults (mean age ≥ 18 years); 2) studies that reported the effects of high- or low-carbohydrate diet compared with other dietary approaches on SBP and DBP in patients with T2DM, following any duration of treatment. The exclusion criteria were: 1) animal-based studies; 2) reviews; 3) posters; 4) letters to the editor; 5) studies on patients with type 1 diabetes or pre-diabetes; 6) studies conducted on patients with gestational diabetes mellitus (GDM); and 7) studies that did not include a control group. The initial search was supplemented by checking the reference lists of the retrieved articles to identify missed studies. Disagreements about the eligibility of any article were solved by discussing with a third author (AA).

Data extraction and quality assessment

Two investigators (PK and RC) extracted data from eligible studies using an Excel spreadsheet. The following data were extracted from each eligible study: first author, publication year, study location, dietary approaches, study design, sample size, and the age, SBP, DBP, body mass index, and sex ratio of the participants. In cases where the data were insufficient for a meta-analysis, we contacted the authors directly to obtain the data.

The Cochrane Collaboration’s tool was used to assess the risk of bias (Higgins et al., 2011). This tool has nine items, of which each are divided into six domains of bias with three rating categories: 1) low risk of bias (alter the results significantly); 2) unclear risk of bias (raises some doubt about the results); and 3) high risk (seriously

weakens confidence in the results). All selected articles were scored by two authors (AA and RC). Any disagreement were resolved by a third assessor (EF).

Data synthesis and statistical analysis

Differences between groups were assessed using the mean and standard deviation (SD) of the interested variables at baseline and post intervention. When the SD of the change was not reported, we calculated it by following formula: $SD = \text{square root} [(SD \text{ pre-intervention})^2 + (SD \text{ post-intervention})^2 - (2R \times SD \text{ pre-intervention} \times SD \text{ post-intervention})]$. A correlation coefficient of 0.8 was assumed as the R-value for the above-mentioned formula. Standard error (SE) was converted to SD by multiplying SE with \sqrt{n} ($n = \text{sample size of each group}$). If the median and range [or 95% confidence interval (CI)] were reported, mean and SD were estimated according to the method by Hozo et al. (2005). We used GetData Graph Digitizer 2.24 software (<http://getdata-graph-digitizer.com/>) to digitize and extract the data in a graphic form. A random effects model was used to calculate the pooled effect size of the outcome data where appropriate. Publication bias was assessed using visual assessment of funnel plots, Begg tests and Egger's regression asymmetry tests. We performed sensitivity analysis using the one-study remove (leave-one-out) approach to estimate the impact of each trial on the pooled effect size. We used Q tests (significance point at $P < 0.05$) and I-square (I^2) tests to examine between-study heterogeneity (Higgins et al., 2003). All analyses were conducted using STATA version

12 (Stata Corporation, College Station, TX, USA). $P < 0.05$ was considered statistically significant.

RESULTS

Study selection

The initial search yielded 610, 497, 1,077, and 343 citations in Cochrane Library, PubMed, Scopus, and Web of Science, respectively (Fig. 1). Of these, 368 articles were excluded due to duplication. Two investigators reviewed the titles and abstracts of the remaining 2,159 articles. Twenty three studies were identified for full-text review. Of these, 7 studies were excluded for the following reasons: included patients with GDM, intervention of diet with exercise, and no available data. Finally, a total of 16 articles were included in this meta-analysis.

Study characteristics

All 16 included studies were double blinded and placebo-controlled, and some had two or more effect sizes (Nielsen et al., 1995; Walker et al., 1995; Heilbronn et al., 1999; Brinkworth et al., 2004; Sargrad et al., 2005; Shah et al., 2005; Daly et al., 2006; Westman et al., 2008; Brehm et al., 2009; Davis et al., 2009; Esposito et al., 2009; Larsen et al., 2011; Krebs et al., 2012; Tay et al., 2015; Watson et al., 2016; Razak and Isaacs, 2017). The included studies were published between 1995 and 2017, with a total sample size of 1,610 patients with T2DM. The duration of intervention varied between 1 and 208

