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High protein diet is of benefit for patients with type 2 diabetes

An updated meta-analysis

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Abstract

Currently, the prevalence of type 2 diabetes is still increasing worldwide and has become a major public health burden. This meta-analysis was performed to further assess high protein (HP) diet on body weight, glycemic control, and cardiovascular disease risk factors in type 2 diabetes.

A literature search was conducted in PubMed and Embase databases up to June 2018. The pooled standard mean difference (SMD) and the corresponding 95% confidence interval (CI) were calculated using RevMan 5.3 software.

In total, 18 randomized control trials involving 1099 adults with type 2 diabetes were included. Pooled results indicated that HP diet could not significantly affect blood pressure of patients with type 2 diabetes, compared with low protein (LP) diet. However, the overall analyses showed the significant effect of HP diet on triglycerides reduction (SMD = -0.20, 95% CI = -0.35 to -0.05, P = .01) in patients with type 2 diabetes, compared with LP diet. Subgroup analyses showed that the ratio of energy from fat and carbohydrate in diet could affect the effect of HP diet on weight and triglyceride.

HP diet could be indicated to obtain beneficial results in weight loss and lipid metabolism.

Abbreviations: BMI = body mass index, CI = confidence interval, HDL = high-density lipoprotein cholesterol, HP = high protein, HPLC = high protein low carbohydrate, HPLCHF = high protein low carbohydrate high fat, LDL = low-density lipoprotein cholesterol, LP = low protein, LPHC = low protein high carbohydrate, LPHCLF = low protein high carbohydrate low fat, RCT = randomized control trial, SMD = standard mean difference, TC = total cholesterol, TG = triglycerides.

Keywords: cardiovascular disease risk factors, high protein diet, meta-analysis, type 2 diabetes

1. Introduction

Currently, the prevalence of type 2 diabetes is still increasing worldwide^[1] and has become a major public health burden.^[2] Type 2 diabetes is characterized by insulin resistance in most subjects and approximately 80% of patients with type 2 diabetes are overweight or obese. Obesity and insulin resistance are all associated with the risk factors of cardiovascular diseases.^[3–5] Weight management is a major component of effective diabetes care, which can significantly improve the cardiovascular diseases markers (such as blood pressure, high-density lipoprotein cholesterol [HDL], and triglycerides [TG]) and glycemic control.^[6,7] Thus, long-term weight management is essential for the patients with type 2 diabetes.

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Received: 15 January 2018 / Accepted: 15 October 2018 http://dx.doi.org/10.1097/MD.000000000013149 The dietary approach to weight loss and treating type 2 diabetes is commonly used in clinical practice. Many studies suggest nutrient composition (both in energy restriction and energy balance) of dietary strategies may be important and affect glucose and lipid profile in diabetes patients.^[8–11] However, the optimal diet for people with diabetes is still unknown. High protein (HP) diet has been frequently used for weight loss in obese people. Currently, some studies have proved that a HP intake can enhance weight loss, glycemic control, and cardiovascular disease risk factors.^[6,12,13] A previous meta-analysis has proved beneficial effects on weight loss, HbA1c, and blood pressure.^[14] However, the controversies still exist among recent published studies.^[12,15–17]

We speculated that the HP diet is benefit for the diabetes patients. Therefore, we performed this updated meta-analysis to further confirm the effect of HP diet on weight loss, glycemic control, and cardiovascular disease risk factors. In addition, the secondary purpose was to assess the effect of ratio of energy from carbohydrate and fat in diets on the results by subgroup analysis.

2. Materials and methods

2.1. Search strategy

A literature search was conducted in PubMed and Embase databases up to June 2018. The following key words were used: ("type 2 diabetes" or "diabetes") and ("diet" or "diets" or "dietary" or "protein" or "high protein") and "randomized." In addition, we also manually scanned the reference lists of some relevant reviews to select additional studies.

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2.2. Inclusion and exclusion criteria

All included studies should meet the following criteria: the study type was randomized control trial (RCT); participants were patients with diabetes; the HP and low protein (LP) diets were applied and compared; the intervention of HP diet was kept for ≥ 1 month (or 4 weeks); the weight loss, glycemic control, blood lipids change, or blood pressure change after diet intervention in each group was investigated.

The exclusion criteria were: comparison was not performed based on diet composition; the ratio of energy from protein in diet intervention was equal between groups; duplicated publications; no available data; and letters, comments, or reviews.

2.3. Data extraction and quality assessment

Two investigators independently reviewed the full texts of included studies and assessed their quality. Differences were resolved by discussion to ensure consistency. The following data should be recorded in a predesigned form: first author, year of publication, country, sample size, age, sex, the duration of intervention, diets component, and the outcomes.

In addition, the design, execution, and reporting of the included studies were assessed using the Cochrane risk of bias tool, which included the following items: random sequence generation and allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias).

2.4. Statistical analysis

All analyses were performed using RevMan 5.3 software. The chi-squared and I^2 tests were used to assess the heterogeneity among studies. A *P* value < .1 or $I^2 > 50\%$ indicated the existence of significant heterogeneity. An appropriate statistical model

(random- or fixed-effects model) was used to calculate the pooled standard mean difference (SMD) as well as the corresponding 95% confidence interval (CI) based on the results of heterogeneity testing. In addition, the subgroup analyses were performed based on the diet composition. The sensitivity analysis was performed to evaluate the stability of the results by removing each individual study from the pooled analysis. The publication bias was assessed using the funnel plot.

3. Results

3.1. Characteristics of included studies

After the initial literature search, totally 1022 articles were found (450 from PubMed and 572 from Embase). After excluding duplicates, 318 potentially relevant articles remained. Among them, 230 irrelevant articles were removed by scanning the titles; 59 articles were excluded by reading abstracts based on the inclusion and exclusion criteria. Then 11 articles were excluded by reading the full texts. Finally, 18 studies^[11-13,15-29] were included in this meta-analysis. In addition, no additional studies were selected by manual search (Fig. 1).

The characteristics of these included studies were shown in Table 1. A total of 1099 adults with diabetes were reanalyzed in this meta-analysis. The publication year was from 2002 to 2018. These studies were, respectively, conducted in Australia (n=7), the United States (n=6), New Zealand (n=1), Greece (n=1), Sweden (n=1), and the United Kingdom (n=2). The subjects were all patients with type 2 diabetes. The duration of diet intervention ranged from 4 weeks to 24 months. The baseline weight/body mass index (BMI) was similar between groups in each included study. In addition, risk of bias in most studies was low or unclear, but high risk of performance bias was shown in all the included studies due to no blinding of subject or implementer (see Supplementary Table 1, http://links.lww.com/MD/C616 and



Figure 1. Literature search and study selection.

Author, year	County	Study type	Duration of intervention	Subject	Group	Radio of prote carbohydrate, an	ein, nd fat	Sample size	Age (mean \pm SD [*] /SEM [#])	Sex, F/M	Weight/BMI (mean \pm SD [*] /SEM [#])
Wycherley, 2010	Australia	RCT	16 wk	Overweight and obese patients with type 2 diabetes	HP	32:47:18	HPLCLF	12	$55.0 \pm 8.4^{*}$	NA	102.7±15.4 [*] /35.6±3.8 [*]
					LP	18:53:22	LPHCHF	16			$97.0 \pm 10.6^{*}/34.8 \pm 4.9^{*}$
Parker, 2002 Australia RCT 12 wh		12 wk	Patients with type 2 diabetes	HP	28:42:28	HPLC	26	F: 58.7±2.2 M: 63.4±1.7 [#]	17/9	97.7±17.4 [#]	
					LP	16:55:26	LPHC	28	F: 60.9±2.3 M: 64.2±3.8 [#]	18/10	91.4±18.2 [#]
Jesudason, 2013	Australia	RCT	12 mo	Patients with type 2 diabetes and renal disease	HP	30:40:30	HPLC	21	59.4±2.2 [#]	6/15	108.1±5.0 [#]
					LP	20:50:30	LPHC	24	$62.4 \pm 1.7^{\#}$	4/20	104.7±3.8 [#]
Luger, 2013	Australia	RCT	12 wk	Patients with type 2 diabetes	HP	23-27:38-43:32-35	HPLCHF	22	61.0±5.7*	8/14	$94.1 \pm 15.6^{*}/33.0 \pm 4.2^{*}$
					LP	17-20:43-50:29-34	LPHCLF	22	$63.7 \pm 5.2^{*}$	16/6	91.5±20.2 [*] /33.6±5.3 [*]
Sargrad, 2005	USA	RCT	8 wk	Patients with type 2 diabetes	HP	27:43:30	HPLC	6	$48 \pm 5.5^{\#}$	5/1	$94.9 \pm 6.4^{\#}/33 \pm 2^{\#}$
					LP	19:51:30	LPHC	6	$47 \pm 1.9^{\#}$	4/2	$97.5 \pm 9.6^{\#}/36 \pm 3^{\#}$
Brinkworth, 2004	Australia	RCT	12 wk	Obese adults with type 2 diabetes	HP	30:40:30	HPLC	19	$60.9 \pm 1.8^{\#}$	11/8	96.2±4.0 [#] /33.6±1.2 [#]
					LP	15:55:30	LPHC	19	$62.7 \pm 1.8^{\#}$	12/7	91.2±4.3 [#] /33.3±1.3 [#]
Krebs, 2012	os, 2012 New Zealand RCT 12 mo		Patients with type 2 diabetes	HP	30:40:30	HPLC	207	$57.7 \pm 9.9^{*}$	95/112	$103.4 \pm 19.7^{*}/36.6 \pm 6.7^{*}$	
					LP	15:55:30	LPHC	212	$58.0 \pm 9.2^{*}$	73/139	$101.9 \pm 20.1^{*}/36.7 \pm 6.4^{*}$
Khoo, 2011	Australia	RCT	8 wk	Obese men with type 2 diabetes	HP	NA	HPLF	12	$62.3 \pm 5.9^*$	0/12	$109.6 \pm 14.9^{*}/35.6 \pm 4.8^{*}$
					LP	NA	LPHF	19	$58.1 \pm 11.4^{*}$	0/19	$112.7 \pm 19.2^{*}/35.1 \pm 4.3^{*}$
Papakonstantinou, 2010	Greece	RCT, crossover design	4 wk	Obese individuals with newly diagnosed type 2 diabetes	HP	30:51:19	HPHCLF	17	$46\pm3^{\#}$	12/5	$93 \pm 4^{\#}/34 \pm 1^{\#}$
					LP	18:40:42	LPLCHF				
Gannon, 2004	USA	RCT, crossover design	5 wk	Patients with type 2 diabetes	HP	30:20:50	HPLCHF	8	63.3	0/8	$98 \pm 4.5^{\#}$
					LP	15:55:30	LPHCLF		*	0/8	$99 \pm 4.5^{\#}$
Westman, 2008	USA	RCT	24 wk	Patients with type 2 diabetes	HP	28:13:59	HPLCHF	21	51.2±6.1	14/7	$108.4 \pm 20.5^{\circ}/37.8 \pm 6.7^{\circ}$
					LP	20:44:36	LPHCLF	29	50.0 ± 8.4	23/9	$105.2 \pm 19.8^{\circ}/37.9 \pm 6.0^{\circ}$
Guldbrand, 2012	Sweden	RCT	24 mo	Patients with type 2 diabetes	HP	30:20:50	HPLCHF	30	61.2±9.5	16/14	91.4±19 /31.6±5.0
					LP	10-15:55-60:10	LPHCLF	31	62.7 ± 11	18/13	$98.8 \pm 21 / 33.8 \pm 5.7$
Rock, 2014	USA	RCT	12 mo	Patients with type 2 diabetes	HP	25:45:30	HPLCHF	77	57.3±8.6	37/40	106.4±18.3 /36.2±4.7
					LP	20:60:20	LPHCLF	74	55.5 ± 9.2	35/39	105.4 ± 17.8 /36.2 ± 4.3
Tay, 2014	Australia	RCT	52 wk	Obese adults type 2 diabetes	HP	28:14:58	HPLCHF	58	58±7	21/37	$101.7 \pm 14.4^{\circ}/34.2 \pm 4.5^{\circ}$
					LP	17:53:30	LPHCLF	57	58 ± 7	28/29	101.6 ± 15.8 /35.1 ± 4.1
Nuttall, 2012	USA	RCT, crossover design	5 wk	Men with type 2 diabetes	HP	30:30:40	HPLCHF	8	NA	0/8	97.2
					LP	15:55:30	LPHCLF				97.6
Gannon, 2003	USA	RCT	5 wk	Type 2 diabetes	HP	30:40:30	HPLC	12	61	2/10	31
		DOT	04	0	LP	15:55:30	LPHC	12	E4 0 [#]	2/10	070 474#040 5 **
Nerylee, 2016	UK	KCI	24 WK	Ubese adults with type 2 diabetes	HP	29:34:31	HPLCHF	32	54±8"	15/17	9/.3±17.1"/34.3±5.4"
D.1 0000		DOT	0	T O	LP	21:48:24	LPHCLF	29	55±8"	13/16	$101.5 \pm 16.1^{#}/34.4 \pm 4.7^{#}$
Daiy, 2006	UK	KUI	3 mo	Type 2 diabetes	HP	26.4:33.5:40.1	HPLCHF	51	$58.2 \pm 1.55''$	26/25	$101.6 \pm 1.84^{"/3}5.4 \pm 0.7^{"}$
					LP	20.9:45.2:32.9	LPHULF	51	59.1±1.48″	21/24	102.3 ± 2.49"/36.7 ± 1.26"

BMI = body mass index, HP = high protein, HPHCLF = high protein high carbohydrate low fat, HPLC = high protein low carbohydrate, HPLCHF = high protein low carbohydrate high fat, HPLCF = high protein low fat, LP = low protein, LPHC = low protein high carbohydrate, LPHCHF = low protein high carbohydrate low fat, LPHCF = low protein high carbohydrate low

Fig. 2). Detection or other bias risk may exist in some studies due to less rigorous study design or procedure.

3.2. Effect of HP diet on weight loss

Most of these included studies investigated the effect of HP diet on weight loss. No significant heterogeneity was found among these studies ($I^2=0\%$, P>.10), so the pooled SMDs were calculated by fixed-effects model. Results showed that the HP diet did not significantly affect the body weight compared with LP diet (SMD = -0.09, 95% CI = -0.21 to 0.04, *P* = .17, Fig. 3A). Similarly, there was also no significant difference between HP and LP groups in BMI (SMD = -0.06, 95% CI = -0.24 to 0.12, *P* = .49, Fig. 3B), fat mass (SMD = -0.01, 95% CI = -0.18 to 0.15, *P* = .88, Fig. 3C), and fat-free mass (SMD = -0.04, 95% CI = -0.27 to 0.20, *P* = .76, Fig. 3D). These results indicated that

A Risk of bias graph



в Risk of bias graph



Figure 2. Risk of bias graph and risk of bias summary.

the weight loss of patients with type 2 diabetes HP diet could not affected by the ratio of energy from protein in diet.

3.3. Effect of HP diet on glycemic control

Figure 4 shows the results of meta-analysis for effect of HP diet on glycemic control. No significant evidence of heterogeneity among studies was found in the analysis for fasting glucose, fasting insulin, and HbA1c ($I^2 < 50\%$, P > .10). Thus, the fixed-effects model was applied, respectively. The pooled estimate indicated that the change of fasting glucose (SMD=-0.08, 95% CI=-0.21 to 0.06, P=.25, Fig. 4A), fasting insulin (SMD=-0.04, 95% CI=-0.24 to 0.17, P=.71, Fig. 4B), and HbA1c (SMD=-0.07, 95% CI=-0.20 to 0.06, P=.27, Fig. 4C) after HP and LP diets were similar, suggesting that the ratio of energy from protein in diets did not affect the glycemic control in patients with type 2 diabetes.

