# **Original Article**

# Long-Term Effects of 4 Popular Diets on Weight Loss and Cardiovascular Risk Factors

# A Systematic Review of Randomized Controlled Trials

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**Background**—We conducted a systematic review to examine the efficacy of the Atkins, South Beach, Weight Watchers (WW), and Zone diets, with a particular focus on sustained weight loss at ≥12 months.

Methods and Results—We systematically searched MEDLINE, EMBASE, and the Cochrane Library of Clinical Trials to identify randomized controlled trials (RCTs) published in English with follow-up ≥4 weeks that examined the effects of these 4 popular diets on weight loss and cardiovascular risk factors. We identified 12 RCTs (n=2559) with follow-up ≥12 months: 10 versus usual care (5 Atkins, 4 WW, and 1 South Beach) and 2 head-to-head (1 of Atkins, WW, and Zone, and 1 of Atkins, Zone, and control). At 12 months, the 10 RCTs comparing popular diets to usual care revealed that only WW was consistently more efficacious at reducing weight (range of mean changes: −3.5 to −6.0 kg versus −0.8 to −5.4 kg; P<0.05 for 3/4 RCTs). However, the 2 head-to-head RCTs suggest that Atkins (range: −2.1 to −4.7 kg), WW (−3.0 kg), Zone (−1.6 to −3.2 kg), and control (−2.2 kg) all achieved modest long-term weight loss. Twenty-four-month data suggest that weight lost with Atkins or WW is partially regained over time.

Conclusions—Head-to-head RCTs, providing the most robust evidence available, demonstrated that Atkins, WW, and Zone achieved modest and similar long-term weight loss. Despite millions of dollars spent on popular commercial diets, data are conflicting and insufficient to identify one popular diet as being more beneficial than the others. (Circ Cardiovasc Qual Outcomes. 2014;7:815-827.)

**Key Words:** diet, carbohydrate-restricted ■ weight loss

A wide variety of diets are available to promote weight loss and improve cardiovascular risk factors, such as lipid levels, blood pressure, and glycemia. Among them, 4 are particularly popular among North Americans. Millions of copies of Atkins, South Beach (SB), and Zone instructional books have been sold, <sup>1-3</sup> and over a million Weight Watchers (WW) members attend its weekly group meetings globally. <sup>4</sup> These diets contribute to a North American weight loss market estimated at >\$66 billion for 2013. <sup>5</sup>

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Each diet has its own philosophy and macronutrient targets. Atkins is a 4-phase diet based on very low carbohydrate intake, with unlimited protein and fat consumption. SB is a 3-phase modified low-carbohydrate high-protein diet. It focuses on controlling carbohydrate intake, as well as eating

lean proteins, mono- or polyunsaturated fats, and low-glycemic index carbohydrates.<sup>2</sup> WW is a food, physical activity, and behavior modification plan that uses a personalized points system to provide caloric intake restriction and weekly group sessions led by plan graduates.<sup>6</sup> Zone is a low-carbohydrate diet that recommends the consumption of low-fat proteins, low-glycemic load carbohydrates, and small amounts of good fat (eg, olive oil, avocado).<sup>3</sup>

The efficacy of these 4 popular commercial diets has been examined in several randomized controlled trials (RCTs), both comparing them to usual care and to each other. However, they provided heterogeneous results. Despite their popularity and their substantial contribution to a billion-dollar industry, the efficacy of these diets in promoting sustained weight loss and improving cardiovascular risk factors remains unclear. Our objective was to examine the efficacy of these 4 diets

Received November 5, 2013; accepted September 18, 2014.

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 $The \ Data \ Supplement is available at \ http://circoutcomes.ahajournals.org/lookup/suppl/doi:10.1161/CIRCOUTCOMES.113.000723/-/DC1.$ 

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Circ Cardiovasc Qual Outcomes is available at http://circoutcomes.ahajournals.org

DOI: 10.1161/CIRCOUTCOMES.113.000723

#### WHAT IS KNOWN

- The obesity epidemic and its accompanying health consequences in North America and worldwide are well-established.
- The efficacy of popular commercial diets at achieving sustained weight loss and improving cardiovascular risk factors remains unclear.