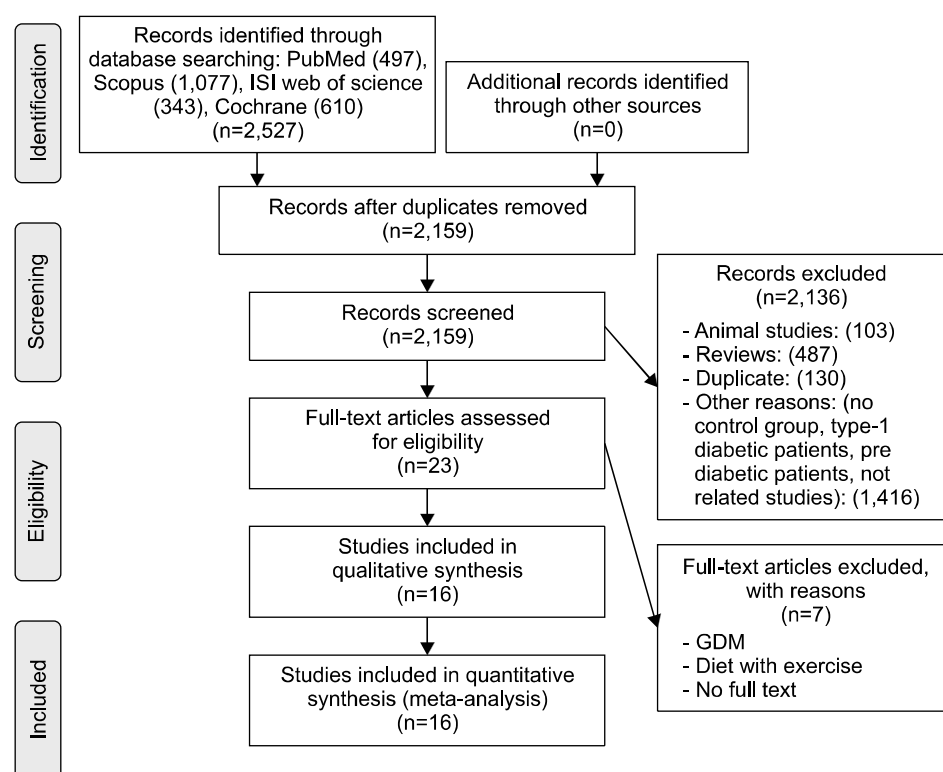


Fig. 1. Flow diagram of the literature search (Moher et al., 2009).

Table 1. Characteristics of the studies included in the meta-analysis

References	Country	Study design	Sample size (intervention / control)	Sex	Intervention	Trial duration	Age (intervention / control)	Results (intervention group)
Walker et al. (1995)	Australia	RCT- cross over	T2D patients (24/24)	M/F	High-HCLF diet vs. MF diet	12 weeks	58.3±2.1 / 58.3±2.1	No significant changes in SBP and DBP
Nielsen et al. (1995)	Denmark	RCT- cross over	T2D patients (4/6)	M/F	High-CHO diet vs. high-MUFA diet	3 weeks	66±7.75 / 66±7.75	No significant changes in SBP and DBP
Heilbronn et al. (1999)	Australia	RCT	T2D patients (12/13)	M/F	High-CHO diet vs. high-MUFA diet	1 week 12 weeks	57.5±3.4 / 58.7±2.5	No significant changes in SBP and DBP in different points of the follow-up
Brinkworth et al. (2004)	Australia	RCT	T2D patients (12/10)	M/F	High-CHO diet vs. high-SFA diet	1 week 12 weeks	52.0±2.6 / 51.5±1.6	No significant changes in SBP and DBP
			T2D patients (21/22)	M/F M F	High-CHO diet vs. high-protein diet	16 weeks	52.0±2.6 / 51.5±1.6	No significant changes in SBP and DBP
Daly et al. (2006)	UK	RCT	T2D patients (51/51)	M/F	Low-CHO diet vs. low-fat diet	12 weeks	58.2±1.55 / 59.1±1.48	No significant changes in SBP and DBP
Shah et al. (2005)	USA	RCT- cross over	T2D patients (42/42)	M/F	High-CHO diet vs. high- <i>cis</i> -MUFA diet	2 weeks 3 weeks 4 weeks	58±10 / 58±10	No significant changes in SBP and DBP in different points of the follow-up
			T2D patients (21/21)			5 weeks 6 weeks 14 weeks		
Sargrad et al. (2005)	USA	RCT	T2D patients (6/6)	M/F	High-CHO diet vs. high-protein diet	8 weeks		No significant changes in SBP and DBP
			T2D patients (21/29)	M/F	Low-CHO and ketogenic diet vs. low-glycemic and reduced-calorie diet	24 weeks	51.2±6.1 / 50.0±8.4	No significant changes in SBP and DBP
Davis et al. (2009)	USA	RCT	T2D patients (55/50)	M/F	Low-CHO diet vs. low-fat diet	12 weeks 24 weeks 52 weeks	54±6 / 53±7	No significant changes in SBP and DBP in different points of the follow-up
Brehm et al. (2009)	USA	RCT	T2D patients (52/43)	M/F	High-CHO diet vs. high-MUFA diet	16 weeks 32 weeks 52 weeks	56.5±0.8 / 56.5±0.8	No significant changes in SBP and DBP in different points of the follow-up
			T2D patients (108/107)	M/F	Low-CHO Mediterranean-style diet vs. low-fat diet	52 weeks	52.4±11.2 / 51.9±10.7	Significant reduction in SBP and DBP in different points of the follow-up
Larsen et al. (2011)	Australia	RCT	T2D patients (46/53)	M/F	High-CHO diet vs. high-protein diet	12 weeks 52 weeks	58.8±1.47 / 59.6±1.47	No significant changes in SBP and DBP in different points of the follow-up
Krebs et al. (2012)	New Zealand	RCT	T2D patients (212/207)	M/F	High-CHO diet vs. high-protein diet	24 weeks 104 weeks	58.0±9.2 / 57.7±9.9	No significant changes in SBP and DBP in different points of the follow-up
						52 weeks		

Table 1. Continued

References	Country	Study design	Sample size (intervention / control)	Sex	Intervention	Trial duration	Age (intervention / control)	Results (intervention group)
Tay et al. (2015)	South Australia	RCT	T2D patients (58/57)	M/F	Very low-CHO diet vs. high-CHO diet	52 weeks	58±7 / 58±7	No significant changes in SBP and DBP
Watson et al. (2016)	Australia	RCT	T2D patients (29/32)	M/F	High-CHO diet vs. high-protein diet	12 weeks 24 weeks	55±8 / 54±8	No significant changes in SBP and DBP in different points of the follow-up
Razak and Isaacs (2017)	South Africa	RCT	T2D patients (10/10)	M/F	Low-CHO diet vs. low-fat diet	12 weeks	49.2±6 / 49.6±6	No significant changes in SBP and DBP

RCT, randomized controlled trials; T2D, type 2 diabetics; M, male; F, female; HCLF, high-carbohydrate low-fat; MF, modified-fat; CHO, carbohydrate; MUFA, monounsaturated fatty acid; SFA, high-saturated fatty acid; SBP, systolic blood pressure; DBP, diastolic blood pressure; NR, Not reported.