3.4. Effect of HP diet on lipid metabolism

The effects of HP diet on blood lipid levels were investigated by 14 included studies. There was no significant heterogeneity ($I^2 < 50\%$, P > .10) among these studies in the analysis for total cholesterol (TC), TG, low-density lipoprotein cholesterol (LDL), and HDL, and then the fixed-effects model was applied to pool the data. The results showed that the HP diet could significantly increase the reduction of TG (SMD = -0.20, 95% CI = -0.35 to -0.05, P = .01, Fig. 5B) but not significantly affect the TC (SMD = -0.10, 95% CI = -0.23 to 0.03, P = .13, Fig. 5A), LDL (SMD = -0.06, 95% CI = -0.16 to 0.10, P = .63, Fig. 5D) levels compared with the LP diet.

3.5. Effect of HP diet on blood pressure

Figure 6 shows the pooled estimate for the effect of HP diet on blood pressure. No significant heterogeneity suggested the use of

1202047	HP			LP	-		Std. Mean Difference	Std. Mean Difference
Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV. Fixed, 95% Cl
-5.3	25	19	-5.4	25	19	3.6%	0.00 [-0.63, 0.64]	
-9	8.4	11	-7.4	7.6	14	14.4%	-0.20 [-0.52, 0.12]	
-9.7	01.4	21	-0.0	34.8	24	4.3%	-0.06 [-0.65, 0.52]	
-2	29.00	30	-2.9	29.69	21	4.7%	0.03 [-0.53, 0.59]	
-9	15.0	144	-9.0	19.7	150	2.8%	0.03 [-0.69, 0.75]	
-3.9	23.20	144	-0	24.06	150	28.1%	0.09 [-0.14, 0.32]	
-3.1	21.88	21	-1	28	22	4.1%	-0.08 [-0.68, 0.52]	
-3.55	3.8	31	-0.92	2.4	31	6.5%	-0.82 [-1.29, -0.34]	
-2	17.23	8	-1	17.99	8	1.5%	-0.05 [-1.03, 0.93]	
-8.9	6.2	23	-7.7	6.1	22	4.3%	-0.19 [-0.78, 0.39]	
-4	23.3	1/	-3	23.3	17	3.2%	-0.04 [-0.71, 0.63]	
-5.5	123.3	26	-4.8	131	28	5.2%	-0.01 [-0.54, 0.53]	
-2.5	3.9	6	-2.2	2.2	6	1.1%	-0.09 [-1.22, 1.04]	
-12	6.3	46	-11.5	5.5	47	8.9%	-0.08 [-0.49, 0.32]	
-10.1	28.85	21	-7.9	26.49	29	4.7%	-0.08 [-0.64, 0.48]	
-9	4.8	12	-8.6	4.6	16	2.6%	-0.08 [-0.83, 0.67]	
		520			539	100.0%	-0.09 [-0.21, 0.04]	•
, df = 15	(P = 0.	65); l ² :	= 0%					
.38 (P =	0.17)							-1 -0.5 0 0.5 1 Favours [HP] Favours [LP]
	HP			LP			Std. Mean Difference	Std. Mean Difference
Mear	n SD	Tota	Mean	SD	Total	Weight	IV. Fixed, 95% CI	IV, Fixed, 95% Cl
-3.3	2 7.25	77	-2.7	6.36	74	31.0%	-0.07 [-0.39, 0.25]	
-0.1	8 7.66	30	-1	7.93	31	12.5%	0.03 [-0.48, 0.53]	
-1	1 5.94	21	-0.3	7.49	22	8.8%	-0.12[-0.71, 0.48]	
-3	1 1.87	23	-2 57	1.88	22	9.1%	-0.28 [-0.87 0.31]	
-0.	5.8	17	-2.01	5.8	17	7 0%	-0.17 [-0.84 0.51]	
	2 2 2 2	11	3.5	2 17	37	15 0%	0.13[0.31,0.58]	
-3.		41	-3.0	2.11	37	10.0%	0.13 [-0.31, 0.36]	
-3.	0.00	21	-2.1	0.04	29	10.0%	-0.14 [-0.70, 0.43]	
-0.4	2 1.7	12	-3.1	1.0	10	5.0%	-0.06 [-0.61, 0.69]	
		242			248	100.0%	-0.06 [-0.24, 0.12]	• •
, df = 7	(P = 0.9)	98); l ² =	0%				2	-2 -1 0 1 2
0.69 (P	= 0.49)							Favours [HP] Favours [LP]
	100			220			2010/01/2020/01/2020	
	HP	Tetel		LP	Tetel	141-1-1-4	Std. Mean Difference	Std. Mean Difference
Mean	SD	Total	Mean	SD	Total	weight	IV, Fixed, 95% CI	IV. Fixed. 95% CI
-4.4	16.96	19	-3.9	15.43	19	6.7%	-0.03 [-0.67, 0.61]	1
-3	16.59	144	-3.8	17.56	150	51.9%	0.05 [-0.18, 0.28]	
-2.5	15.7	19	-0.3	19.92	20	6.9%	-0.12 [-0.75, 0.51]	
-7.8	4.8	23	-5.9	5.1	22	7.8%	-0.38 [-0.97, 0.21]	
-3	17.5	17	-2	17.5	17	6.0%	-0.06 [-0.73, 0.62]	
-2.6	4.4	6	-2.2	1.7	6	2.1%	-0.11 [-1.24, 1.02]	
-7.9	6.21	41	-8.6	5.89	37	13.7%	0.11 [-0.33, 0.56]	
-7.1	4	12	-6.5	3.7	16	4.8%	-0.15 [-0.90, 0.60]	
		281			287	100.0%	-0.01 [-0.18, 0.15]	+
f = 7 (P)	= 0.94	; 2 = 00	%					
15 (P = ().88)							-2 -1 0 1 2
								Favours [HP] Favours [LP]
	HP			LP			Std. Mean Difference	Std. Mean Difference
Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV. Fixed, 95% Cl
-0.9	15.6	19	-1.6	17.26	19	14.0%	0.04 [-0.59, 0.68]	
-3	4.49	19	-0.2	5.7	20	13.8%	-0.53 [-1.17, 0.11]	
-1.1	2.4	23	-1.7	2.3	22	16.5%	0.25 [-0.34, 0.84]	
0	17.48	17	-1	17.48	17	12.5%	0.06 [-0.62, 0.73]	
0.4	20.6	6	0.1	21.7	6	4.4%	0.01 [-1.12, 1.14]	
	1.63	41	-1.6	1.68	37	28.6%	-0.12 [-0.56, 0.33]	
-1.8			22	1.9	16	10.1%	0.17 [-0.58, 0.92]	
-1.8	1.5	12	-2.2					
-1.8 -1.9	1.5	12	-2.2		137	100.0%	-0.04 [-0.27 0.20]	•
-1.8 -1.9	1.5	12 137 : 1 ² = 0 ⁴	-2.2		137	100.0%	-0.04 [-0.27, 0.20]	<u>_</u> ,
-1.8 -1.9	1.5 = 0.71)	12 137 ; l ² = 0 ⁴	-2.2		137	100.0%	-0.04 [-0.27, 0.20]	-2 -1 0 1 2
	Mean -5.3 -9 -9.7 -2 -9 -3.9 -3.1 -3.55 -2 -89 -3.1 -3.55 -2 -89 -4 -5.5 -2.5 -12 -10.1 -9 .df = 15 38 (P = Mean -3.3 -3.3 -3.3 -3.3 -3.3 -3.4 -3.3 -3.3 -3.4 -3.3 -3.4 -3.5 -7.8 -7.9 -7.1 ff = 7 (P Mean -0.9 -3 -7.8 -7.9 -7.1 ff = 7 (P Mean -0.9 -3	HP HP Mean SD -5.3 25 -9 8.4 -9.7 61.4 -2 29.06 -9 15.8 -3.9 23.26 -3.1 21.88 -3.55 3.8 -2 17.23 -8.9 6.2 -4 23.3 -5.5 123.3 -5.5 123.3 -2.5 3.9 -10.1 28.85 -9 4.8 df = 15 (P = 0.17) HP Mean SD -3.2 7.25 -0.8 7.66 -1.1 5.94 -3.1 1.87 -3.2 7.25 -3.8 -3.2 -3.2 7.25 -3.8 -3.2 -3.1 1.87 -3.2 7.25 -3.3 16.59 -2.5 15.7 -7.7	HP Mean SD Total -5.3 25 19 -9 8.4 77 -9.7 61.4 21 -2 29.06 30 -9 15.8 12 -3.9 23.26 144 -3.1 21.88 21 -3.55 3.8 37 -2 17.23 8 -8.9 6.2 23 -4 23.3 17 -5.5 123.3 26 -2.5 3.9 6 -10.1 28.85 21 -9 4.8 12 -9 4.8 12 -9 4.8 12 520 0 df = 15 (P = 0.65); P = 3 38 (P = 0.17) HP Mean SD Total -3.2 7.25 77 -0.8 7.66 30 -1.1 5.94 21 -3.1 1.87 23 -2 5.8 17 -3.2 2.28 <	HP Total Mean 5.3 25 19 -5.4 -9 8.4 77 -7.4 -9.7 61.4 21 -6.6 -2 29.06 30 -2.9 -9 15.8 12 -9.6 -3.9 23.26 144 -6 -3.1 21.88 21 -1 -3.55 3.8 37 -0.92 -2 17.23 8 -1 -8.9 6.2 23 -7.7 -4 23.3 17 -3 -5.5 123.3 26 -4.8 -2.5 3.9 6 -2.2 -12 6.3 46 -11.5 -10.1 28.85 21 -7.9 -9 4.8 12 -8.6 50 Total Mean -3.2 -3.1 1.87 23 -2.57 -3.2 7.2.7 -0.3	HP LP Mean SD Total Mean SD -5.3 25 19 -5.4 25 -9 8.4 77 -7.4 7.6 -9.7 61.4 21 -6.6 34.8 -2 29.06 30 -2.9 29.06 -9 15.8 12 -9.6 19.7 -3.9 23.26 144 -6 24.06 -3.1 21.88 21 -1 28 -3.55 3.8 37 -0.92 2.4 -2 17.23 8 -1 7.99 -8.9 6.2 23 -7.7 6.1 -4 23.3 17 -3 23.3 -5.5 123.3 26 -4.8 131 -2.5 3.9 6 -2.2 2.2 -12 6.3 46 -11.5 5.5 -10.1 28.85 21 -7.9 <t< td=""><td>HP LP Mean SD Total Mean SD Total -5.3 25 19 -5.4 25 19 -9 8.4 77 -7.4 7.6 74 -9.7 61.4 21 -6.6 34.8 24 -2 29.06 30 -2.9 29.69 21 -9 15.8 12 -9.6 19.7 19 -3.9 23.2 26 144 -6 24.06 150 -3.1 21.88 21 -1 28 22 -3.55 3.8 37 -0.92 2.4 37 -2 17.23 8 -1 17.99 8 -8.9 6.2 23 -7.7 6.1 22 2.2 6 -12 6.3 46 -11.5 5.5 47 -10.1 28.85 21 -7.9 26.49 29 -3.1 1.6 16</td><td>HP LP Mean SD Total Mean SD Total Weight -5.3 25 19 -5.4 25 19 3.6% -9 8.4 77 -7.4 7.6 74 14.4% -9.7 61.4 21 -6.6 34.8 24 4.3% -2 29.06 30 -2.9 29.69 21 4.7% -9 15.8 12 -9 19.7 19 2.8% -3.1 21.88 21 -1 28 22 4.1% -3.55 3.8 37 -0.92 2.4 37 6.5% -2 17.23 8 -1 17.99 8 1.5% -5.5 123.3 26 -4.8 131 28 5.2% -2.5 3.9 6 -2.2 2.2 6 1.1% -10 2.835 21 -7.7 2.649 29</td><td>$\begin{array}{c c c c c c c c c c c c c c c c c c c$</td></t<>	HP LP Mean SD Total Mean SD Total -5.3 25 19 -5.4 25 19 -9 8.4 77 -7.4 7.6 74 -9.7 61.4 21 -6.6 34.8 24 -2 29.06 30 -2.9 29.69 21 -9 15.8 12 -9.6 19.7 19 -3.9 23.2 26 144 -6 24.06 150 -3.1 21.88 21 -1 28 22 -3.55 3.8 37 -0.92 2.4 37 -2 17.23 8 -1 17.99 8 -8.9 6.2 23 -7.7 6.1 22 2.2 6 -12 6.3 46 -11.5 5.5 47 -10.1 28.85 21 -7.9 26.49 29 -3.1 1.6 16	HP LP Mean SD Total Mean SD Total Weight -5.3 25 19 -5.4 25 19 3.6% -9 8.4 77 -7.4 7.6 74 14.4% -9.7 61.4 21 -6.6 34.8 24 4.3% -2 29.06 30 -2.9 29.69 21 4.7% -9 15.8 12 -9 19.7 19 2.8% -3.1 21.88 21 -1 28 22 4.1% -3.55 3.8 37 -0.92 2.4 37 6.5% -2 17.23 8 -1 17.99 8 1.5% -5.5 123.3 26 -4.8 131 28 5.2% -2.5 3.9 6 -2.2 2.2 6 1.1% -10 2.835 21 -7.7 2.649 29	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

fixed-effects model in the meta-analysis ($I^2 < 50\%$, P > .10). The pooled estimate indicated that the change of diastolic (SMD = -0.08, 95% CI = -0.22 to 0.06, P = .27, Fig. 6A) and systolic (SMD = -0.08, 95% CI = -0.21 to -0.05, P = .25, Fig. 6B) blood pressures was not significantly affected by HP diet in HP group compared with that in LP group.

3.6. Subgroup analysis

In total, 6 studies compared the HP low carbohydrate (HPLC) and LP high carbohydrate (LPHC) diets (which showed similar ratio of energy from fat) and 9 studies compared HPLC high fat (HPLCHF) and LPHC low fat (LPHCLF) diets. The results of subgroup analyses were shown in Table 2.