#### WHAT THE STUDY ADDS

- This systematic review demonstrates that available data
  on the efficacy of popular commercial diets are limited
  and heterogeneous, with 2 head-to-head trials suggesting that Atkins, Weight Watchers, and Zone achieve
  modest and similar long-term weight loss, as well as
  similar effects on cardiovascular risk factor levels.
- South Beach was only assessed in 1 long-term trial, which found no difference in weight loss versus usual care, and no data were reported on its effects on cardiovascular risk factor levels.
- Despite millions of dollars spent in the weight loss industry, available data are conflicting and insufficient to identify one popular diet as being more beneficial than the others.

in promoting weight loss and improving cardiovascular risk factors (ie, anthropometric measures, lipid profiles, blood pressure, and glycemia), with a particular focus on sustained weight loss at  $\geq 12$  months.

## **Methods**

### **Search Strategy**

We systematically searched the MEDLINE, EMBASE, and Cochrane Library of Clinical Trials databases from inception to May 2014 to identify RCTs conducted in adults and published in English that examined the effect of Atkins, SB, Zone, or WW on weight loss and cardiovascular risk factors. These 4 diets were chosen as a representative and pragmatic sample of popular commercial diets: the first 3 are best-selling book-based diets, 1-3 whereas WW, another leading popular commercial diet, involves a contrasting meeting-based approach.<sup>4</sup> Our search involved the following keywords: Atkins, calorie restriction, carbohydrate-restricted, diet, diet fads, diet therapy, fat-restricted, high-fiber, high-protein, low-carbohydrate, low-fat, popular diet, obese, Ornish, overweight, protein-restricted, SB, vegetarian diet, weight loss program, WW, and Zone. Although Ornish was initially included in our search, it is predominantly used and classified by US Medicare as Intensive Cardiac Rehabilitation.7 We thus excluded Ornish from the present study. Finally, we hand-searched references from published RCTs, relevant reviews, and previous meta-analyses for additional RCTs.

#### **Inclusion Criteria**

We included RCTs that examined the effects of Atkins, SB, WW, and Zone (diets described in Table I in the Data Supplement) on weight loss and cardiovascular risk factors with follow-up  $\geq 4$  weeks. A 4-week grace period was allowed for the classification of short- versus long-term RCTs (ie, <12 months versus  $\geq 12$  months) to account for RCTs that measured follow-up in weeks rather than months. We restricted inclusion to RCTs comparing these diets to usual care or to each other. To reduce heterogeneity and specifically examine these 4 popular diets, we also restricted inclusion to reports describing these diets by name or referencing specific manuals for those diets. For multiphase diets, included RCTs must have examined all phases preceding their final weight maintenance phase.

We excluded trials evaluating the effects of popular diets on weight maintenance, with participants with malignancies or post-transplant, without an appropriate active or usual care reference group, and those randomizing participants to an arm where they could preferentially select their diet, unless data from these participants were not combined with those of participants randomized directly to the studied diets.

## **Data Extraction and Analysis**

Data on study characteristics, study population, demographic and clinical characteristics, intervention characteristics, and use of any

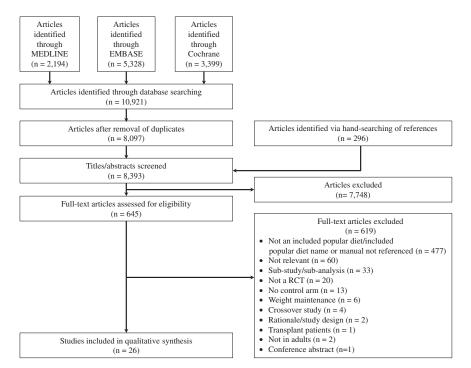


Figure 1. PRISMA flow diagram.