weeks. All studies contained participants of both genders, and the participants ranged in age from 49.2 to 66 years. Six studies were conducted in Australia (Walker et al., 1995; Heilbronn et al., 1999; Brinkworth et al., 2004; Larsen et al., 2011; Tay et al., 2015; Watson et al., 2016), five in USA (Sargrad et al., 2005; Shah et al., 2005; Westman et al., 2008; Brehm et al., 2009; Davis et al., 2009), one in the United Kingdom (Daly et al., 2006), one in Denmark (Nielsen et al., 1995), one in Italy (Esposito et al., 2009), one in South Africa (Razak and Isaacs, 2017), and one in New Zealand (Krebs et al., 2012). Thirteen studies had a parallel study design, and three had a cross-over study design. The types of interventional diet were as follows: high-carbohydrate diet vs. high-MUFA diet (n=4), high-carbohydrate diet vs. high-protein diet (n=5), high-carbohydrate diet vs. high-saturated fatty acids diet (n=1), high-carbohydrate diet vs. modified fat diet (n=1), low-carbohydrate diet vs. low-fat diet (n=4), low-carbohydrate diet vs. high-carbohydrate diet (n=1), and low-carbohydrate diet vs. low-glycemic index diet (n=1). The characteristics of the included studies are summarized in Table 1.

Assessment of risk of bias

The results of the RCTs risk of bias are indicated in Table 2. The assessors agreed on 91 of the 112 items, resulting in 81% agreement rate. After discussing with a third assessor (EF), 100% agreement was reached. One study (Tay et al., 2015) had the lowest risk of bias and reached the highest score (6 out of 7). Of the 16 studies, 10 had a low risk of bias and reached a score of ≥4 out of 7. Lack of blinding of participants and personnel occurred in all the included studies. Further details are presented in the Table 2.

Publication bias and sensitivity analysis

Evaluation of publication bias using funnel plots did not show evidence of publication bias within the studies. Furthermore, based on both the Egger test and the Begg test, there were no statistical evidence of publication bias between the studies. The P-values for the Egger and Begg tests based on the different dietary approaches were as follows: high-carbohydrate diet vs. high-MUFA diet (SBP, P=0.160 and P=0.525; DBP, P=0.533 and P=0.165, respectively), high-carbohydrate diet vs. high-protein diet (SBP, P=0.858 and P=0.961; DBP, P=0.945 and P=0.763, respectively), and low-carbohydrate diet vs. low-fat diet (SBP, P=0.851 and P=0.438; DBP, P=0.452 and P=0.299, respectively) (data not shown). To evaluate the strength of our results, we carried out sensitivity analysis. However, removing each study individual in the sensitivity analysis did not change the pooled effect size.

Table 2. Quality assessment (Cochrane collaboration's tool for assessing risk of bias)

References	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias	Total
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Anything else, ideally pre-specified	
Walker et al. (1995)	Low	High	High	High	High	Low	Low	3/7
Nielsen et al. (1995)	Low	High	High	High	Low	Low	Unclear	3/7
Heilbronn et al. (1999)	Low	High	High	High	Low	Low	Low	4/7
Brinkworth et al. (2004)	Low	High	High	High	Low	Low	High	3/7
Daly et al. (2006)	Low	Low	High	High	High	Low	Unclear	3/7
Shah et al. (2005)	Low	High	High	High	Low	Low	Low	4/7
Sargrad et al. (2005)	Low	Low	High	High	Low	Low	Low	5/7
Westman et al. (2008)	Low	High	High	High	Low	Low	High	3/7
Davis et al. (2009)	Low	Low	High	High	Low	Low	Low	5/7
Brehm et al. (2009)	Low	High	High	High	Low	Low	Low	4/7
Esposito et al. (2009)	Low	High	High	Low	Low	High	Low	4/7
Larsen et al. (2011)	Low	High	High	High	Low	Low	Low	4/7
Krebs et al. (2012)	Low	Low	High	Low	Low	Low	Unclear	5/7
Tay et al. (2015)	Low	Low	High	Low	Low	Low	Low	6/7
Watson et al. (2016)	Low	Low	High	High	Low	Low	Unclear	4/7
Razak and Isaacs (2017)	High	High	High	High	Low	Low	High	2/7

Meta-analysis

The overall pooled net effect of the different dietary approaches on SBP and DBP compared with the high-carbohydrate diet were -2.29 mmHg (95% CI: -3.49 to -1.1) and -1.03 (95% CI: -1.77 to -0.29), respectively (Fig. 2). The high-MUFA diet was more effective in reducing both SBP and DBP than the high-carbohydrate diet [weighted mean differences (WMD) with 95% CI: -4.03 (-5.79 to -2.27); -2.12 (-3.18 to -1.06), respectively] (Fig. 3). Compared with the high-carbohydrate, the high-protein diet was not effective in reducing SBP or DBP [WMD: -1.17 (-2.60 to 0.27); -0.65 (-1.89 to 0.58), respectively] (Fig. 4). Furthermore, all the dietary interventions together were not effective in reducing both SBP and DBP compared with the low-carbohydrate diet [WMD: -0.86 (-3.80 to 2.07); 0.6 (-0.58 to 1.77), respectively] (Fig. 5). In addition, the low-fat diet was not effective in reducing SBP or DBP compared with low-carbohydrate diet [WMD: -2.72 (-6.47 to 1.03); 0.59 (-0.89 , 2.08), respectively] (Fig. 6).