		HP			LP			Std. Mean Difference	Std. Mean Difference
Study or Subaroup	Mean	SD	Tota	Mean	SD	Tota	Weight	IV. Fixed, 95% CI	IV. Fixed. 95% CI
Brinkworth G D 2004	-0.6	2.79	19	-0.6	1.83	19	4.5%	0.00 [-0.64, 0.64]	
Cheryl L Rock 2014	-16	119.79	66	2	71.83	67	15.7%	-0.20 [-0.54, 0.14]	
Khoo J 2011	-1.26	1.06	12	-0.24	0.87	19	3.0%	-1.05 [-1.82, -0.27]	
Krebs J D 2012	0.2	3.55	144	0.4	3.37	150	34.9%	-0.06 [-0.29, 0.17]	-
Luger M 2013	-41.7	74.93	21	-2.1	79	22	4.9%	-0.50 [-1.11. 0.10]	
Gannon 2004	-2.7	2.29	8	-1.2	24	8	1.8%	-0.60 [-1.61, 0.40]	
Nervlee W 2016	-2.1	2.9	23	-25	2.8	22	5.3%	0.14 [-0.45, 0.72]	
Papakonstantinou E 2010	-0.8	1.11	17	-	1.73	17	4.0%	0 13 [-0 54 0 81]	
Parker B 2002	-0.74	2.65	26	-0.43	3 2 0 1	28	6.4%	-0 13 [-0 66 0 40]	
Sargrad K R 2005	0	4.7	6	-1.6	3.3	e	1.4%	0.36 [-0.78, 1.51]	
Tay J 2014	-0.7	1.96	41	-1.5	1.86	37	9.0%	0.41 [-0.04, 0.86]	
Westman E C 2008	-19.9	88.4	21	-16	5 79.4	29	5.8%	-0.05 [-0.61, 0.52]	
Wycherley T P 2010	-2.5	2.7	12	-2.2	2 2.2	16	3.2%	-0.12 [-0.87, 0.63]	
Total (95% CI)			416			440	100.0%	-0.08 [-0.21, 0.06]	•
Heterogeneity: $Chi^2 = 15.7$	1 df = 12	P = 0	20). 12 =	24%		110	100.070		
Test for everall effect: 7 =	1, UI - 12	0.25)	20), 1	24 /0					-2 -1 0 1 2
Test for overall effect. 2 -	1.15 (F -	0.23)							Favours [HP] Favours [LP]
A									
		HP			LP		S	td. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Fixed, 95% CI	IV. Fixed. 95% Cl
Brinkworth G D 2004	0.2	10.77	19	1.9	15.6	19	10.4%	-0.12 [-0.76, 0.51]	
Khoo J 2011	6.96	4.51	12	-4.13	32.05	19	7.9%	0.43 [-0.31, 1.16]	
Nerylee W 2016	-9.6	10.1	23	-7.9	10.3	22	12.3%	-0.16 [-0.75, 0.42]	
Papakonstantinou E 2010	-1	11.62	17	0	5.81	17	9.3%	-0.11 [-0.78, 0.57]	
Parker B 2002	-3	50.5	26	-17	63.5	28	14.7%	0.24 [-0.30, 0.78]	
Sargrad K R 2005	-11	72.8	6	-19	66.8	6	3.3%	0.11 [-1.03, 1.24]	
Tay J 2014	-5.8	5.88	41	-4.9	5.9	37	21.3%	-0.15 [-0.60, 0.29]	
Westman E C 2008	-6	11.57	21	-2.2	9.48	29	13.2%	-0.36 [-0.93, 0.21]	
Wycherley T P 2010	-3.5	2.8	12	-4.1	4.2	16	7.5%	0.16 [-0.59, 0.91]	
Total (95% CI)			177			193	100.0%	-0.04 [-0.24, 0.17]	•
Heterogeneity: Chi ² = 4.67.	df = 8 (P	P = 0.79	: 1 ² = 09	10				CENTRY STREET, AND AND	
Test for overall effect: $Z = C$).37 (P =	0.71)							-2 -1 0 1 2
		54 Y 182							Favours [HP] Favours [LP]
	14							I Marco Difference	Old Mars Difference
Chudu an Culuman	Mann	CD T	atal N	L	P T	4-1 10	Ste	a. Wean Difference	Std. Mean Difference
Study or Subgroup	wean	SU I	otal IV	lean	50 10	Dial V	veight	IV. Fixed, 95% CI	IV. Fixed, 95% CI
Brinkworth G D 2004	-0.5	1.26	19	-0.5 1	.92	19	4.1%	0.00 [-0.64, 0.64]	
Cheryl L. Rock 2014	-0.7	1.62	66	-0.3 1	.88	67	14.3%	-0.23 [-0.57, 0.11]	
Guldbrand H 2012	0	4.39	30	0.2 4	1.23	31	6.6%	-0.05 [-0.55, 0.46]	
Krebs J D 2012	0.1	1.77	144	0.1 1	1.75	150	31.8%	0.00 [-0.23, 0.23]	
Luger M 2013	-0.3	1.99	21	-0.2 1	1.36	21	4.5%	-0.06 [-0.66, 0.55]	
M. E. Daly 2006	-0.55	1.03	37 -	0.23 (0.79	37	7.9%	-0.34 [-0.80, 0.11]	
Gannon 2003	-0.3	0.35	12	-0.8	0.7	12	2.3%	0.87 [0.03, 1.72]	
Nerylee W 2016	-1.34	1.01	23	-1.5 1	1.03	22	4.9%	0.15 [-0.43, 0.74]	
Parker B 2002	-0.54	5.81	26 -	0.51 5	5.13	28	5.8%	-0.01 [-0.54, 0.53]	The second s
Sargrad K R 2005	-1	2.49	6	-1.3 1	1.57	6	1.3%	0.13 [-1.00, 1.27]	
Tay J 2014	-1	0.82	41	-1 (0.76	37	8.4%	0.00 [-0.44, 0.44]	
Westman E C 2008	-1.5	2.34	21	-0.5	2.83	29	5.2%	-0.37 [-0.94, 0.19]	
Wycherley T P 2010	-1.8	1.6	12	-1.1	0.6	16	2.8%	-0.60 [-1.37, 0.17]	
Total (95% CI)		10111	458			75 1	00.0%	-0.07 [-0.20.0.06]	•
Hotorogonoitu Chi2 - 44	14 df -	10 /0 -	0.50	12 - 00/		10 1	00.070		
Test for overall effect: Z	= 1.10 (F	P = 0.27)	r = 0%	0				-2 -1 0 1 2 Favours (HP) Favours (LP)
C									Favours [HP] Favours [LP]
C									

Figure 4. Meta-analysis for effect of high protein diet on fasting glucose (A), fasting insulin (B), and HbA1c (C).

In subgroup analyses, the significant effect of HP diet on TG disappeared in subgroup analysis of HPLC versus LPHC diets (SMD = -0.13, 95% CI = -0.52 to 0.25, P = .51), which were inconsistent with the overall analyses. Meanwhile, the inconsistent results with the overall meta-analyses were also found in the subgroup analyses for weight. These results showed significant effect of HPLCHF diet on weight loss

compared with LPHCLF diet (SMD = -0.21, 95% CI = -0.38 to -0.04, P = .02).

3.7. Sensitivity analysis and publication bias

Sensitivity analysis showed that after omitting the data of the studies of Krebs 2012 (SMD = -0.15, 95% CI = -0.30 to -0.01,