Table 1. Baseline Characteristics of Participants in Long-Term (≥12 mo) Trials

	Participants	ants					Nutritional	Everoise					BMI
Study	Randomized	Analyzed	Duration, wk	Population	Ar	Arms	Counseling	Prescription	Age, y	Female, %	White, %	Weight, kg	kg/m²
Atkins													
Foster (2003) <sup>11</sup>	63	63*	52	Obese, otherwise healthy	Atkins	High-carbohydrate/ LFD with LEARN†	Yes	No	44.1	68.3	76.2	98.5	34.1
Davis (2009) <sup>12</sup>	105	105‡	52	BMI ≥25, T2DM	Atkins	LFD modeled after Diabetes Prevention Program with CR	Yes	NO	53.5	78.1	14.3	97.1	36.0
Goldstein (2011) <sup>13</sup>	52	308	52	BMI: 30–39.9, T2DM	Modified Atkins	ADA diet with CR	Yes	No	56.0	51.9	N R	92.0	33.2
					after 4-week Dieta Hyperten:	after 4-week Dietary Approach to Stop Hypertension run-in							
Shai (2008)⁴¶	213	213#	104	BMI ≥27 aged 40–65 y, or T2DM, or coronary heart disease	Atkins	AHA LFD with CR	Yes	No	51.5	11.7	N.	91.6	30.7
Foster (2010) <sup>15</sup>	307	307**	104	BMI: 30–40, otherwise healthy	Atkins with comprehe progr	Atkins LFD with CR with comprehensive behavioral program††	Yes	Yes	45.5	8.79	70.7	103.4	36.1
South Beach													
Swenson (2007) <sup>16</sup>	32#	26§§	52	Severely obese postgastric bypass	South Beach	AHA LFD	Yes	Yes	40.9‡‡	#9.06	84.4##	184.9‡‡	48.9‡‡
Weight Watchers													
Pinto (2013)™¶	26	111111111111111111111111111111111111111	48	BMI: 27–50 aged 30–65 y	WW	BWL intervention¶¶	Yes for BWL intervention	Yes	49.1	89.5	NR	98.1	35.9
Jebb (2011) <sup>18</sup>	772	772#	52	BMI: 27–35 with ≥1 other risk factor for obesity-related disease##	WW	Standard care at general practice	Yes for standard care	No	47.4	86.5	N.	86.7	31.4
Jolly (2011)¹٩¶***	170	170+++	52	Overweight/obese ± comorbidities‡‡‡	WW	Nurse-led individual support at general practice	Yes for individual support	NO	50.6	70.0	88.2	92.9	33.6
Heshka (2003) <sup>20</sup>	423	423§§§	104	BMI: 27–40, ± comorbidities	WW	Self-help Y	Yes for self-help	No	44.5	84.6	N	93.6	33.7 (Continued)

Continued Table 1.

	Participants	ants						Nutritional	Exercise					
Study	Randomized	Analyzed	Randomized Analyzed Duration, wk Population	Population		Arms		Counseling	Prescription Age, y Female, % White, % Weight, kg BMI, kg/m²	Age, y	Female, %	White, %	Weight, kg	BMI, kg/m²
Head-to-Head Dansinger (2005)²¹¶	120	120##	52	BMI: 27–42, with ≥1 cardiometabolic	Atkins	WW	Zone	Yes	ON N	49.0	53.3	73.3	98.7	34.7
Gardner (2007)²²¶	235	235##	52	BMI: 27-40, premenopausal, otherwise healthy	Atkins	Zone	LEARN†	Yes	No	40.7	100	72.3	85.0	31.3

ADA indicates American Diabetes Association, AHA, American Heart Association; BMI, body mass index; BWL, behavioral weight loss; CR, calorie restriction; LFD, low-fat diet; NR, not reported; T2DM, type 2 diabetes mellitus; and WW, Weight Watchers.

|Very low carbohydrate content of 25 g/d for the first 6 wk postrandomization increased to 40 g/d thereafter, with unrestricted calorie, protein, or fat intake and encouraging participants to increase their fat consumption through foods rich in monounsaturated fatty acids

Repeated-measures analysis of variance (ANOVA) with baseline observation carried forward (BOCF)

<sup>-</sup>The LEARN Program for Weight Management manual contains 16 lessons addressing different aspects of weight management

thrention-to-treat (ITT) analysis with hierarchical linear models to analyze all available data.

SRepeated-measures ANOVA ignoring dropouts.

<sup>¶</sup>Trial had other arms that were not included.

<sup>#</sup>ITT analysis with last observation carried forward (LOCF)

<sup>++</sup>Delivered in-person to participants through group sessions held throughout the study follow-up, and comprising topics on behavioral skills (eg, self-monitoring, stimulus control, relapse management); an exercise prescription; \*\*Random-effects linear model fitted to all available data for each variable for all 307 participants.

and daily multivitamin supplements.

<sup>#</sup>Modified ITT analysis including 32 patients who completed ≥1 postoperative assessment (baseline assessment completed by n=43)

<sup>|| ||</sup> Linear mixed models including all participants and using all available data.