Subgroup analysis

The subgroup analysis indicated that, in comparison to the high-carbohydrate diet, the overall pooled net effect of the different dietary approaches on SBP and DBP were significant in long-term intervention (Table 3). The effect of the high-MUFA diet on both SBP and DBP compared with the high carbohydrate diet was significant in both long- and short-term intervention (Table 3). However, there was no significant effect on either SBP or DBP of long-term or short-term intervention with the high-pro-

tein diet compared with the high-carbohydrate diet (Table 3). Due to the low number of studies, subgroup analysis comparing the overall different dietary approaches and low-fat diet with the low-carbohydrate diet was not performed.

DISCUSSION

In our systematic review and meta-analysis of 16 trials including 1,610 patients with T2DM, we showed that dietary modifications were more effective in reducing both SBP and DBP than high carbohydrate diets. Indeed, diets high in MUFA diet more effective in reducing both SBP and DBP than high carbohydrate diets; however, high protein diets were not effective. Furthermore, we found that some dietary approaches, such as low fat diets, were no more beneficial for reducing SBP or DBP compared with low carbohydrate diets.

The prevalence of CVD, the most common cause of death in western societies, is rapidly increasing amongst patients with T2DM (Colosia et al., 2013). High blood pressure is a major risk factor for CVD, especially in diabetics (Colosia et al., 2013). Lowering blood pressure is an important factor for preventing CVD; a decrease in SBP of approximately 10 mmHg can reduce the risk of CVD by 20%, stroke by 27%, and heart failure by 28% (Ettihad et al., 2016). Additionally, a decrease in DBP of approximately 5 mmHg is associated with a lower risk of stroke (32%) and ischemic heart disease (20%) (Law et al., 2003). In a previous meta-analysis, a revealed in SPB

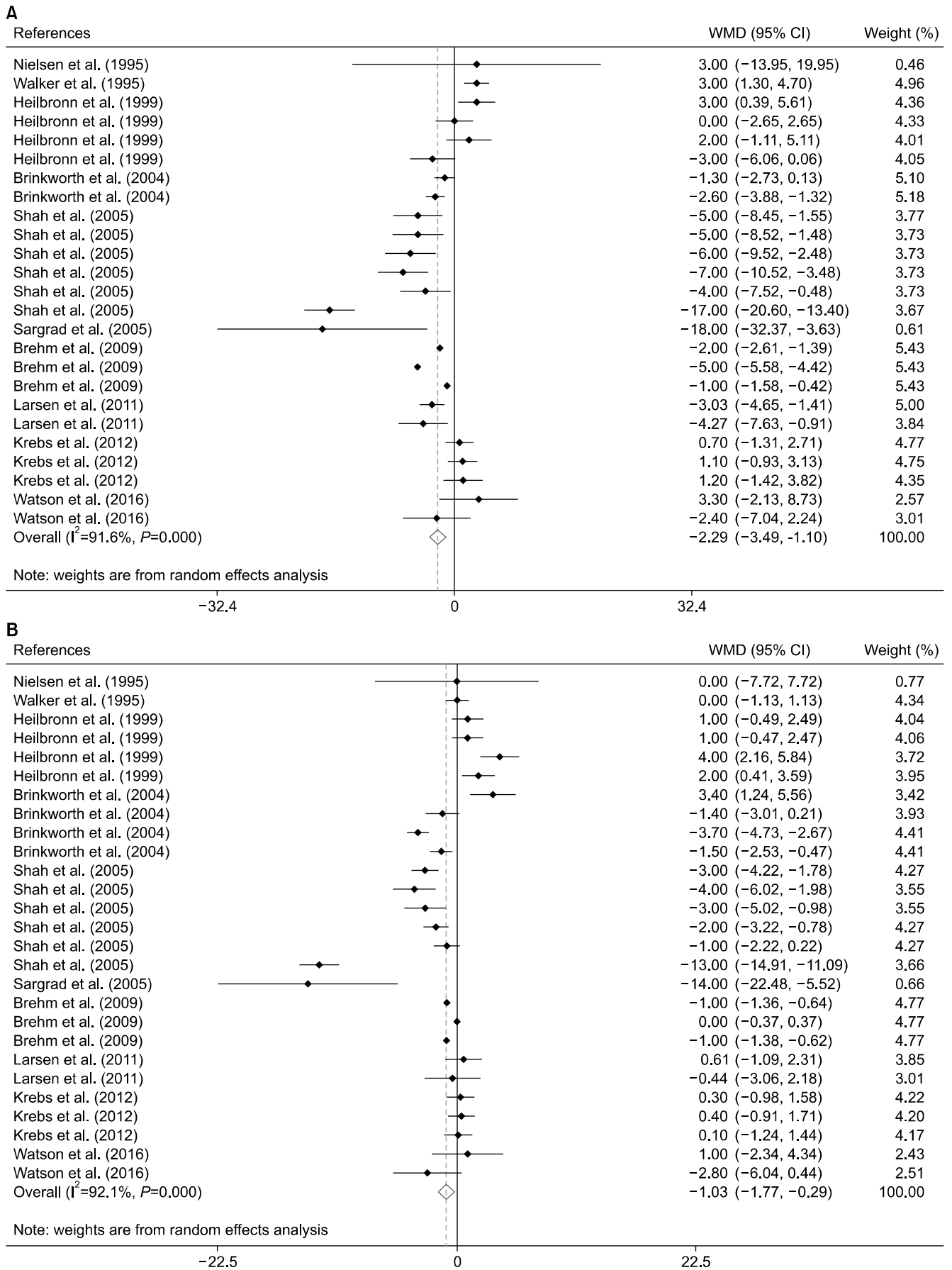


Fig. 2. Forest plot of the overall pooled net effect of different dietary approaches compared with the high-carbohydrate diet on (A) systolic blood pressure and (B) diastolic blood pressure.