Stock as Substratus Num Total Num			ЦВ			IP			Std Moon Difforence	Std Moon Difference
Breisendi G 2 2004 0.07 128 09 0.41 1.35 19 0 425 0.20 10.40 0.4128 0.53 Guddman (1 2012 0.41 134 0.30 0.43 133 0 0.75 0.05 0.128 0.53 Guddman (1 2012 0.41 134 0.30 0.43 133 0 0.75 0.05 0.128 0.53 Guddman (1 2012 0.41 134 0.30 0.43 133 0 0.75 0.05 0.128 0.53 User M 2013 0.42 157 21 0.41 107 120 445 0.425 0.53 Hand P 2012 2010 0.45 1157 0 0.45 1157 0 425 0.400 0.59 Hand P 2012 0.45 1157 0 0.45 1157 0 425 0.400 0.45 Hand P 2012 0.45 0.45 1157 0 0.45 1157 0 425 0.400 0.45 Hand P 2012 0.45 0.45 1157 0 0.45 1157 0 425 0.400 0.45 Hand P 2012 0.45 0.45 1157 0 0.45 1157 0 425 0.400 0.45 Hand P 2012 0.45 0.45 1157 0 425 0.400 0.45 Hand P 2012 0.45 0.45 1157 0 425 0.400 0.45 Hand P 2012 0.45 0.45 1157 0 425 0.45 0.45 10.45 0.05 Hand P 2012 0.45 0.45 1157 0 435 0.55 0.45 0.05 11.55 0.05 0.55 Hand P 2012 0.45 0.45 0.45 0.25 0.55 0.400 0.15 0.55 0.55 Hand P 2012 0.45 0.45 0.45 0.55 0.55 0.55 0.55 0.55	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Fixed, 95% CI	IV. Fixed, 95% CI
Clang L. Bodz 2014 double net X 2016 double net X	Brinkworth G D 2004	-0.37	1.26	19	-0.1	1.35	19	4.2%	-0.20 [-0.84, 0.44]	
Outbinent 2012 -0.1 1.33 30 -0.75 -0.05	Cheryl L. Rock 2014	11	49.08	66	13	49.91	67	14.7%	-0.04 [-0.38, 0.30]	-
$ \begin{array}{c} \text{Nool 2011} & 0.23 & 1.95 & 12 & 169 & 1.65 & 19 & 2.26 & \\ \text{Norther J 2010} & 0.24 & 1.24 & 4.07 & 1.37 & 19 & 2.25 & \\ \text{Norther J 2010} & 0.24 & 0.44 & 0.07 & 1.37 & 19 & 0.25 & \\ \text{Norther J 2010} & 0.4 & 0.48 & 23 & 0.00 & 0.47 & 22 & 456 & 0.071, 137, 0.18 \\ \text{Pagatomistrices II2010} & 0.7 & 1.32 & 17 & 0.6 & 0.95 & 17 & 3.86 & 0.061, 1.65, 0.09 \\ \text{Pagatomistrices II2010} & 0.4 & 1.48 & 0.22 & 1.56 & 1.28 & 0.001, 0.44 & 0.44 & 0.47 & 1.37 & 0.18 \\ \text{Pagatomistrices II2010} & 0.4 & 0.48 & 22 & 4.56 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.08 & 1.28 & 0.012, 1.46 & 0.012, 1.013 & 0.014 & 0.014, 0.028 & 0.012, 1.46 & 0.014$	Guldbrand H 2012	-0.1	1.34	30	-0.3	1.33	31	6.7%	0.15 [-0.35, 0.65]	
$ \begin{array}{c} \text{Cress J 2012} & 423 & 128 & 144 & 4.17 & 1.57 & 150 & 22.56 & 0.05 (128.0, 164 \\ \hline \begin{tabular}{ll} & 424 & 157 & 124 & 0.11 & 105 & 226 & 566 & 1056 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 127 & 201 & 0.05 & 173 & 366 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 127 & 0.0 & 0.05 & 173 & 366 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 127 & 0.0 & 0.05 & 173 & 366 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 127 & 0.0 & 0.05 & 123 & 0.05 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 127 & 0.0 & 0.05 & 123 & 0.05 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 127 & 0.0 & 0.05 & 123 & 0.05 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 126 & 0.0 & 0.05 & 123 & 0.05 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 100 & 0.05 & 0.05 & 123 & 0.05 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 100 & 118 & 0.05 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 100 & 118 & 0.05 & 0.05 (128.0, 106 \\ \hline \begin{tabular}{ll} & 426 & 100 & 118 & 0.05 & 0.05 (128.0, 0.05 \\ \hline \begin{tabular}{ll} & 426 & 0.05 & 128 & 0.05 & 0.05 (128.0, 0.05 \\ \hline \begin{tabular}{ll} & 426 & 0.05 & 128 & 0.05 & 0.05 & 0.05 (128.0, 0.05 \\ \hline \begin{tabular}{ll} & 426 & 0.05 & 128 & 0.05 & 0.05 & 0.05 & 0.05 \\ \hline \begin{tabular}{ll} & 426 & 0.05 & 128 & 0.05 & 0.05 & 0.05 & 0.05 \\ \hline \begin{tabular}{ll} & 426 & 0.05 &$	Khoo J 2011	-0.23	1.93	12	1.69	1.65	19	2.8%	-1.06 [-1.84, -0.29]	
Lager M 2013, 42 2 157 21 4.0 107 20 45% 407 (489.0.54) Peakent B 2020 40 17 132 17 40 40 51 7 13 25 4 50 102 (140.0.58) Peakent B 2020 40 11 57 6 408 1 57 6 102 12 40 108 25 55% 40 15 (200 144.0.58) Peakent B 2020 40 11 57 6 408 1 57 6 102 12 40 108 25 55% 40 15 (201 44.0.58) Provide (17 201 40 10 66 10 204 40 40 40 10 20 12 40 10 20 10 100 144.0.104 14 14 10 100 144 14 14 14 14 14 14 14 14 14 14 14 14	Krebs J D 2012	-0.24	1.29	144	-0.17	1.37	150	32.5%	-0.05 [-0.28, 0.18]	
Nerview 7.01%	Luger M 2013	-0.2	1.57	21	-0.1	1.07	20	4.5%	-0.07 [-0.69, 0.54]	
Parameter Journel and Journel 2010 Off Parameter Journel 2010	Nervice W 2016	-0.4	0.48	23	-0.03	0.47	22	4.6%	-0.77 [-1.37, -0.16]	
Particle 2020 1 2000 303 1:17 25 0.00 1:18 25 0.59% 0.21 [073,033] Try J 2014 0.01 0.65 41 0.01 0.02 37 8.6% 0.00 [0.44,0.44] Wycheniae [12:00 4.4 48.2 1:4 8.6 0:22 28 5.6% 0.00 [0.44,0.44] Wycheniae [12:00 4.4 48.2 1:4 8.6 0:22 28 5.6% 0.00 [0.44,0.44] Wycheniae [12:00 4.4 48.2 1:4 8.6 0:22 28 5.6% 0.00 [0.44,0.44] Wycheniae [12:00 4.4 48.2 1:4 8.6 0:22 28 5.6% 0.00 [0.44,0.44] Wycheniae [12:01 4.4 48.2 1:4 5.6 1.9 - 0.46]; F= 0% Test for overall efficit. 2 = 1.5 (F = 0.46); F= 0.5 (F = 0.46); F	Nuttall F Q 2012	-20	48	17	-22	45.0	17	1.8%	-0.08 [-1.06, 0.90]	
Seguad SP 2005 -0.81 1.57 6 0.38 1.57 6 0.38 1.57 6 0.38 1.57 6 0.38 1.57 6 0.38 0.00 [-4.4, 0.41, 1.3] Westman E 2 000 -4.4 4.46.02 21 -3.6 6.0.22 23 6.6% 0.02 [-4.3, 0.59] Total (SS C) -4.44 4.46.02 21 -5.8 6.32 29 5.4% 0.02 [-4.3, 0.59] Yethory PT2010 -0.40 [-1.03) -4.46 440 100.0% -4.16 [-4.23, 0.03] Total (SS C) -4.46 -4.00 [-4.23, 0.16] -4.16 [-4.23, 0.03] -7.25 [-2.00, 1/2] -7.25 [-2.0, 0.03] A MP LP Std. Mean Difference Std. Mean Difference N. Enced, 95% CI Fibrowerh (D.2011) -3.63 10.7% 10.55% -0.28 [-0.40, 0.36] -7.25 [-0.40, 0.36] Microwerh (D.2011) -3.71 [2.86 0.61 2.5 5% -0.28 [-0.40, 0.36] -7.25 [-2.00, 0.7] Liper M 2013 -0.65 1.5 7.71 [0.5 0.81] 2.5 5% -0.28 [-0.40, 0.36] <td>Papakonstantinou E 2010</td> <td>-0.7</td> <td>1.52</td> <td>26</td> <td>-0.01</td> <td>1.95</td> <td>28</td> <td>5.0%</td> <td>-0.06 [-0.76, 0.39]</td> <td></td>	Papakonstantinou E 2010	-0.7	1.52	26	-0.01	1.95	28	5.0%	-0.06 [-0.76, 0.39]	
	Sargrad K R 2005	-0.33	1.57	6	-0.81	1.57	6	1.3%	0.00 [-1 13 1 13]	
Weetman E C 2008 -4.4 46.02 21 6.8 0.22 2.9 5.4% 0.02 0.24% 0.06% Total (85% Cl) -4.4 6.8 12 0.7 0.6 16 3.0% 0.14 [0.61, 0.60] Total (85% Cl) -4.6 -4.69 100.0% 4.10 [4.23, 0.03]	Tay .1 2014	-0.1	0.65	41	-0.1	0.62	37	8.6%	0.00 [-0.44, 0.44]	
$ \begin{aligned} $	Westman E C 2008	-4.4	48.02	21	-5.8	63.22	29	5.4%	0.02 [-0.54, 0.59]	
Total (8%): Cl) 446 449 100.0% 0.10 (-0.23, 0.03) A 449 100.0% 0.10 (-0.23, 0.03)	Wycherley T P 2010	-0.6	0.8	12	-0.7	0.6	16	3.0%	0.14 [-0.61, 0.89]	
The formal effect Z = 1.5 (P = 0.5) Test for overall effect Z = 1.5 (P = 0.5) A A A Me Bit Mean Difference Bit Mean Difference	Total (95% CI)			446			460	100 0%	0 10 [-0 23 0 03]	
Test for overall effect 2 = 1.53 (P = 0.1 1.50) 2 -1 0 1 2	Heterogeneity: Chi ² = 12.81	df = 13	(P = 0	46) 12 =	0%		403	100.070	-0.10[-0.25, 0.05]	
A Surfa or Subgroup Mean SD Total Mean SD Total Weight V. Fixed, 95% C V. Fix	Test for overall effect: Z = 1	.53 (P =	0.13)	10), 1	070					-2 -1 0 1 2 Favours [HP] Favours [LP]
HP LP Std. Mean Difference Std. Mean Difference Std. Mean Difference Std. Mean Difference N. Fixed, 28% CI Study.cor. Subgroup Mean 50 Total Weight M. Fixed, 28% CI N. Fixed, 28% CI Study.cor. Subgroup Mean 50 Total Weight M. Fixed, 28% CI N. Fixed, 28% CI Study.cor. Subgroup Mean 50 Total Weight M. Fixed, 28% CI N. Fixed, 28% CI Study.cor. Subgroup Mean 50 Total Mean 50 Total Study.cor. Subgroup Mean Micro.2 0.01 0.03 0.04 12 0.05 0.04 12 6.05 0.04 22 0.05 0.04 12 0.06 0.04 12 0.06 0.05 0.05 1.03 1.03 1.03 0.02 0.03 0.04 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03 1.03	Δ									the second second second second second
Study as Subgroup Mann SD Total Weight W. Fined State Study as Subgroup Manne The SD Total Weight W. Fined State Study as Subgroup Manne SD Total Weight Chery L. Rock 2014 -37 115 116 316 367 15 423 168 0.411 Chery L. Rock 2014 -33 117 119 316 857 10 435 0.226 108 0.011 10 118 118 117 119 316 857 0.026 0.026 0.031 117 119 316 857 0.026 0.036 0.031 117 119 316 857 0.026 0.036 0.037 10 119 118 119 119 118 119 119 118 119 119 118 119 119 118 119 119 119 119 119 119 119 119 119 119 119 119 119 119 119 119	<u>^</u>		UD			1.0			Std Mass Difference	Ctd Mean Difference
Benksoni C D 2004 -0.42 118 19 0.16 0.87 19 5.5% -0.23 0.03 0.03 0.03 Guddmard H2012 -0.2 1.65 30 -0.1 1.19 31 8.9% -0.07 (-0.57, 0.43) Guddmard H2012 -0.2 1.65 30 -0.1 1.19 31 8.9% -0.26 (-0.80, 0.47) Luger M2013 -0.60 -0.60 -0.47 1.28 2.18 37 1.07% -0.28 (-0.80, 1.07) Neryler W2016 -0.4 0.66 2.23 0.60 0.41 2.28 0.60 0.64 2.27 0.50 0.50 0.16 0.50 0.51 1.07% 0.28 (-0.80, 1.06%, 0.41 0.16	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV Fixed 95% Cl	IV Fixed 95% Cl
Charyd L. Roak 2014 37 117.17 86 -16 122.33 67 194.45 -017 [0.31, 0.17] dedwared H2012 -0.2 165 30 -0.1 119 31 884 07 10.57, 0.43 Khoo J 2011 -0.63 0.34 12 -0.55 0.27 19 4.3% -0.26 [0.96, 0.47] M.E. Day 2004 -0.67 1.39 37 -0.25 1.58 37 10.7% -0.26 [0.9, 0.35] M.E. Day 2004 -0.67 1.39 37 -0.25 1.58 37 10.7% -0.26 [0.38, 0.7] Parker B 2002 -0.67 1.39 37 -0.25 1.58 37 10.7% -0.26 [0.38, 0.7] Parker B 2002 -0.41 7.21 2 8 -48 75.89 8 2.2% 0.09 [0.58, 107] Parker B 2002 -0.34 0.81 22 -0.63 1.48 28 75% -0.26 [0.58, 0.41] Parker B 2002 -0.34 0.81 22 -0.5 1.76 2.5 (0.50, 0.52] Parker B 2002 -0.54 0.41 1 22 -0.6 1.11 16 4.5% -0.02 [1.53, 0.44] Parker B 2002 -0.54 0.41 1 22 -0.6 1.11 16 4.5% -0.02 [1.05, 0.42] Wychenity IP 2010 -0.4 1 1 12 -0.6 1.11 16 4.5% -0.02 [1.05, 0.42] Parker B 2002 -0.10 105 19 0.27 70% -0.32 [1.06, 0.24] Wychenity IP 2010 -0.4 1 1 12 -0.6 1.11 16 4.5% -0.02 [1.05, 0.43] Parker B 2002 -0.11 155 91 -0.03; 17 144 197 147% -0.04 [1.03, 0.20] Cherly IL, Rock 2014 -0.44 4.462 2 66 4.41 77 147% -0.04 [1.03, 0.20] Cherly IL, Rock 2014 -0.48 4.1 12 -0.3 0.27 19 3.0% -0.78 (-1.54, -0.03] Parker B 2002 -0.11 105 19 0.22 1.11 19 150 2.25% 0.03 [0.00, 0.23] Cherly IL, Rock 2014 -0.44 4.462 2 66 4.41 1 07 147% -0.04 [1.03, 0.20] Cherly IL, Rock 2014 -0.48 4.81 12 -1.51 43.78 20 4.5% 0.02 [0.05, 0.50] Wychenky IP 2010 -0.54 0.34 12 -0.3 0.27 19 3.0% -0.78 (-1.54, -0.03] Cherly IL, Rock 2014 -0.48 4.81 12 -1.51 43.78 20 4.5% 0.02 [0.05, 0.50] Cherly IL, Rock 2014 -0.44 0.48 23 -0.00 4.72 24 4.7% -0.61 [-1.03, 0.20] Cherly IL, Rock 2014 -0.44 0.48 22 -0.3 0.27 19 3.0% -0.78 (-1.54, -0.03] Cherly IL, Rock 2014 -0.44 0.48 22 -0.3 0.27 19 3.0% 0.18 [-0.57, 0.39] Cherly IL, Rock 30.45 (0.44 0.47 22 4.7% -0.61 [-1.70, 0.08] Parker B 2002 -0.19 0.43 1.44 0.05 1.77 0.47% -0.04 [-0.30, 0.35] Cherly IL, Rock 30.45 (0.43 1.44 0.05 1.77% -0.016 [-0.60, 0.45] Parker B 2002 -0.19 0.43 1.44 0.05 1.77 0.78 (-0.16 [-0.60, 0.45] Parker B 2002 -0.19 0.43 1.44 0.02 2.26 5.45% 0.00 [-0.70, 0.83] Parker	Brinkworth C.D. 2004	0.42	1 19	10	0.18	0.97	10	5 5%	0 23 [0 86 0 41]	