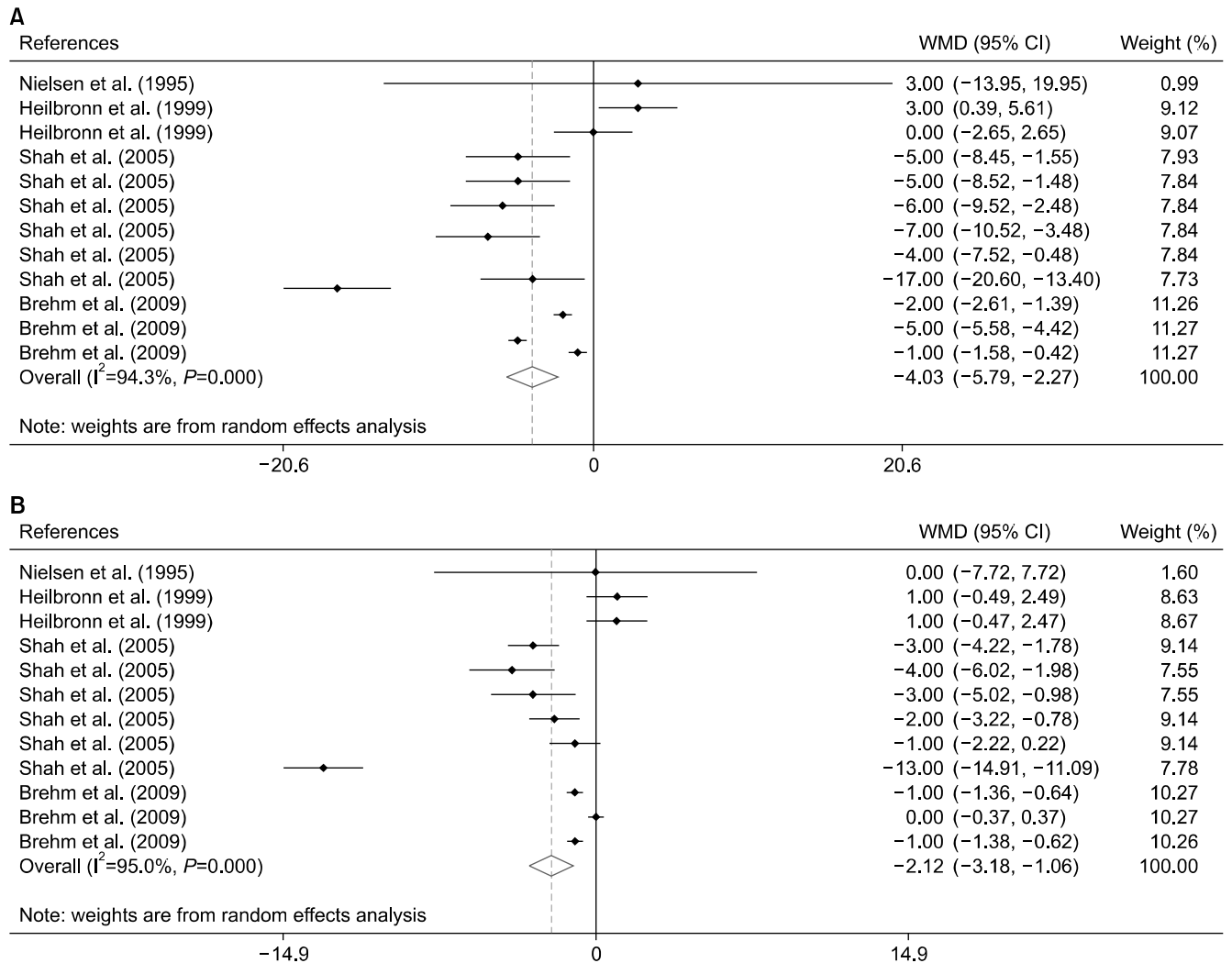


Fig. 3. Forest plot of the effect of the high-monounsaturated fatty acid diet compared with the high-carbohydrate diet on (A) systolic blood pressure and (B) diastolic blood pressure.

of 2 mmHg was associated with a 10% lowered risk of death due to the stroke (Lewington et al., 2002).

Our meta-analysis indicated that other dietary interventions reduce SBP and DBP by -2.29 mmHg and -1.03 mmHg, respectively, compared with a high-carbohydrate diet. In a 2015 meta-analysis (Gay et al., 2016), healthy dietary modifications were associated with significant reductions in both SBP and DBP (-3.07 mmHg and -1.81 mmHg, respectively). Furthermore, in a recent meta-analysis (Schwingshackl et al., 2019), dietary approaches to stop hypertension, Mediterranean, low-carbohydrate, Palaeolithic, high-protein, low-glycaemic index, low-sodium, and low-fat diets shown to be more effective than a control diet for reducing SBP and DBP in hypertensive and pre-hypertensive individuals. Consistent with the results in our current study, low-fat diets were not shown to significantly decrease SBP or DBP compared with low-carbohydrate diets (Schwingshackl et al., 2019). Moreover, we showed that high protein diets are not effective in reducing SBP and DBP compared with high-car-

bohydrate diets. Previous meta-analyses have shown conflicting results regarding the effect of high-protein diets on blood pressure. For example, one meta-analysis showed that high protein diets do not significant effect SBP or DBP compared with low-protein diets (Schwingshackl and Hoffmann, 2013). However, in another meta-analysis, which included pre-hypertensive and hypertensive participants, indicated that high-protein diets are significantly more effective in reducing both SBP and DBP compared with control diets (Schwingshackl et al., 2019). These differences may be partly due to the differences in the participants included in the meta-analyses, and the groups compared.

In our meta-analysis, we showed that a high-MUFA diet had an incremental blood pressure lowering effect of -4.03 mmHg and -2.12 mmHg for SBP and DBP, respectively, compared with a high-carbohydrate diet. Our results are in line with the meta-analysis by Schwingshackl et al., (2019) that demonstrated a significant difference between high and low-MUFA diets with

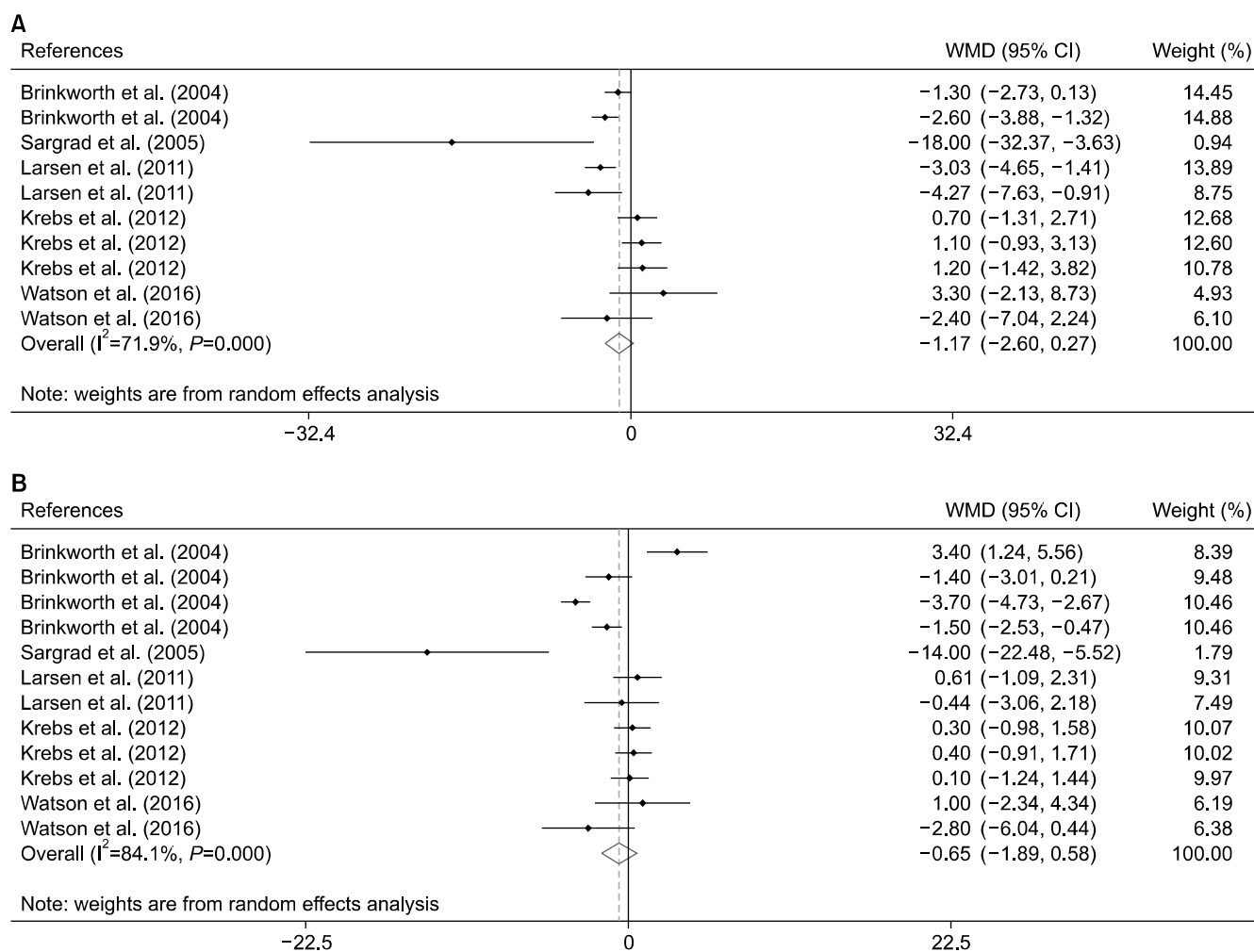


Fig. 4. Forest plot of the effect of the high-protein diet compared with the high-carbohydrate diet on (A) systolic blood pressure and (B) diastolic blood pressure.

respect to both SBP and DBP (-2.26 mmHg and -1.15 mmHg, respectively). In another meta-analysis, a high-carbohydrate diet was associated with higher SBP and DBP than diets rich in MUFA (Shah et al., 2007). However, a recent meta-analysis indicated that high-MUFA diets did not reduce SBP or DBP compared with high carbohydrate diets (Jovanovski et al., 2019). It should be noted that all these meta-analyses included populations without health restrictions, and our study is the first systematic review and meta-analysis in this area that particularly focused on T2DM patients.