Conditioner H2012 -0.2 1.16 30 0.1 1.19 31 8.9% -0.07 [0.57, 0.43] Loger M2013 -0.68 131.1 19 -1.3 128.56 21 5.9% -0.28 [0.69, 0.47] Nerylee W2016 -0.4 0.66 0.41 22 6.6% 0.21 [0.38, 0.79] Nerylee W2016 -0.4 0.66 1.9 7.9% -0.08 [0.68, 1.07] Papakonstantinou E 2010 -0.5 0.82 1.7 0.4 0.06 [0.87, 1.15, 0.24] Starter S 2020 -0.34 0.49 41 0.01 0.62 37 100.26, 0.41 Starter S 2020 -0.34 0.49 41 0.01 0.62 37 100.26 1.16 16 4.9% 0.31 [0.857, 0.39] Vectrier T 2 0.64 1.1 16 0.49 1.16 0.49 1.06 0.21 [0.457, 0.43] Tel (SWS) C1 -33 37 357 100.28 77 0.32 [0.80, 0.42] -0.32 [0.48, 0.24] -0.32 [0.48, 0.24]	Cheryl L Rock 2014	-0.42	117 17	66	-0.10	132 30	67	10 4%	-0.23 [-0.80, 0.41]	
Nono. 2011 Chemological Model Olds Olds <tholds< th=""> Ol</tholds<>	Guldbrand H2012	-0.2	1.65	30	-10	1 10	31	8 9%	-0.07 [-0.57, 0.43]	
Lunger M 2013 HE Day 2004 HE	Khoo 12011	-0.63	0.34	12	-0.55	0.27	10	4 3%	-0.26 [-0.99, 0.47]	
ME C Day 2004 -0.67 138 37 -0.25 158 37 10.7% -0.28 (-0.74, 0.18) ME C Day 2012 -14 72.12 8 -48 75.98 8 2.3% 0.09 (-0.8, 1.07) Parker B 2002 -0.34 0.81 126 -0.23 1.13 12 75.0% -0.12 (-0.79, 0.53) Syngad K R 2005 -1.99 7.13 6 -1.97 7.16 -1.97 4.16 1.8% -0.00 (-1.13, 1.13) Total (8% Ci) -33 7.75 5.1 1.97 2.06 1.11 16 4.0% 0.18 (-0.57, 0.33) Total (8% Ci) -337 357 100.0% -0.20 (-0.35, 0.05) -2.25 (-0.8, 0.24) B HP LP Std. Mean Difference Md. Man Difference Md. Man Difference B Charl Rock 2.1 1.05 1.9 2.27 1.41 1.9 4.1% -0.38 (-1.00, 0.28) Charl Rock 2.1 Me 4.22 6.0 1.9 3.0 2.29 0.05 1.05 0.05 1.05 1.05 1.05 1.05 0.05 1.06	Luger M 2013	-50.8	131 1	19	-137	129.86	21	5.8%	-0.28 [-0.90, 0.35]	
Navybee W 2016 - 0.4 0.98 23 - 0.6 0.94 22 6.6% 0.211 (0.38, 0.78] Papakonstantinou E 2010 - 0.5 0.62 17 - 0.4 0.95 17 5.0% - 0.12 (0.79, 0.65] Papakonstantinou E 2010 - 0.5 0.62 17 - 0.4 0.95 17 5.0% - 0.12 (0.79, 0.55] Sargad K 2005 - 1.99 7.13 6 - 1.97 4.16 6 1.5% - 0.00 (-1.3, 1.13] Try J 2014 - 0.4 0.49 41 - 0.01 0.62 37 7.0% - 0.70 (-1.15, 0.24] Westman E C 2008 4.75 77.58 21 - 1.93 179.69 29 7.0% - 0.32 (-0.80, 0.24] Westman E C 2008 4.75 77.58 21 - 1.93 179.69 29 7.0% - 0.32 (-0.80, 0.24] Westman E C 2008 4.75 77.58 21 - 1.93 179.69 29 7.0% - 0.32 (-0.80, 0.24] Westman E C 2008 4.75 77.58 21 - 1.93 179.69 29 7.0% - 0.32 (-0.80, 0.24] Unchall (95% C) Binkworth O 2004 - 0.19 125 19 0.27 1.44 19 4.1% - 0.38 (-0.03) Heterogeneity: Ch ² = 8.8, d = 13 (P = 0.80); P = 0%; Test for overall effect: Z = 2.56 (P = 0.01) Binkworth O 2004 - 0.19 1.25 19 0.27 1.44 19 4.1% - 0.38 (-0.02) Heterogeneity: Ch ² = 0.04 1 125 - 0.04 19 0.27 1.44 19 4.1% - 0.38 (-0.02) Heterogeneity: Ch ² = 0.04 1 125 - 0.04 19 0.27 19 9 3.0% - 0.76 (-1.56, -0.03) Heterogeneity: Ch ² = 0.04 1 135 9 - 0.27 19 9 3.0% - 0.76 (-1.57, -0.03) Heterogeneity: Ch ² = 0.04 1 145 2 - 0.6 19 9 0 11 0.77 0.04 (-0.20, 0.23) Heterogeneity: Ch ² = 0.04 1 135 9 - 0.33 0.27 19 9 3.0% - 0.76 (-1.57, -0.03) Heterogeneity: Ch ² = 0.04 1.03 8.13 0 - 0.16 (-2.0, 0.28) Heterogeneity: Ch ² = 0.04 1.03 8.13 0 - 0.05 17 3.7% 0.016 (-0.20, 0.28) Heterogeneity: Ch ² = 1.02 0.44 6.30 1.27 6 1.3% 0.04 (-1.02, 0.28) Heterogeneity: Ch ² = 1.02 0.44 6.30 1.27 6 1.3% 0.04 (-1.02, 0.28) Heterogeneity: Ch ² = 1.02 0.44 6.30 1.27 6 1.3% 0.04 (-1.02, 0.28) Heterogeneity: Ch ² = 1.02 0.44 6.30 1.27 6 1.3% 0.04 (-1.02, 0.28) Heterogeneity: Ch ² = 1.02 0.44 6.30 1.27 6 1.3% 0.04 (-1.02, 0.08) Heterogeneity: Ch ² = 1.02 0.44 1.02 0.52 37 8.6% 0.016 (-0.70, 0.48) Heterogeneity: Ch ² = 1.02 0.44 1.02 0.52 37 8.6% 0.016 (-0.70, 0.48) Heterogeneity: Ch ² = 1.02 0.45 1.12 0.00 0.44 19 4.2% 0.016 (-0.70, 0.48) Heterogeneity: Ch ² = 1.02 0.45 1.	M E Daly 2004	-0.67	1.39	37	-0.25	1.58	37	10.7%	-0.28 [-0.74, 0.18]	
Number P 202012 41 72.12 8 44 75.89 8 2.23% 0.009 (0.88, 10.7) Parker B2002 -0.34 0.81 26 -0.23 1.43 28 7.50% -0.01 (0.13, 1.13) Syngrad KR 2005 -1.99 7.13 6 -1.97 4.66 6 1.85% -0.00 (1.13, 1.13) Tay J 2014 -0.4 0.44 4.11 0.13 2.03 7.05% -0.22 (1.04) 0.44 Wethmare E 2:008 4.75 7.758 2.1 377 100.05% -0.20 (1-33, 1.03) Total (B%C C) -0.30 (1=0.01) -0.37 337 100.05% -0.20 (1-33, 4.05) B P LP Std. Mean Difference N. Fixed. 95% CI M. Fixed. 95% CI	Nerviee W 2016	-0.4	0.96	23	-0.6	0.94	22	6.6%	0.21 [-0.38, 0.79]	
Papakonstantinuc E 2010 -0.6 0.82 17 -0.4 0.35 17 5.0% -0.212 10.79 0.55] Papakonstantinuc E 2010 -0.4 0.81 126 -0.32 1.43 28 7.7% -0.09 (-0.33, 0.44) Wycheffey TP 2010 -0.4 0.81 126 -0.32 1.43 28 7.7% -0.09 (-0.33, 0.44) Wycheffey TP 2010 -0.4 1 12 -0.6 1.1 16 4.0% -0.18 (-0.7, 0.33) Heterogeneity: Ch ⁺ = 8.8, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.8); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B Heterogeneity: Ch ⁺ = 8.9, d = 13 (P = 0.60); Z = 0.41 (P = 0.30); D Test for overall effect: Z = 0.94 (P = 0.3); C C Heterogeneity: Ch ⁺ = 13 (P = 0.67); P = 0% Test for overall effect: Z = 0.94 (P = 0.3); C C Heterogeneity: Ch ⁺ = 13 (P = 0.67); P = 0%; Test for overall effect: Z = 0.94 (P = 0.3); C Heterogeneity: Ch ⁺ = 10.23, d = 13 (P = 0.67); P = 0%; Test for overall effect: Z = 0.94 (P = 0.3); C Heterogeneity: Ch ⁺ = 10.23, d = 13 (P = 0.67); P = 0%; Test for overall effect: Z = 0.94 (P = 0.3); C Heterogeneity: Ch ⁺ = 10.23, d = 13 (P = 0.67); P = 0%; Test for overall effect: Z = 0.94 (P = 0.3); C Heterogeneity: Ch ⁺ = 13.95 (P = 0.57); F = 0%; Test for overall effect: Z = 0.94 (P = 0.3); C Heterogeneity: Ch ⁺ = 13.95 (P = 0.57); F = 2%; Test for overall effect: Z = 0.94 (P = 0.3); C Heterog	Nuttall F Q 2012	-41	72.12	8	-48	75.89	8	2.3%	0.09 [-0.89, 1.07]	
Parker B 2002 Sargand K R 2002 199 A 24 0.41 0.41 26 0.23 1.43 28 7.9% 0.00 [0.83, 0.44] Tary J 2014 0.4 0.49 0.49 41 0.01 0.62 37 10.7% 0.70 [1.15, 0.24] Westman E C 2008 0.75, 77.85 21 - 193 176.69 29 7.0% 0.02 [0.83, 0.45] Total (8% C) 11 12 0.6 1.1 16 4.0% 0.18 [0.57, 0.83] Total (8% C) 12 0.6 0, 13 17 0.0% 0.28 [0.35, 0.45] Total (8% C) 13 0 0.4 1 12 0.6 1.1 16 4.0% 0.18 [0.57, 0.83] 14 08% C) 14 08% C) 14 08% C) 15 0.04 0.19 1.05 19 0.0% 15 0.04 0.19 1.05 19 0.27 1.44 19 4.1% 0.03 [1.00, 0.58 1.00, 0.28] 14 0.04 0.41 10.5 19 0.27 1.44 19 4.1% 0.04 [0.38, 0.30] 15 0.04 0.19 1.05 19 0.27 1.44 19 4.1% 0.04 [0.38, 0.30] 15 0.00 0.4 0.19 1.05 19 0.27 1.44 19 4.1% 0.04 [0.38, 0.30] 15 0.00 0.4 0.19 1.05 19 0.27 1.44 19 4.1% 0.04 [0.38, 0.30] 15 0.00 0.4 0.19 1.05 19 0.27 1.44 19 4.1% 0.04 [0.38, 0.30] 15 0.00 0.4 0.19 1.05 19 0.27 1.44 19 4.1% 0.04 [0.38, 0.30] 15 0.00 0.4 0.19 1.05 19 0.27 1.44 19 4.1% 0.04 [0.38, 0.30] 15 0.00 0.4 0.19 1.15 13 0.3 0.99 01 6.7% 0.00 [0.50, 0.50] 15 0.00 1.00 0.4 0.19 0.05 10.00 0.28 0.00 0.16 0.20, 0.20 0.05 1 15 0.00 0.42 0.0 0.11 10 7.03 0.90 01 6.27 0.02 [0.00 0.16 0.0, 0.50] 14 0.04 0.47 0.27 [1.54, 4.03] 14 0.1 0.64 0.24 0.04 0.47 0.22 1.9 15 0.30 0.46 0.7 3.7% 0.06 [1.21, 0.01] 14 0 1.2 0.5 11.1 17 7.0 3.04 05 17 3.7% 0.06 [1.21, 0.01] 14 0 1.0 0.5 0.44 1.0 0.2 0.5 112 0.30 0.5 116 3.0% 0.01 [1.20, 0.01] 15 0.05 0.44 1.00 0.17 0.89 0 15 0.05 0.44 1.00 0.15 0.27 0.43 1.40 0.02 0.60 0.47 0.72 [1.54, 0.03] 15 0.05 0.13 0.58 2.1 2.26 6.05 2.47 % 0.04 [1.10, 1.70, 0.89] 15 0.07 0.01 0.53 0.5 16 3.0% 0.18 [2.57, 0.33] 15 0.02 0.02 1.3 0.5 16 3.0% 0.18 [2.57, 0.33] 15 0.02 0.02 1.3 0.5 16 3.0% 0.18 [2.57, 0.33] 15 0.02 0.01 0.35 12 0.20 0.5 116 3.0% 0.18 [2.57, 0.33] 15 0.02 0.01 0.35 12 0.20 0.5 12 0.30 0.5 16 3.0% 0.18 [2.57, 0.33] 15 0.02 0.01 0.35 12 0.05 11 0.07 0.42 0.5 119 0.07 10.27 0.41 0.00 0.00 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0	Papakonstantinou E 2010	-0.5	0.62	17	-0.4	0.95	17	5.0%	-0.12 [-0.79, 0.55]	
Sargnad KR 2005 - 1.99 7.13 6 -1.97 4.16 6 1.9% -0.00[-113.1.13] Try J 2014 -0.4 0.49 41 -0.01 0.62 37 10.7% -0.70[-1.15, -0.24] Westman EC 2008 -67.5 77.58 21 -19.3 176.69 29 7.0% -0.22 [0.88, 0.24] Wycherley TP 2010 -0.4 1 12 -0.6 1.1 16 4.0% 0.18 [0.57, 0.83] Heterogeneity: Chi ⁺ = 8.69, df = 13 (P = 0.8); P = 0%. Test for overall effect Z = 2.56 (P = 0.01) B HP LP Std. Mean Difference Std. Mean Diffe	Parker B 2002	-0.34	0.81	26	-0.23	1.43	28	7.9%	-0.09 [-0.63, 0.44]	
Tay J 2014 -0.4 0.4 0.4 0.4 0.4 0.62 37 10.7% -0.70 (11.5) - 0.24 Weshman E C 2006 -0.75 77.58 21 - 1.93 175.69 29 70.% -0.72 (15.15, -0.24) Wichnriey T P 2010 -0.4 1 12 -0.6 1.1 16 40% 0.18 (-0.57, 0.83) Total (95% CI) -3.37 337 100.0% -0.20 (-0.35, -0.65) Favour, IPP Favour, IPP Favour, IPP Favour, IPP B HP LP Std. Mean Difference Std. Mean Difference Std. Mean Difference Study or Subgroup Man SD Total Weight V. Fixed, 95% CI V. Fixed, 95% CI Cheryl, Rock 2014 44 46.22 66 64.41 67 17.7% -0.01 (-0.50, 0.03) Krob J 2010 -0.17 1.16 16.376 20 4.5% -0.03 (-0.50, 0.50) - Luger M 2013 -4.3 4.881 21 -5.1 4.376 20 4.5% -0.06 (-1.70, 0.68) Payakonsaninous 2010 -0.6 21.0 20.6 2.4 7%	Sargrad K R 2005	-1.99	7.13	6	-1.97	4.16	6	1.8%	-0.00 [-1.13, 1.13]	
Weistmark E C 2008 -0.75 77.58 21 -19.3 17.86.9 29 7.0% $-0.22 [0.89, 0.24]$ Wycherfey TP 2010 -0.4 1 12 -0.6 1.1 16 4.0% $0.18 [-0.57, 0.83]$ Heterogeneity: Chi ² = 8.08, df = 13 (P = 0.80); P = 0%. Test for overall effect: Z = 2.56 (P = 0.01) HP LP Std. Mean Difference Std. Mean Differenc	Tay J 2014	-0.4	0.49	41	-0.01	0.62	37	10.7%	-0.70 [-1.15, -0.24]	
Wycherfey T P 2010 -0.4 1 12 -0.6 1.1 16 4.0% 0.18 [-0.57, 0.93] Total (8% C) 337 357 100.0% -0.20 [-0.35, -0.65] Heterogeneity: Ch ² = 5.69, d = 13 (P = 0.80); P = 0% Test for overall effect: Z = 2.56 (P = 0.01) B HP LP Std. Mean Difference Std. Mean Difference Std. Mean Difference Std. Mean Difference Without 4 4622 66 6 44.1 67 14.7% -0.04 [-0.38, 0.30] Culubrand H2012 -0.31 1.15 30 -0.3 0.99 31 6.7% -0.04 [-0.38, 0.30] Culubrand H2012 -0.31 1.15 30 -0.3 0.99 31 6.7% -0.04 [-0.38, 0.30] Culubrand H2012 -0.31 1.15 30 -0.04 0.42 12 4.7% -0.04 [-0.38, 0.30] Culubrand H2012 -0.31 1.15 30 -0.04 0.47 12 4.7% -0.04 [-0.38, 0.30] Culubrand H2012 -0.31 1.15 30 -0.04 0.47 22 4.7% -0.04 [-0.48, 0.36] Haw 2013 -4.3 4.88 1 21 -5.1 43.76 20 4.5% -0.03 [-0.00, 0.45] Haw 2013 -4.3 4.88 1 21 -5.1 43.76 20 4.5% -0.02 [-0.60, 0.63] Hyelse W2016 -0.3 0.48 23 -0.04 0.47 22 4.7% -0.04 [-1.07, 0.39] Parkors famious E2 010 -0.5 1.11 17 -0.3 0.95 17 3.7% -0.04 [-1.07, 0.39] Parkors famious E2 010 -0.2 0.6 12 -0.3 0.5 16 3.0% 0.18 [-0.57, 0.93] Wycherley T P 2010 -0.2 0.6 12 -0.3 0.5 16 3.0% 0.18 [-0.57, 0.93] Total (8% C) -0.22 0.65 12 -0.3 0.5 16 3.0% 0.18 [-0.57, 0.93] Total (95% C) -0.20 0.6 12 -0.3 0.5 16 3.0% 0.18 [-0.57, 0.93] Total (95% C) -0.20 0.6 12 -0.3 0.5 16 3.0% 0.18 [-0.57, 0.93] Total (95% C) -0.44 0.20 3.1 19 0.03 -11 19 4.2% -0.06 [-0.19, 0.07] HP C Std. Mean Difference Std. Mean Difference M4 0.02 0.31 19 0.03 -11 19 4.2% -0.16 [-0.70, 0.48] Heterogeneity: Ch ² = 10.23 0.45 6 30 0.11 0.43 31 6.7% 0.24 [-0.27, 0.74] Khoo J 2011 -0.06 0.1 12 0.07 0.09 19 2.2% -0.07 [-0.30, 0.18] HP Aver B 2002 -0.01 0.43 144 0.02 0.37 150 32.2% -0.07 [-0.30, 0.18] Heterogeneity: Ch ² = 10.23 0.5 10 3.04 119 4.2% -0.36 [-0.70, 0.48] Heterogeneity: Ch ² = 10.23 0.56 30 0.11 0.43 31 6.7% 0.24 [-0.27, 0.44] Heterogeneity: Ch ² = 10.3, 178 0 22 0.12 0.2 28 6.03 (-0.37 16.03, 0.48] Heterogeneity: Ch ² = 10.0 0.0 0.1 12 (-0.05, 0.34 8 1.5% -0.06 [-0.19, 0.07] H2 2 4.0 0.0 0.04 0.17 12 0.22 0.05 0.33 119	Westman E C 2008	-67.5	77.58	21	-19.3	179.69	29	7.0%	-0.32 [-0.89, 0.24]	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Wycherley T P 2010	-0.4	1	12	-0.6	1.1	16	4.0%	0.18 [-0.57, 0.93]	
$ \begin{aligned} & \text{Heterogeneity: Chi^2 = 8.69, df = 13 (P = 0.80); F = 0% \\ \text{Test for overall effect: Z = 2.56 (P = 0.01) \\ \hline \\ B \\ \hline \\ & \text{Study or Subgroup} & \frac{\text{Mean}}{\text{SD}} & \frac{\text{SD}}{\text{Total}} & \frac{\text{Mean}}{\text{Mean}} & \frac{\text{SD}}{\text{SD}} & \frac{\text{Total}}{\text{Mean}} & \frac{\text{Mean}}{\text{SD}} & \frac{\text{SD}}{\text{Total}} & \frac{\text{Mean}}{\text{Mean}} & \frac{\text{SD}}{\text{SD}} & \frac{\text{Total}}{\text{Mean}} & \frac{\text{Mean}}{\text{SD}} & \frac{\text{SD}}{\text{Total}} & \frac{\text{Mean}}{\text{Mean}} & \frac{\text{SD}}{\text{SD}} & \frac{\text{Total}}{\text{Mean}} & \frac{\text{SD}}{\text{Mean}} & \frac{\text{SD}}{\text{SD}} & \frac{\text{Total}}{\text{Mean}} & \frac{\text{SD}}{\text{Mean}} & \frac{\text{SD}}{\text{SD}} & \frac{\text{Total}}{\text{Mean}} & \frac{\text{SD}}{\text{Mean}} & \frac{\text{SD}}{\text{Man}} & \frac{\text{SD}} & \frac{\text{SD}}{\text{Man}} & \frac{\text{SD}$	Total (95% CI)			337			357	100.0%	-0.20 [-0.35, -0.05]	•
Test for overall effect: Z = 2.56 (P = 0.01) B HP LP Std. Mean Difference Std. Yor Subgroup Mean D D Total Mean D D D D D D D D D D D D D D D D D D D	Heterogeneity: Chi ² = 8.69, d	f = 13 (P	= 0.80)	; ² = 0 ⁴	%					-2 -1 0 1 2
B Study or Subgroup Mean SD Total Mean SD Total Weight IV. Fixed, 95% CI V. Fixed, 95% CI	Test for overall effect: Z = 2.5	6 (P = 0	.01)							Favours [HP] Favours [LP]
HP LP Std. Mean Difference Std. Mean Difference Std. Mean Difference Std. Mean Difference Brinkworth G D 2004 -0.19 1.05 19 0.27 1.44 19 4.1% -0.38 (-1.00, 0.28) V. Fixed, 95% CI Charj L, Rock 2014 4 4622 66 64 14 67 1.7% -0.04 (-0.38, 0.30) 0.01 (-0.50, 0.50) Guidbrand H 2012 -0.31 1.15 30 -0.3 0.27 1.44 19 3.0% -0.02 (-0.50, 0.50) Krebs J 2012 -0.11 1.16 1.44 -0.21 1.19 150 3.25% 0.02 (-0.60, 0.63) Payleer W2016 -0.3 0.48 2.3 -0.00 0.47 2.2 4.5% 0.02 (-0.60, 0.68) Parker B 2002 -0.19 1.07 2.6 0.09 1.59 2.8 5.9% -0.20 (-0.74, 0.33) Vestmare C 2006 1.3 3.6.78 21 -2.8 6.9 5.9 5.4% 0.07 (-0.49, 0.63) Vesterider Y P 2010 -0.2 <td< td=""><td>B</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></td<>	B									
Study or Subgroup Mean SD Total SSD Total Mean SD Total SSD Total SSD			HP			LP			Std. Mean Difference	Std. Mean Difference
Brinkworth G D 2004 Chery L. Rock 2014 4 6522 Guldbrand H 2012 -0.3 1.15 30 -0.3 0.99 31 6.7% -0.00 [-0.50, 0.30] Creating L. Schwarz 12 -0.3 0.44 2012 -0.3 0.44 2012 -0.3 0.44 2012 -0.3 0.48 21 -0.3 0.47 22 4.7% -0.61 [-1.54, -0.03] Krebs J D 2012 -0.17 -0.3 0.48 23 -0.004 -0.05 -0.78 [-1.54, -0.03] Krebs J D 2012 -0.17 -0.3 0.48 23 -0.004 -0.09 -1.77 -0.05 -0.78 -0.78 -0.06 [-1.21, -0.01] -0.05 -0.17 -0.05 -0.78 -0.06 [-1.07, 0.08] -0.06 [-1.07, 0.08] -0.06 [-1.07, 0.08] -0.06 [-1.01, 0.05] -0.06 [-1.01, 0.05] -0.06 [-0.19, 0.07] -2 -1 -1 -2 -1 -2	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
Cheryl L. Rock 2014 4 46.22 66 6 44.1 67 14.7% -0.04 [0.38, 0.30] Guldbrand H 2012 0.3 1.15 30 -0.3 0.99 31 6.7% 0.00 [0.50, 0.50] Khou J 2011 -0.54 0.34 12 -0.3 0.27 19 3.0% -0.78 [-1.54, -0.3] Wrest J D 2012 -0.17 1.16 144 -0.2 119 150 32.5% 0.03 [0.20, 0.25] Luger M 2013 -4.3 48.61 21 -5.1 43.76 20 4.5% 0.02 [0.60, 6.83] Nerylee W 2016 -0.3 0.48 23 -0.004 0.47 22 4.7% -0.61 [-1.21, -0.01] Nutail F Q 2012 -0.19 1.07 26 0.09 159 28 5.9% -0.20 [0.74, 0.33] Sargrad K R 2005 -0.32 0.64 6 -0.36 1.27 6 1.3% 0.04 [-1.01, 1.17] Total (95% CI) -0.2 0.6 12 -0.3 0.5 16 3.0% 0.18 [-0.27, 0.93] Total (95% CI) -446 46 0.03 0.31 19 0.25 54.5% CI W. Fixed 95% CI W. F	Brinkworth G D 2004	-0.19	1.05	19	0.27	1.44	19	4.1%	-0.36 [-1.00, 0.28]	
Guldbrand H 2012 -0.3 1.15 30 -0.3 0.99 31 6.7% 0.00 [-0.50, 0.50] Krebs J D 2012 -0.17 1.16 144 -0.2 1.19 150 32.5% 0.03 [-0.60, 0.63] Nerylee W 2016 -0.3 0.48 23 -0.004 0.47 22 4.7% -0.61 [-1.21, -0.01] Nutal F Q 2012 -16 50.97 8 -12 32.98 8 1.8% -0.09 [1-07, 0.89] Papakonstantinou E 2010 -0.5 1.11 7 -0.3 0.95 17 3.7% -0.19 [-0.86, 0.48] Parker B 2002 -0.19 1.07 26 0.09 1.59 28 5.9% -0.20 [0.74, 0.33] Sargrad K R 2005 -0.32 0.64 6 -0.36 1.27 6 1.3% 0.04 [-1.10, 1.17] Tay J 2014 -0.1 0.65 41 -0.2 0.62 37 8.6% 0.16 [-0.27, 0.63] Westman E C 2008 1.3 36.78 21 -2.8 69.05 29 5.4% 0.07 [-0.49, 0.63] Westman E C 2008 1.3 36.78 21 -2.8 69.05 29 5.4% 0.07 [-0.49, 0.63] Total (95% CI) 446 469 100.0% -0.06 [-0.19, 0.07] Heterogeneity: Ch ² = 10.23, df = 13 (P = 0.67); P = 0% Test for overall effect: Z = 0.94 (P = 0.35) C	Cheryl L. Rock 2014	4	46.22	66	6	44.1	67	14.7%	-0.04 [-0.38, 0.30]	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Guldbrand H 2012	-0.3	1.15	30	-0.3	0.99	31	6.7%	0.00 [-0.50, 0.50]	
Notes to 2012 0.11 1.10 1.41 4.02 1.13 100 22.5% 0.03 [-2.50 0.03 [-2.50 0.02] Nerylee W 2016 0.3 0.48 23 -0.004 0.47 22 4.7% -0.05 [-1.20 , 0.03] Nerylee W 2016 0.3 0.48 23 -0.004 0.47 22 4.7% -0.05 [-1.20 , 0.01 Papakonstantinou E 2010 0.5 1.11 17 -0.3 0.95 17 3.7% -0.09 [-1.07 , 0.99] Papakonstantinou E 2010 0.5 1.11 17 -0.3 0.95 17 3.7% -0.09 [-1.07 , 0.89] Parker B 2002 0.19 1.07 26 0.09 1.59 28 5.9% 0.20 [-0.74 , 0.33] Sargrad K R 2005 -0.32 0.64 6 -0.36 1.27 6 1.3% 0.04 [-1.10 , 1.17] Tay J 2014 0.1 0.65 41 -0.2 0.62 37 8.6% 0.16 [-0.29 , 0.60] Westman E C 2008 1.3 36.78 21 -2.8 6.90.5 29 5.4% 0.07 [-0.49 , 0.63] Wycherley T P 2010 0.2 0.6 12 0.3 0.5 16 3.0% 0.18 [-0.57 , 0.39] Total (95% CI) 446 469 100.0% -0.06 [-0.19 , 0.07] Heterogeneity: Ch ^P = 10.23, df = 13 (P = 0.67); P = 0% Test for overall effect Z = 0.94 (P = 0.35) C HP LP Std. Mean Difference Std. Mean Difference Std. Mean Difference Std. Mean Difference Std. Mean Difference Nervice (HP) Favours [LP] HP LP Std. Mean Difference Std. Mean Difference Nervice (HP) Favours [LP] HP LP Std. Mean Difference Nervice (J = 0.20, 0.1 12 0.07 0.09 19 2.8% -1.35 [-2.16 , 0.54] Khoo J 2011 -0.06 0.1 12 0.07 0.09 19 2.8% -1.35 [-2.16 , 0.54] Krebs J D 2012 -0.01 0.43 144 0.02 0.37 150 32.5% -0.07 [-0.30 , 0.16] Nervice W 2016 0.03 0.14 123 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 123 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.14 23 0.1 0.14 22 4.5% -0.08 [-0.64], 0.58] Nervice W 2016 0.03 0.1	Krobe 1 D 2012	-0.54	0.34	144	-0.3	1.10	150	3.0%	-0.78 [-1.54, -0.03]	-
Logo m 2/10 4.3 0.04 2.3 0.04 0.07 0.05 0.06 0.07 0.05	Luger M 2013	-4.3	48.81	21	-0.2	43.76	20	4 5%	0.03 [-0.20, 0.23]	
Nutlail F 2012 -16 50.07 8 -12 32.98 8 1.8% -0.00 [-1.07, 0.8] Papakonstantinou E 2010 0.5 1.11 17 -0.3 0.55 17 3.7% -0.19 [-1.07, 0.8] Parker B 2002 -0.19 1.07 26 0.09 1.59 28 5.9% -0.20 [-0.74, 0.33] Sargrad K R 2005 -0.32 0.64 6 -0.26 0.57 8.6% 0.16 [-0.29, 0.60] Westman E C 2008 1.3 8.78 21 -2.8 69.05 29 5.4% 0.07 [-0.49, 0.63] Wycherley T P 2010 -0.2 0.6 12 -0.3 0.5 16 3.0% 0.18 [-0.57, 0.93] Total (95% Cl) 446 469 100.0% -0.06 [-0.19, 0.07] -2 -1 0 1 2 -1 2 7 3.7% 0.18 [-0.57, 0.93] Total (95% Cl) 446 469 100.0% -0.06 [-0.19, 0.07] -2 -1 0 1<2 Favours [LP] Favours [LP] C Ele Std. Mean Difference Std. Mean Difference <td>Nervice W 2016</td> <td>-4.3</td> <td>0.48</td> <td>23</td> <td>-0.004</td> <td>0.47</td> <td>20</td> <td>4.3%</td> <td>-0.61 [-1.21 -0.01]</td> <td></td>	Nervice W 2016	-4.3	0.48	23	-0.004	0.47	20	4.3%	-0.61 [-1.21 -0.01]	
Papakonstantinou E 2010 -0.5 1.11 17 -0.3 0.35 -0.19 0.08 0.19 0.08 Parker B 2002 -0.19 1.07 26 0.09 1.59 28 5.9% -0.20 0.10 0.74 0.33 Sargrad K R 2005 -0.32 0.64 6 -0.36 1.27 6 1.3% 0.04 1.11 17 Tay J 2014 -0.1 0.65 41 -0.2 0.62 37 8.6% 0.16 1.09, 0.63 Westman E C 2008 1.3 36.78 21 -2.8 69.05 29 5.4% 0.07 -4.09, 0.63 Wycherley T P 2010 -0.2 0.6 12 -0.3 0.51 100.0% -0.06 -0.19, 0.07 Heterogeneity: Ch ² = 10.23, df = 13 (P = 0.67); P = 0% Test for overall effect: Z = 0.94 (P = 0.35) Std. Mean Difference Std. Mean Difference Not Mean <	Nuttall E O 2012	-16	50.97	8	-12	32.98	8	1.8%	-0.09 [-1.07 0.89]	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Papakonstantinou E 2010	-0.5	1.11	17	-0.3	0.95	17	3.7%	-0.19 [-0.86, 0.48]	
Sargrad K R 2005 -0.32 0.64 6 -0.36 1.27 6 1.3% 0.04 [-1.10, 1.17] Tay J 2014 -0.1 0.65 41 -0.2 0.62 37 8.6% 0.16 [-0.29, 0.60] Westman E C 2008 1.3 36.78 21 -2.8 69.05 29 5.4% 0.07 [-0.49, 0.63] Wycherley T P 2010 -0.2 0.6 12 -0.3 0.5 16 3.0% 0.18 [-0.57, 0.93] Total (95% CI) 446 469 100.0% -0.06 [-0.19, 0.07] -2 -1 0 1 2 rest for overall effect: Z = 0.94 (P = 0.35) C Fixed provements Std. Mean Difference Std. Mean Difference IV. Fixed, 95% CI IV. Fixed, 95% CI Brinkworth G D 2004 -0.02 0.31 19 0.26% -1.35 [-2.16, -0.54] IV. Fixed, 95% CI IV. Fixed, 95% CI IV. Fixed, 95% CI Brinkworth G D 2004 -0.02 0.31 19 0.26% -1.35 [-2.16, -0.54] IV. Fixed, 95% CI IV. Fixed, 95% CI Brinkworth G D 2012 -0.01 12 0.07 0.09 19 2.	Parker B 2002	-0.19	1.07	26	0.09	1.59	28	5.9%	-0.20 [-0.74, 0.33]	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Sargrad K R 2005	-0.32	0.64	6	-0.36	1.27	6	1.3%	0.04 [-1.10, 1.17]	
Westman E C 2008 1.3 36.78 21 -2.8 69.05 29 5.4% 0.07 $[-0.49, 0.63]$ Wycherley T P 2010 -0.2 0.6 12 -0.3 0.5 16 3.0% 0.18 $[-0.57, 0.93]$ Total (95% Cl) 446 469 100.0% -0.06 $[-0.19, 0.07]$ Heterogeneity: ChP = 10.23, df = 13 (P = 0.67); P = 0% Total Weight VL Fixed, 95% Cl V. Fixed, 95% Cl C HP LP Std. Mean Difference V. Fixed, 95% Cl V. Fixed, 95% Cl Brinkworth G D 2004 -0.02 0.31 19 0.03 0.31 19 4.2% -0.16 [-0.79, 0.40] Guidbrand H 2012 0.23 0.56 30 0.11 0.43 31 6.7% 0.24 [-0.27, 0.41] Guidbrand H 2012 0.23 0.56 30 11.4 20.58 20 4.5% -0.07 [-0.27, 0.41] Guidbrand H 2012 0.23 0.56 10 10.42 23.5% -0.07 [-0.30, 0.15] -0.98 [-0.64, 0.58] Nerylee W 2016 0.03 1.4 20.05 20.36	Tay J 2014	-0.1	0.65	41	-0.2	0.62	37	8.6%	0.16 [-0.29, 0.60]	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Westman E C 2008	1.3	36.78	21	-2.8	69.05	29	5.4%	0.07 [-0.49, 0.63]	