A possible mechanism for high carbohydrate diet leading to higher blood pressure than high-MUFA diet is due to increased levels of insulin. Previous studies have shown that a high-carbohydrate diet increases the level of insulin by 10% compared with high-MUFA diets, with the effect persisting for 14-weeks (Garg et al., 1994). It is well known that hyperinsulinemia increases the activity of the sympathetic nervous system, which increases vascular resistance, cardiac output, heart rate, and retention of Na^+ and, eventually, increases blood pressure (Facchini

et al., 1996). Furthermore, a high-MUFA diet has been shown to improve cardiovascular risk factors. A previous meta-analysis indicated that replacing carbohydrates with MUFA improves blood levels of triglycerides, low-density lipoproteins and high-density lipoproteins (HDL) (Mensink et al., 2003). In addition, a further meta-analysis revealed that high-MUFA diets reduce plasma levels of triacylglycerols, and increase HDL concentrations in patients with diabetes mellitus (Garg, 1998). Several studies have shown biological interrelations between blood pressure and blood lipids, and have correlated high blood pressure with increased atherogenic plasma lipid fractions (Bønaa and Thelle, 1991). Therefore, it can be speculated that a high-MUFA diet could be effective in reducing blood pressure through this mechanism.

This systematic review and meta-analysis has several strengths. First, this is the first meta-analysis to assess the effects of different dietary approaches compared with a high/low-carbohydrate diet on blood pressure in patients with T2DM. Second, we included RCTs that examined complementary endpoints, therefore providing a

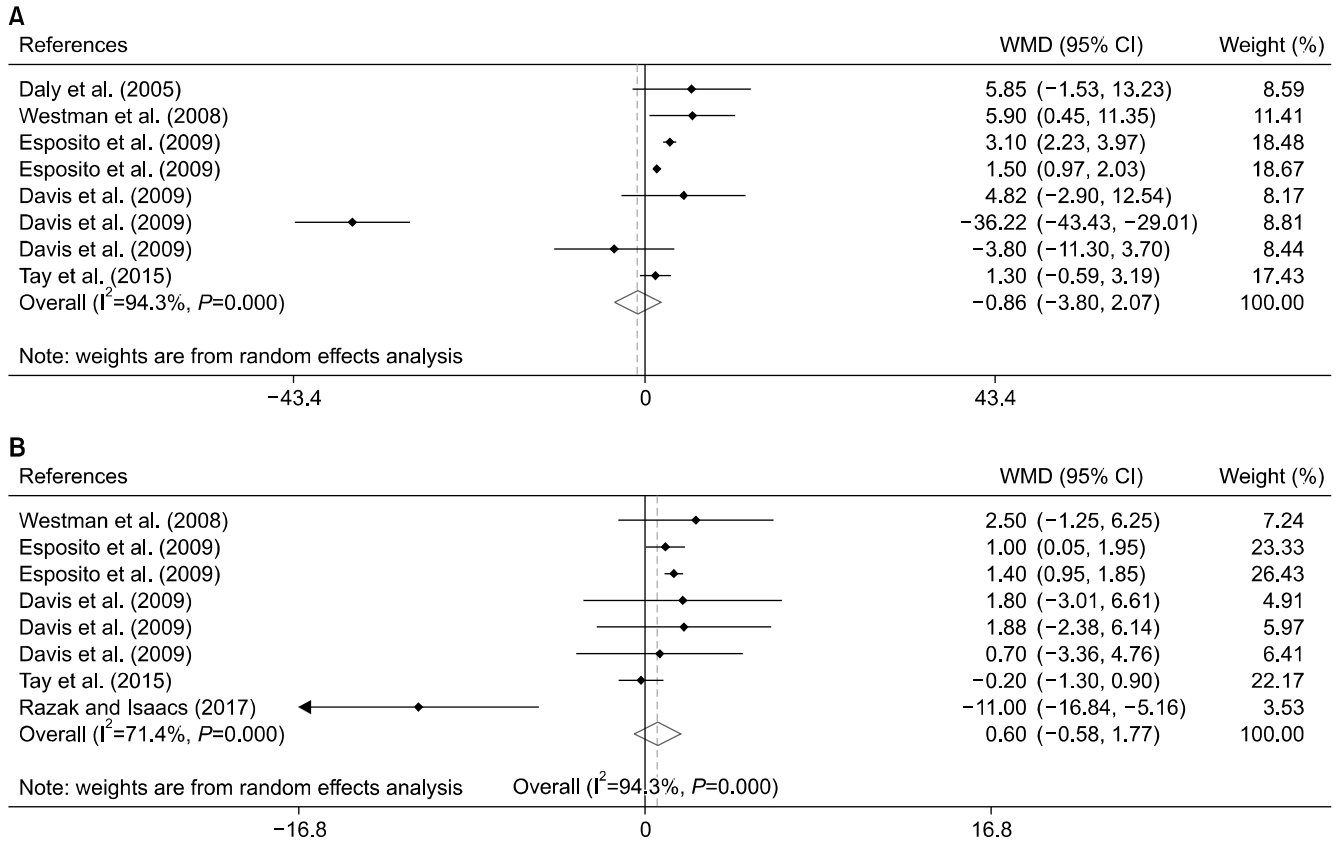


Fig. 5. Forest plot of the overall pooled net effect of different dietary approaches compared with the low-carbohydrate diet on (A) systolic blood pressure and (B) diastolic blood pressure.