Total (95% Cl) 446 469 100.0% -0.06 [-0.19, 0.07] Heterogeneity: ChP = 10.23, df = 13 (P = 0.67); P = 0% Test for overall effect: Z = 0.94 (P = 0.35) -2 -1 0 1 2 Test for overall effect: Z = 0.94 (P = 0.35) Ferrore Std. Mean Difference V.F. Ked. 95% Cl V.F. Ked. 95% Cl Brinkworth G D 2004 -0.02 0.31 19 0.33 0.31 19 4.2% -0.16 [-0.79, 0.48] Cheryl L. Rock 2014 15 14.38 66 14 14.2 67 14.7% 0.07 [-027, 0.41] Guldbrand H 2012 0.23 0.56 30.011 0.43 14.4 20.45% -0.04 [-0.20, 0.15] Luger M 2013 0.81 7.788 21 1.42 2.5% -0.37 [-0.64, 1.34] Parker B 2002 -0.01 0.25 26 0.01 2.26 2.36% 0.26 [-0.23, 0.69] 1.42 Westman E C 2008 5.61 14.59 21 0 7.8% 0.25 [-0.20, 0.69] -2 -1 2 2.5%	Wycherley T P 2010	-0.2	0.6	12	-0.3	0.5	16	3.0%	0.18 [-0.57, 0.93]	
Heterogeneity: Chi ² = 10.23, df = 13 (P = 0.67); P = 0% Test for overall effect: Z = 0.94 (P = 0.35) C Study or Subgroup Mean SD Total Mean St Total Mean Difference Std. Mean Difference Brinkworth G D 2004 -0.02 oil 1 V. Fixed, 95% CI Derive Weath V. Fixed, 95% CI V. Fixed, 95% CI Brinkworth G D 2004 -0.02 oil 1 V. Fixed, 95% CI Brinkworth G D 2004 -0.02 oil 1 A: 0.03 oil 2 Std. Mean Difference Brinkworth G D 2004 -0.02 oil 1 4.35 CI V. Fixed, 95% CI Brinkworth G D 2004 -0.02 oil 1 A: 0.03 Oil 4 14.2 C Oil 0.03 0.11 0.43 6.7 -0.01 Oil 0.25 Oil 0.26	Total (95% CI)			446			469	100.0%	-0.06 [-0.19, 0.07]	•
Test for overall effect: Z = 0.94 (P = 0.35) -2 -1 0 1 2 Favours [LP] Favours [LP] Favours [LP] Study or Subgroup Mean SD Total Weight IV. Fixed, 95% CI Diversity of Subgroup Std. Mean SD Total Weight IV. Fixed, 95% CI Diversity of Subgroup Std. Mean SD Total Weight IV. Fixed, 95% CI Diversity of Subgroup Std. Mean Std. Mean Difference Mean SD Total Weight IV. Fixed, 95% CI Colspan="2">IV. Fixed, 95% CI Other Subgroup Std. Mean Difference Std. Mean Difference IV. Fixed, 95% CI IV. Fixed, 95% CI IV. Fixed, 95% CI IV. Fixed, 95% CI IV. Fixed, 95% CI <td>Heterogeneity: Chi² = 10.23,</td> <td>df = 13</td> <td>(P = 0.6</td> <td>7); 12 =</td> <td>0%</td> <td></td> <td></td> <td></td> <td></td> <td></td>	Heterogeneity: Chi ² = 10.23,	df = 13	(P = 0.6	7); 12 =	0%					
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Brinkworth G D 2004 -0.02 0.31 19 0.03 0.31 19 4.2% -0.16 [-0.79, 0.48] Cheryl L. Rock 2014 15 14.38 66 14 14.2 67 14.7% 0.07 [-0.27, 0.41] Guldbrand H 2012 0.23 0.56 30 0.11 0.43 14.7% 0.02 [-0.27, 0.41] Guldbrand H 2012 0.23 0.56 30 0.11 0.43 14.4 0.02 0.37 150 32.5% -0.03 [-0.64, 0.54] Krobs J D 2012 -0.01 0.43 14.4 0.02 0.37 150 32.5% -0.03 [-0.64, 0.58] Nerylee W 2016 0.03 0.14 23 0.1 0.14 22 4.8% -0.49 [-1.09, 0.10] Nutall F Q 2012 -1 8 4 8 1.7% 0.35 [-0.64, 1.34] Papakonstantinou E 2010 0.1 0.425 26 0.01 2.6 28 6.0% -0.08 [-0.61, 0.46] Sargrad K R 2005 -0.08 0.66 6 0.05 0.34 8 1.5% -0.25 [-0.20, 0.69] Westman E C 2	Study or Subgroup	Mear	n SD	Tota	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV. Fixed, 95% Cl
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Guldbrand H 2012 0.23 0.56 30 0.11 0.43 31 6.7% 0.24 {-0.27, 0.74} Knoo J 2011 -0.06 0.1 12 0.07 0.09 19 2.6% -1.35 {-2.16, 0.54} Krebs J 2012 -0.01 0.43 144 20.02 0.37 1.09 19 2.6% -0.07 {-0.30, 0.15} Luger M 2013 0.8 17.88 21 1.4 20.58 20 4.5% -0.03 {-0.64, 0.58} Nerylee W 2016 0.03 0.14 23 0.1 0.14 22 4.8% -0.49 {-1.09, 0.10} Nuttal F Q 2012 -1 8 4 6 8 1.7% -0.18 {-0.65, 0.49} Papakonstantinou E 2010 -0.1 0.62 17 0 0.45 17 3.7% -0.08 {-0.66, 1.04, 6} Sargrad K R 2005 -0.06 66 6 0.05 0.34 8.5% 0.25 {-0.20, 0.69} Westman E C 2008 5.6 14.59 21 0 7.8 8.5% 0.23 {-0.23, 0.90} Wyertery T P 2010 0 0.2 12	Cheryl L. Rock 2014	15	5 14.38	66	14	14.2	67	14.7%	0.07 [-0.27, 0.41]	
Khoo J 2011 -0.06 0.1 12 0.07 0.09 19 2.8% -1.35 [-2.16, -0.54] Krebs J D 2012 -0.01 0.43 144 0.02 0.37 150 32.5% -0.07 [-0.30, 0.15] Luger M 2013 0.81 7.88 21 1.4 20.58 20 4.5% -0.03 [-0.64, 0.58] Nerylee W 2016 0.03 0.14 23 0.1 0.14 22 4.8% -0.49 [-1.09, 0.10] Nuttall F Q 2012 -1 8 8 4.7% 0.35 [-0.64, 1.34] Papakonstantinou E 2010 -0.1 0.62 17 0.45 17 3.7% -0.08 [-0.61, 0.46] Sargrad K R 2005 -0.08 0.66 6 -0.05 0.34 8 1.5% -0.08 [-0.12, 1.00] Tay J 2014 0.1 0.16 41 0.06 0.16 3.0% 0.00 [-0.75, 0.75] Westman E C 2008 5.6 14.59 21 0 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% CI) 446 471 100.0% -0.03 [-0.6, 0.10] -2	Guldbrand H 2012	0.23	3 0.56	30	0.11	0.43	31	6.7%	0.24 [-0.27, 0.74]	
Krebs J D 2012 -0.01 0.43 144 0.02 0.37 150 32.5% -0.07 [-0.30, 0.15] Luger M 2013 0.8 17.88 21 1.4 20.58 20 4.5% -0.03 [-0.64, 0.58] Nerylee W 2016 0.03 0.11 423 0.1 0.14 23 0.1 0.44 24 8.% -0.04 [-1.08, 0.08] Nutal F Q 2012 -1 8 8 -4 8 8 1.7% 0.35 [-0.64, 1.34] Papakonstantinou E 2010 -0.1 0.25 26 0.04 -0.08 [-0.65, 0.49] 9 Parker B 2002 -0.01 0.25 26 0.05 0.34 8 1.5% -0.06 [-1.12, 1.00] Sargrad K R 2005 -0.08 0.66 6 -0.25 2.5.3% 0.33 [-0.23, 0.90] Wycherley T P 2010 0 0.2 12 0 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% Cl) 446 471 100.0% -0.03 [-0.6, 0.10] -2 -1 0 2 Heterogeneity: Chi ² = 18.15, df = 13 (P = 0.63) 12 </td <td>Khoo J 2011</td> <td>-0.06</td> <td>6 0.1</td> <td>12</td> <td>0.07</td> <td>0.09</td> <td>19</td> <td>2.6%</td> <td>-1.35 [-2.16, -0.54]</td> <td></td>	Khoo J 2011	-0.06	6 0.1	12	0.07	0.09	19	2.6%	-1.35 [-2.16, -0.54]	
Luger M 2013 0.8 17.88 21 1.4 20.58 20 4.5% -0.03 [-0.64, 0.58] Nerylee W 2016 0.03 0.14 23 0.1 0.14 22 4.8% -0.49 [-1.09, 0.10] Nuttali F Q 2012 -1 8 8 -4 8 8 1.7% -0.35 [-0.64, 1.34] Papakonstantinou E 2010 -0.1 0.62 17 0 0.45 17 3.7% -0.18 [-0.85, 0.49] Parker B 2002 -0.01 0.25 26 0.01 0.26 28 6.0% -0.08 [-0.61, 0.46] Sargrad K 2005 -0.08 0.66 6 -0.05 0.34 8 1.5% -0.06 [-1.12, 1.00] Tay J 2014 0.1 0.16 41 0.06 0.16 37 8.5% 0.25 [-0.20, 0.69] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Westman E C 2010 0 0.2 12 0 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% CI) 446 471 100.0% -0.03 [-0.16, 0.10] Heterogeneity: Chi ² = 18.15, df = 13 (P = 0.15); l ² = 28% Test for overall effect: Z = 0.49 (P = 0.63) Fauture F (HP) E-average II P)	Krebs J D 2012	-0.0	1 0.43	144	0.02	0.37	150	32.5%	-0.07 [-0.30, 0.15]	*
Nerviee W 2016 0.03 0.14 23 0.1 0.14 22 4.8% -0.49 [-1.09, 0.10] Nuttall F Q 2012 -1 8 8 4 8 8 1.7% 0.05 [-0.64, 1.34] Papakonstantinou E 2010 -0.1 0.62 17 0.45 1.7% 0.05 [-0.64, 1.34] Papakonstantinou E 2010 -0.1 0.62 17 0.7% -0.18 [-0.85, 0.49] Parker B 2002 -0.01 0.25 26 0.01 0.26 28 6.0% -0.08 [-0.61, 0.46] Sargrad K R 2005 -0.08 0.66 6 -0.05 0.34 8 1.5% -0.06 [-1.12, 1.00] Tay J 2014 0 1.0 16 41 0.06 0.63 0.25 [-0.20, 0.69] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Wyestmery T P 2010 0 0.2 16 3.0% 0.00 [-0.75, 0.75] -2 -1 0 1 2	Luger M 2013	0.8	8 17.88	21	1.4	20.58	20	4.5%	-0.03 [-0.64, 0.58]	
Nutal F Q 2012 -1 8 8 -4 8 8 1.7% 0.35 [0.64, 1.34] Papakonstantinou E 2010 -0.1 0.62 17 0 0.45 17 3.7% -0.18 [0.85, 0.49] Parker B 2002 -0.01 0.25 26 0.01 0.26 28 6.0% -0.08 [0.65, 0.49] Sargrad K R 2005 -0.08 0.66 6 -0.05 0.34 8 1.5% -0.06 [-1.12, 1.00] Tay J 2014 0.1 0.16 41 0.06 0.16 3.78% 0.25 [-0.20, 0.69] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Wycherley T P 2010 0 0.2 12 0 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% Cl) 446 471 100.0% -0.03 [-0.16, 0.10] -2 -1 0 1 Heterogeneity: Chi ² = 18.15, df = 13 (P = 0.63) Fauruse HPI Eavoure HPI Eavoure HPI Eavoure HPI Eavoure HPI	Nerylee W 2016	0.03	3 0.14	23	0.1	0.14	22	4.8%	-0.49 [-1.09, 0.10]	
Papakonstantinou E 2010 -0.1 0.62 17 0 0.45 17 3.7% -0.18 [-0.85, 0.49] Parker B 2002 -0.01 0.25 26 0.01 0.26 28 6.0% -0.08 [-0.61, 0.46] Sargrad K R 2005 -0.08 6.66 6 -0.05 0.34 8 1.5% -0.06 [-1.12, 1.00] Tay J 2014 0.1 0.16 41 0.06 0.16 37 8.5% 0.25 [-0.20, 0.69] Westman E C 2008 5.6 14.59 21 0.17.89 29 5.3% 0.33 [-0.23, 0.90] Weyterley T P 2010 0 0.2 12 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% CI) 446 471 100.0% -0.03 [-0.16, 0.10] -2 -1 0 1 2 Heterogeneity: Chi ² = 18.15, df = 13 (P = 0.15); l ² = 28% -2 -1 0 1 2 Test for overail effect: Z = 0.49 (P = 0.63) -2 -1 0 1 2	Nuttall F Q 2012	-	1 8	8	-4	8	8	1.7%	0.35 [-0.64, 1.34]	
Parker B 2002 -0.01 0.25 26 0.01 0.26 28 6.0% -0.08 [-6.61, 0.46] Sargrad K R 2005 -0.08 0.66 6 -0.05 0.34 8 1.5% -0.06 [-1.12, 1.00] Tay J 2014 0.1 0.16 41 0.06 0.16 37 8.5% -0.25 [-0.20, 0.69] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Wycherley T P 2010 0 0.2 12 0 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% CI) 446 471 100.0% -0.03 [-0.16, 0.10] Heterogeneity: Chi ² = 18.15, df = 13 (P = 0.15); l ² = 28% Test for overall effect: Z = 0.49 (P = 0.63) Favoure FLIP	Papakonstantinou E 2010	-0.1	1 0.62	17	0	0.45	17	3.7%	-0.18 [-0.85, 0.49]	
Sargrad K R 2005 -0.08 0.66 6 -0.05 0.34 8 1.5% -0.06 [-1.12, 1.00] Tay J 2014 0.1 0.16 41 0.06 0.16 37 8.5% 0.25 [-0.20, 0.69] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Wycherley T P 2010 0 0.2 12 0 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% Cl) 446 471 100.0% -0.03 [-0.16, 0.10] -2 -1 0 1 Heterogeneity: Chi² = 18.15, df = 13 (P = 0.15); I² = 28% Test for overall effect: 2 = 0.49 (P = 0.63) Faurures [HP] Eavores [HP] Faurure [HP]	Parker B 2002	-0.0*	1 0.25	26	0.01	0.26	28	6.0%	-0.08 [-0.61, 0.46]	
Tay J 2014 0.1 0.16 41 0.06 0.16 37 8.5% 0.25 [-0.20, 0.69] Westman E C 2008 5.6 14.59 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Wycherley T P 2010 0 0.2 12 0 2.16 3.0% 0.00 [-0.75, 0.75] Total (95% CI) 446 471 100.0% -0.03 [-0.16, 0.10] Heterogeneity: Chi² = 18.15, df = 13 (P = 0.15); l² = 28% -2 -1 0 1 2 Test for overall effect: Z = 0.49 (P = 0.63) Faurure [HP] Faurure [HP] Faurure [HP] Faurure [HP] Faurure [HP] Faurure [HP]	Sargrad K R 2005	-0.08	0.66	6	-0.05	0.34	8	1.5%	-0.06 [-1.12, 1.00]	
wessman E C 2008 5.6 14.39 21 0 17.89 29 5.3% 0.33 [-0.23, 0.90] Wycherley T P 2010 0 0.2 12 0 0.2 16 3.0% 0.00 [-0.75, 0.75] Total (95% CI) 446 471 100.0% -0.03 [-0.16, 0.10] Heterogeneity: Chi² = 18.15, df = 13 (P = 0.15); l² = 28% -2 -1 0 1 2 Test for overall effect: Z = 0.49 (P = 0.63) -2 -1 0 1 2	Tay J 2014	0.1	0.16	41	0.06	0.16	37	8.5%	0.25 [-0.20, 0.69]	
Total (95% Cl) 446 471 100.0% -0.03 [-0.16, 0.10] Heterogeneity: Chi ² = 18.15, df = 13 (P = 0.15); l ² = 28% -2 -1 0 1 Test for overall effect: 2 = 0.49 (P = 0.63) -2 -1 0 1 2 Fast for overall effect: 2 = 0.49 (P = 0.63) -2 -1 0 1 2	Westman E C 2008	5.6		21	0	17.89	29	5.3%	0.33 [-0.23, 0.90]	
Total (95% Cl) 446 471 100.0% -0.03 [-0.16, 0.10] • Heterogeneity: Chi ² = 18.15, df = 13 (P = 0.15); l ² = 28% -2 -1 0 1 2 Test for overall effect: Z = 0.49 (P = 0.63) -2 -1 0 1 2	Tyononoy I F 2010		0.2	12	. 0	0.2	10	5.0 %	0.00[-0.10, 0.10]	
Test for overall effect: Z = 0.49 (P = 0.63) - 2 0.76 - 2 0.76 - 2 0.70 - 2	Total (95% CI)	5 df - 4	3/0-0	446	- 200/		471	100.0%	-0.03 [-0.16, 0.10]	
	Test for overall effect: Z =	0.49 (P	= 0.63)	(15); 1*	- 20%					-2 -1 0 1 2 Favours (HP) Favours (I P)