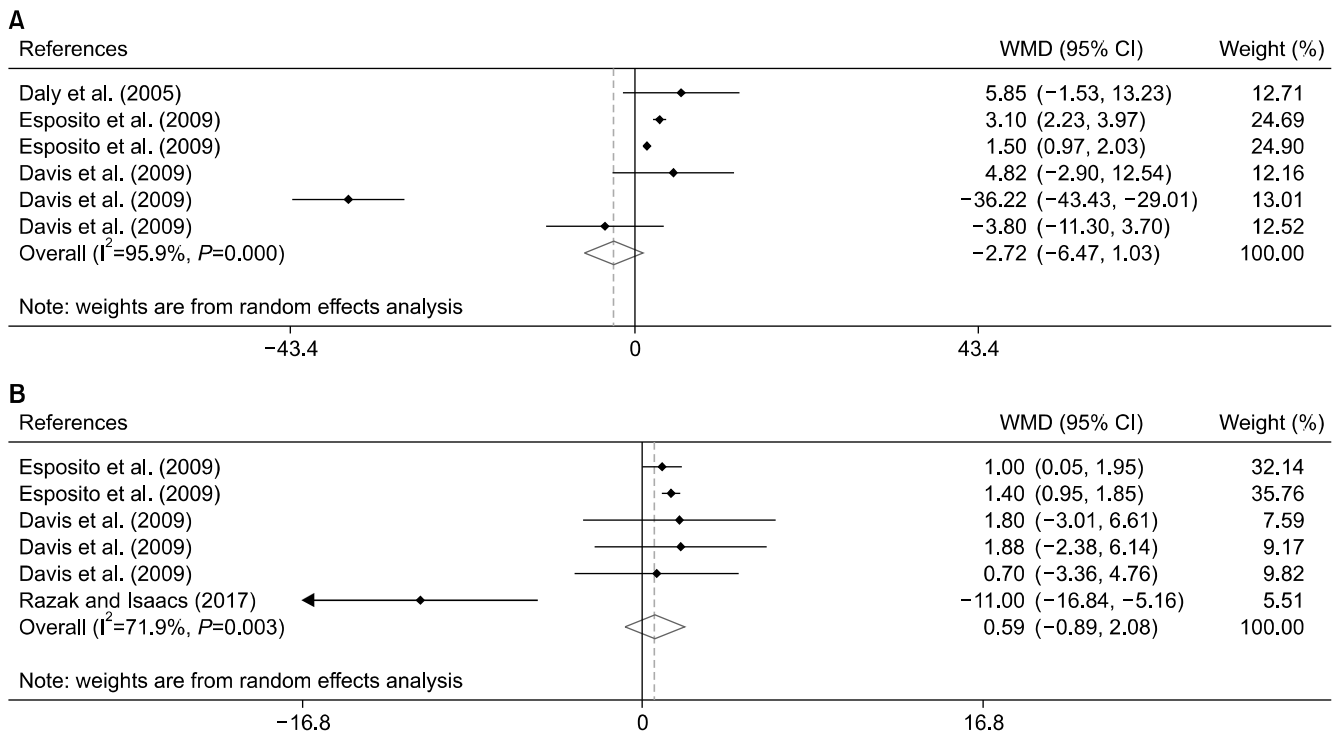


Fig. 6. Forest plot of the effect of the low-fat diet compared with the low-carbohydrate diet on (A) systolic blood pressure and (B) diastolic blood pressure.

Table 3. Subgroup analyses

Trial duration (week)	No.	WMD (95% CI)	<i>P</i> within group	<i>P</i> heterogeneity	<i>I</i> ² (%)
SBP					
Overall pooled net effect of different dietary approaches vs. the high-carbohydrate diet on SBP					
≤12	14	−2.02 (−4.16, 0.13)	0.6	<0.001	84.1
>12	11	−2.64 (−4.22, −1.06)	0.001	<0.001	94.8
High-MUFA diet vs. the high-carbohydrate diet on SBP					
≤12	8	−3.14 (−6.01, −0.27)	0.03	<0.001	80.3
>12	4	−5.32 (−8.02, −2.62)	<0.001	<0.001	98.1
High-protein diet vs. the high-carbohydrate diet on SBP					
≤12	3	−3.04 (−10.02, 3.94)	0.39	0.01	78.3
>12	7	−1.16 (−2.59, 0.27)	0.22	0.003	69.4
DBP					
Overall pooled net effect of different dietary approaches vs. the high-carbohydrate diet on DBP					
≤12	14	−0.55 (−1.80, 0.71)	0.391	<0.001	86.1
>12	13	−1.51 (−2.51, −0.51)	0.003	<0.001	94.9
High-MUFA diet vs. the high-carbohydrate diet on DBP					
≤12	8	−1.47 (−2.81, −0.14)	0.03	<0.001	81.2
>12	4	−3.19 (−4.97, −1.42)	<0.001	<0.001	98.3
High-protein diet vs. the high-carbohydrate diet on DBP					
≤12	3	−2.12 (−7.14, 2.89)	0.41	<0.001	82.2
>12	9	−0.63 (−1.95, 0.68)	0.34	<0.001	85.6

WMD, weighted mean difference; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; MUFA, mono-unsaturated fatty acid.

comprehensive review on this topic. Third, this review is based on an up to date literature search from a large number of databases and included 16 studies with 1,503 participants. However, this meta-analysis is limited by the low number of trials that were available for each dietary approaches, which limits the strength of the conclusions for each dietary approach. However, this study should be helpful for guiding future studies.

In conclusion, the results of this systematic review and meta-analysis have important clinical and public health implications, and indicate that adopting healthful dietary modifications may be an effective method for controlling high blood pressure in T2DM patients in comparison to consuming a high carbohydrate diet. Our results demonstrated that a high-MUFA diet was more effective in reducing both SBP and DBP than a high-carbohydrate diet whereas other dietary approaches were not effective. However, further well-designed studies are needed to confirm these results.

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AUTHORS' CONTRIBUTIONS

AA and RC designed the study. PK and FF reviewed and selected the articles. PK and FF extracted needed data from articles. AA performed data analysis and interpretation. RC drafted the manuscript. EF and MJG revised the article for important intellectual content. All authors have read and approved the final manuscript.

AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

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