D

Figure 5. Meta-analysis for effect of high protein diet on total cholesterol (A), triglycerides (B), low-density lipoprotein cholesterol (C), and high-density lipoprotein cholesterol (D).

P=.04), the result of analysis for weight was changed; after excluding the study of Tay 2014, the results of analyses for TG (SMD=-0.14, 955 CI=-0.30 to 0.02, P=.09) were affected.

In addition, the funnel plot (based on the data of weight) showed the study of Daly 2006 significantly deviate from

the central axis (Fig. 7). However, sensitivity analysis showed no change of study result after excluding the study of Daly 2006.

4. Discussion

In this meta-analysis, the results were inconsistent with that in the previous meta-analysis.^[14] In the present meta-analysis, results

	i navan ⁸	HP	50005	a contract of	LP		5	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV. Fixed, 95% CI
Brinkworth G D 2004	-4.9	11.73	19	2.5	9.28	19	4.6%	-0.69 [-1.34, -0.03]	
Cheryl L. Rock 2014	-4	15.63	66	-7	14.49	67	17.0%	0.20 [-0.14, 0.54]	
David R Jesudason 2013	-3	46.9	21	4	61	24	5.7%	-0.13 [-0.71, 0.46]	
Guldbrand H 2012	-5	13.61	30	-6	14.2	31	7.8%	0.07 [-0.43, 0.57]	
Krebs J D 2012	-0.3	14.02	144	-0.4	29.03	150	37.8%	0.00 [-0.22, 0.23]	
Luger M 2013	-6.7	10.99	21	-1.6	15.2	22	5.4%	-0.38 [-0.98, 0.23]	
Nerylee W 2016	-7.7	6.7	23	-4.9	6.6	22	5.7%	-0.41 [-1.00, 0.18]	
Nuttall F Q 2012	0	14.1	8	-5	14.1	8	2.0%	0.34 [-0.65, 1.32]	
Papakonstantinou E 2010	-8	14.8	17	-3	9.19	17	4.3%	-0.40 [-1.08, 0.28]	et al a ser a s
Westman E C 2008	-8.1	14.99	21	-5.6	15.44	29	6.2%	-0.16 [-0.72, 0.40]	
Wycherley T P 2010	-10	6	12	-7	6	16	3.4%	-0.49 [-1.25, 0.28]	
Total (95% CI)			382			405	100.0%	-0.08 [-0.22, 0.06]	•
Heterogeneity: Chi ² = 11.54.	df = 10 (P = 0.3	2); $ ^2 =$	13%				3	
Test for overall effect: $Z = 1$	09(P = 0)	.27)		500.00X					-1 -0.5 0 0.5 1
									Favours [HP] Favours [LP]
		HP			LP			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	HP	Total	Mean	LP SD	Total	Weight	Std. Mean Difference IV. Fixed, 95% CI	Std. Mean Difference IV. Fixed. 95% Cl
Study or Subgroup Brinkworth G D 2004	Mean -4.6	HP SD 16.39	Total 19	Mean 3.7	LP 50 21.62	Total	Weight 4.3%	Std. Mean Difference IV. Fixed, 95% Cl -0.42 [-1.07, 0.22]	Std. Mean Difference IV. Fixed, 95% Cl
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014	Mean -4.6 -4	HP 5 16.39 24.98	Total 19 66	Mean 3.7 -6	LP 5 21.62 5 44.13	Tota 19 67	Weight 4.3% 15.4%	Std. Mean Difference IV. Fixed, 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40]	Std. Mean Difference IV. Fixed. 95% Cl
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012	Mean -4.6 -4 -9	HP 5 16.39 24.98 20.51	Total 19 66 30	Mean 3.7 -6 -11	LP 21.62 44.13 18.38	Tota 19 67 31	Weight 4.3% 15.4% 7.1%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60]	Std. Mean Difference IV. Fixed. 95% Cl
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012	Mean -4.6 -4 -9 2.2	HP 5 16.39 24.98 20.51 2 27	Total 19 66 30 144	Mean 3.7 -6 -11 1	LP 21.62 44.13 18.38 24.87	Total 19 67 31 150	Weight 4.3% 15.4% 7.1% 34.1%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.66 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27]	Std. Mean Difference IV. Fixed, 95% Cl
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013	Mean -4.6 -4 -9 2.2 -6.2	HP 5 16.39 24.98 20.51 27 19.4	Total 19 66 30 144 21	Mean 3.7 -6 -11 1 0.4	LP 21.62 44.13 18.38 24.87 20.39	Tota 19 67 31 150 22	Weight 4.3% 15.4% 7.1% 34.1% 4.9%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28]	Std. Mean Difference IV. Fixed. 95% Cl
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006	Mean -4.6 -4 -9 2.2 -6.2 -12.3	HP 5 16.39 24.98 20.51 2 27 19.4 8.6	Total 19 66 30 144 21 23	Mean 3.7 -6 -11 1 0.4 -9.8	LP 5 21.62 6 44.13 18.38 24.87 20.39 8 8.9	Total 19 67 31 150 22 22	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.2%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31]	Std. Mean Difference
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W 2016	Mean -4.6 -4 -9 2.2 -6.2 -12.3 -6.24	HP 50 516.39 24.98 20.51 27 19.4 8.6 37	Total 19 66 30 144 21 23 18	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29	LP 21.62 44.13 18.38 24.87 20.39 8.9 16.1	Total 19 67 31 150 22 22 37	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.2% 5.6%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33]	Std. Mean Difference IV. Fixed. 95% CI
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W. 2016 Nuttall F Q 2012	Mean -4.6 -4 -9 2.2 -6.2 -12.3 -6.24 -8	HP <u>SD</u> 16.39 24.98 20.51 27 19.4 8.6 37 20.4	Total 19 66 30 144 21 23 18 8	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29 -6	LP 21.62 44.13 18.38 24.87 20.39 8.9 16.1 5 36	Total 19 67 31 150 22 22 37 8	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.2% 5.6% 1.9%	Std. Mean Difference IV. Fixed. 95% CI -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.06 [-1.04, 0.92]	Std. Mean Difference IV, Fixed, 95% Cl
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W 2016 Nuttall F Q 2012 Papakonstantinou E 2010	Mean -4.6 -9 2.2 -6.2 -12.3 -6.24 -8 -12	HP SD 16.39 24.98 20.51 27 19.4 8.6 37 20.4 20.66	Total 19 66 30 144 21 23 18 8 17	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29 -6 -4	LP SD 21.62 44.13 18.38 24.87 20.39 8.9 16.1 5 366 20.66	Tota 19 67 31 150 22 22 37 8 17	Weight 4.3% 15.4% 7.1% 34.1% 5.2% 5.6% 1.9% 3.9%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.08 [-1.04, 0.92] -0.38 [-1.06, 0.30]	Std. Mean Difference
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W 2016 Nuttall F Q 2012 Papakonstantinou E 2010 Tay J 2014	Mean -4.6 -9 2.2 -6.2 -12.3 -6.24 -8 -12 -7.1	HP SD 16.39 24.98 20.51 27 19.4 8.6 37 20.4 20.66 11.6	Total 19 66 30 144 21 23 18 8 17 41	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29 -6 -4 -5.8	LP SD 21.62 44.13 18.38 24.87 20.39 8.9 16.1 5 366 20.66 11.17	Total 19 67 31 150 22 22 37 8 17 8 17 37	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.6% 1.9% 3.9% 9.0%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.06 [-1.04, 0.92] -0.38 [-1.06, 0.30] -0.11 [-0.56, 0.33]	Std. Mean Difference
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W. 2016 Nuttall F Q 2012 Papakonstantinou E 2010 Tay J 2014 Westman E C 2008	Mean -4.6 -4 -9 2.2 -6.2 -12.3 -6.24 -8 -12 -7.1 -16.6	HP 5 16.39 24.98 20.51 27 19.4 8.6 37 20.4 20.66 11.6 20.1	Total 19 66 30 144 21 23 18 8 17 41 21	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29 -6 -4 -5.8 -10.7	LP 21.62 44.13 18.38 24.87 20.39 3 8.9 16.1 3 66 20.66 11.17 23.2	Total 19 67 31 150 22 22 37 8 17 37 29	Weight 4.3% 15.4% 7.1% 4.9% 5.2% 5.6% 1.9% 3.9% 9.0% 5.6%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.06 [-1.04, 0.92] -0.38 [-1.06, 0.30] -0.11 [-0.56, 0.33] -0.26 [-0.83, 0.30]	Std. Mean Difference
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W 2016 Nuttall F Q 2012 Papakonstantinou E 2010 Tay J 2014 Westman E C 2008 Wycherley T P 2010	Mean -4.6 -9 2.2 -6.2 -12.3 -6.24 -8 -12 -7.1 -16.6 -16	HP 5 16.39 24.98 20.51 27 19.4 8.6 37 20.4 20.66 11.6 20.1 3 13	Total 19 66 30 144 21 23 18 8 17 41 21 21	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29 -6 -4 -5.8 -10.7 -13	LP 21.62 44.13 18.38 24.87 20.39 8.9 16.1 5 36 20.66 5 11.17 23.2 8 11	Total 19 67 31 150 22 22 37 8 17 37 29 16	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.2% 5.6% 1.9% 3.9% 9.0% 5.6% 3.2%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.06 [-1.04, 0.92] -0.38 [-1.06, 0.30] -0.11 [-0.56, 0.33] -0.26 [-0.83, 0.30] -0.25 [-1.00, 0.51]	Std. Mean Difference
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W 2016 Nuttall F Q 2012 Papakonstantinou E 2010 Tay J 2014 Westman E C 2008 Wycherley T P 2010 Total (95% CI)	Mean -4.6 -9 2.2 -6.2 -12.3 -6.2 -12.3 -6.2 -8 -12 -7.1 -16.6 -16	HP 5 16.39 24.98 20.51 27 19.4 8.6 37 20.4 20.66 11.6 20.1 5 13	Total 19 66 30 144 21 23 18 8 17 41 21 12 12 420	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29 -6 -4 -5.8 -10.7 -13	LP 21.62 44.13 18.38 24.87 20.39 8.9 16.1 3 36 20.66 20.66 20.66 11.17 23.2 3 11	Total 19 67 31 150 22 22 37 8 17 37 37 16 16 455	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.6% 3.9% 9.0% 5.6% 3.2% 100.0%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.06 [-1.04, 0.92] -0.38 [-1.06, 0.30] -0.11 [-0.56, 0.33] -0.26 [-0.83, 0.30] -0.25 [-1.00, 0.51] -0.08 [-0.21, 0.05]	Std. Mean Difference
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W 2016 Nuttall F Q 2012 Papakonstantinou E 2010 Tay J 2014 Westman E C 2008 Wycherley T P 2010 Total (95% CI) Heterogeneity: Chi ² = 6.11	Mean -4.6 -4 -9 2.2 -6.2 -12.3 -6.24 -8 -12 -7.1 -16.6 -16	HP 5 16.39 24.98 20.51 27 19.4 8.6 37 20.4 20.66 11.6 20.1 5 13 (P = 0.8	Total 19 66 30 144 21 23 18 8 17 41 21 21 21 22 420 07); ² =	Mean 3.7 -6 -11 1 4 -9.8 -0.29 -6 -4 -5.8 -10.7 -13 0%	LP 21.62 44.13 18.38 24.87 20.39 8.9 16.1 3.66 20.66 11.17 23.2 11	Total 19 67 31 150 22 22 37 8 17 37 29 16 455	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.2% 5.6% 1.9% 3.9% 9.0% 5.6% 3.2% 100.0%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.06 [-1.04, 0.92] -0.38 [-1.06, 0.30] -0.11 [-0.56, 0.33] -0.26 [-0.83, 0.30] -0.25 [-1.00, 0.51] -0.08 [-0.21, 0.05]	Std. Mean Difference
Study or Subgroup Brinkworth G D 2004 Cheryl L. Rock 2014 Guldbrand H 2012 Krebs J D 2012 Luger M 2013 M. E. Daly 2006 Nerylee W 2016 Nuttall F Q 2012 Papakonstantinou E 2010 Tay J 2014 Westman E C 2008 Wycherley T P 2010 Total (95% CI) Heterogeneity: Chi ² = 6.11 Test for overall effect: Z =	Mean -4.6 -4 -9 2.2 -6.2 -12.3 -6.24 -8 -12 -7.1 -16.6 -16	HP 5D 16.39 24.98 20.51 20.51 20.4 20.66 11.6 20.1 5 13 (P = 0.8 5 0.25)	Total 19 66 30 144 21 23 18 8 17 41 21 12 21 12 27); l ² =	Mean 3.7 -6 -11 1 0.4 -9.8 -0.29 -6 -4 -5.8 -10.7 -13 0%	LP 50 51 51 51 51 51 51 51 51 51 51	Total 19 67 31 150 22 22 22 37 8 17 37 8 17 37 8 17 37 8 17 37 8 17 455	Weight 4.3% 15.4% 7.1% 34.1% 4.9% 5.6% 1.9% 3.9% 5.6% 3.2% 100.0%	Std. Mean Difference IV. Fixed. 95% Cl -0.42 [-1.07, 0.22] 0.06 [-0.28, 0.40] 0.10 [-0.40, 0.60] 0.05 [-0.18, 0.27] -0.33 [-0.93, 0.28] -0.28 [-0.87, 0.31] -0.24 [-0.80, 0.33] -0.06 [-1.04, 0.92] -0.38 [-1.06, 0.30] -0.21 [-0.56] -0.08 [-0.21, 0.05] -0.08 [-0.21, 0.05]	Std. Mean Difference IV. Fixed, 95% CI

Figure 6. Meta-analysis for effect of high protein diet on diastolic (A) and systolic (B) blood pressures.

Table 2

Results of subgroup analysis.

Parameters	Subgroups	SMD [95% CI], P	ŕ, p
Weight	HPLC vs. LPHC	0.05 [-0.14, 0.24], .60	0%, .99
-	HPLCHF vs. LPHCLF	-0.21 [-0.38, -0.04], .02	11%, .34
BMI	HPLCHF vs. LPHCLF	-0.05 [-0.24, 0.14], .58	0%, .92
Fat mass	HPLC vs. LPHC	0.03 [-0.18, 0.24], .76	0%, .94
	HPLCHF vs. LPHCLF	-0.08 [-0.39, 0.23], .62	0%, .42
Fat-free mass	HPLC vs. LPHC	0.03 [-0.52, 0.59], .90	0%, .97
	HPLCHF vs. LPHCLF	-0.11 [-0.42, 0.20], .47	36%, .21
Fasting glucose	HPLC vs. LPHC	-0.05 [-0.25, 0.15], .62	0%, .89
5.5	HPLCHF vs. LPHCLF	-0.06 [-0.27, 0.15], .57	42%, .13
Fasting insulin	HPLC vs. LPHC	0.09 [-0.29, 0.48], .64	0%, .69
	HPLCHF vs. LPHCLF	-0.21 [-0.51, 0.09], .16	0%, .84
HbA1c	HPLC vs. LPHC	0.05 [-0.14, 0.24], .62	0%, .42
	HPLCHF vs. LPHCLF	-0.15 [-0.33, 0.03], .10	0%, .78
TC	HPLC vs. LPHC	-0.09 [-0.28, 0.11], .39	0%, .93
	HPLCHF vs. LPHCLF	-0.07 [-0.27, 0.12], .44	0%, .43
TG	HPLC vs. LPHC	-0.13 [-0.52, 0.25], .51	0%, .93
	HPLCHF vs. LPHCLF	-0.23 [-0.41, -0.06], .01	3%, .41
LDL	HPLC vs. LPHC	-0.04 [-0.24, 0.16], .68	0%, 065
	HPLCHF vs. LPHCLF	-0.04 [-0.23, 0.15], .67	0%, .62
HDL	HPLC vs. LPHC	-0.08 [-0.28, 0.11], .41	0%, 1.00
	HPLCHF vs. LPHCLF	0.10 [-0.09, 0.29], .31	0%, .47
Diastolic blood pressure	HPLC vs. LPHC	-0.08 [-0.28, 0.13], .46	47%, .15
	HPLCHF vs. LPHCLF	-0.02 [-0.23, 0.19], .87	9%, .36
Systolic blood pressure	HPLC vs. LPHC	-0.01 [-0.22, 0.21], .95	45%, .18
	HPLCHF vs. LPHCLF	-0.10 [-0.28, 0.08], .28	0%, .90

BMI = body mass index, CI = confidence interval, HDL = high-density lipoprotein cholesterol, HPLC = high protein low carbohydrate, HPLCHF = high protein low carbohydrate high fat, LDL = low-density lipoprotein cholesterol, LPHC = low protein high carbohydrate high carbohydrate low fat, SMD = standard mean difference, TC = total cholesterol, TG = triglycerides.



showed that the HP diet could not significantly improve the weight loss, glycemic control of patients with type 2 diabetes but there may be significant effect of HP diet on lipid metabolism. The inconsistent results may be caused by the difference in included studies. The present studies included more studies and the sample size was larger than that in the previous study.^[14] Moreover, beside body weight, BMI, fat mass, and fat-free mass were also assessed in this meta-analysis to provide more evidences for the effect of HP diet on weight loss; fasting insulin was also analyzed to show the effect of HP diet on glycemic control. In addition, sensitivity analyses and subgroup analyses all indicated consistent results with the overall analysis for the parameters of weight loss and glycemic control. Thus, this meta-analysis provided more evidences to prove no significant effect of HP diet on weight loss and glycemic control in patients with type 2 diabetes, compared with LP diet.

The results also showed that HP diet could significantly affect the TG level of patients with type 2 diabetes, when compared with the LP diets. Sensitivity analysis showed that, after excluding the study of Tay 2014 (HPLCHF vs. LPHCLF), the results changed. Meanwhile, subgroup analyses by HPLC versus LPHC (equal ratio of energy from fat) showed the inconsistent results with the overall analyses. These results indicated that the ratio of energy from fat or carbohydrate in diet may affect the effect of HP diet on TG level. As known for us, HF diets can induce the change of lipid metabolism.^[30,31] Moreover, it was reported different carbohydrate and types of fat intake could result in different TG levels.^[32,33] Thus, it is important to further explore the effect of ratio of energy from fat or carbohydrate in diet on the results and confirm the optimal nutrition component. Similarly, for weight, sensitivity analysis showed that, after excluding the study of Krebs 2012 (HPLC vs. LPHC), the significant effect of HP diet on weight loss presented. Subgroup analyses also showed that the effect of HP diet on weight may be affected by the ratio of energy from fat or carbohydrate in diet. The patients received HPLCHF diet is benefit for weight loss than LPHCLF. More studies should be performed to confirm the results of this study.

In addition, TG is one of the risk factors of cardiovascular diseases.^[34,35] These results indicated HP diet is of benefit for the improvement of risk factors of cardiovascular diseases, and then decrease the risk of cardiovascular diseases in patients with type 2 diabetes. Thus, the HP diet may be benefit for reducing risk of cardiovascular diseases in patients with type 2 diabetes. The investigation on it will be performed in future studies.

There were some limitations in this meta-analysis. First, the treatment time of these studies was greatly different, from 4 weeks to 24 months, which could be another barrier for subgroup analysis. Second, there were many confounding factors (such as country, ethnicity, study design, duration of intervention), which may affect the results of this meta-analysis. Besides, nonsignificant different was found in weight loss, glycemic control, and blood pressure, which may be caused by the impact of some important variables that influence the metabolism sex, age, and duration of intervention. Thus, the results of this study should be further verified by more RCTs with larger sample size and longer follow up.

5. Conclusion

In conclusion, HP diet could be indicated to obtain beneficial results in weight loss and lipid metabolism. Based on the radio in all the included studies, the HP diet with about 30% protein is appropriate. The broader implications of HP diet on patients with type 2 diabetes should be further investigated.

Author contributions

Conceptualization: Wen-Ting Zhao, Ting-Ting Zhao. Data curation: Wen-Ting Zhao. Formal analysis: Wen-Ting Zhao. Funding acquisition: Ting-Ting Zhao. Investigation: Yu Luo. Methodology: Yu Luo, Ying Zhang, Ting-Ting Zhao. Project administration: Yu Luo, Ting-Ting Zhao. Software: Wen-Ting Zhao, Yun Zhou.

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