<sup>||</sup>Emphasizing behavioral skills and comprising closed-group meetings led by BWL expert; moderate CR dietary intervention with <25% fat; and an exercise prescription.

<sup>##</sup>Central adiposity, T2DM not insulin-treated, family history of diabetes mellitus, previous gestational diabetes mellitus, impaired glucose tolerance or fasting glycemia, mild-to-moderate dyslipidemia, hypertension treatment, polycystic ovarian syndrome or infertility with no other apparent cause than weight, lower-limb osteoarthritis, and abdominal hernia

<sup>\*\*\*</sup>Twelve-week dietary intervention

<sup>#</sup>Trial eligibility: South Asians without comorbidity BMI > 25, with comorbidity, BMI > 23; white Europeans/all other ethnic groups without comorbidities BMI > 30, with comorbidities, BMI > 28.

<sup>§§§</sup>ITT analysis with LOCF or linear interpolation and BOCF for participants with no follow-up data.

<sup>|| ||</sup> Fasting glucose 26.1 mmol/L, total cholesterol >5.2 mmol/L, low-density lipoprotein cholesterol >3.4 mmol/L, high-density lipoprotein cholesterol <1.0 mmol/L, triglycerides <1.7 mmol/L, systolic blood pressure <145 mm Hg, diastolic blood pressure ≥90 mm Hg, or current use of medication for hypertension, diabetes mellitus, or dyslipidemia

cointerventions (eg, exercise, nutritional counseling) were independently extracted by 2 reviewers using a standardized form, with disagreements resolved by consensus or by a third reviewer. Nutritional counseling was defined as any additional, clearly specified one-onone or group meeting with registered dietitians, nutritionists, or other healthcare professionals or research staff, with training or experience in obesity management. Outcome data were extracted for the longest follow-up time available; for studies with 24-month follow-up, 12-month data were also extracted. In studies where authors used multiple statistical methods, we extracted the results of their primary analysis. Our primary end point was sustained weight loss, defined as mean weight change at ≥12 months, reported in kg or as mean percentage change. Secondary end points included mean change and mean percentage change in body mass index, body fat, waist circumference, waist-to-hip ratio, fasting glucose, fasting insulin, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, systolic blood pressure (SBP), diastolic blood pressure (DBP), and the prevalence of adverse events. Close examination of extracted data revealed significant clinical heterogeneity; quantitative meta-analyses were, therefore, not undertaken.<sup>8,9</sup> Finally, RCT quality was assessed using the Cochrane Collaboration's tool for assessing risk of bias10 independently by 2 reviewers, with disagreements resolved by consensus or by a third reviewer.

#### Results

#### Search Results

Our search yielded 8393 potentially relevant publications (Figure 1). After screening titles and abstracts, 645 were retrieved for full-text review. Of those, 26 RCTs met our inclusion criteria.

#### **Study Characteristics**

Of the 26 included RCTs, 14 (n=1016) had short-term follow-up (<12 months) (Table II in the Data Supplement) and 12 (n=2559) had long-term follow-up (≥12 months)<sup>11-22</sup> (Table 1). Ten long-term RCTs were versus usual care (5 Atkins, 4 WW, and 1 SB), and 2 were head-to-head (1 of Atkins, WW, and Zone; 1 of Atkins, Zone, and control; Table 1). There was significant heterogeneity in study populations, control interventions, as well as specific components and delivery of the popular diets, which prevented quantitative synthesis. Finally, most of the 26 included RCTs had an unclear risk of bias in

the domains of allocation concealment, blinding, and incomplete data reporting. Six and 5 RCTs, respectively, had high risks of bias in the latter 2 domains (Figure 2), largely because of their poor or incomplete outcome collection and high rate of loss to follow-up.

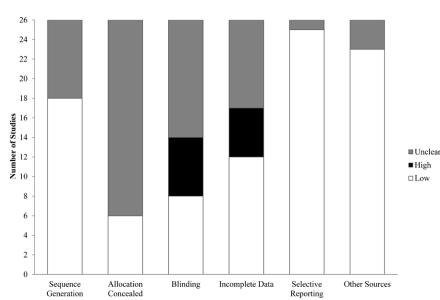
## **Participant Characteristics**

The majority of the 26 included RCTs assessed the effects of popular diets in otherwise healthy overweight or obese individuals, whose mean age ranged from 35.5 to 56.0 years (median: 45.0 years; Table II in the Data Supplement; Table 1). Mean weight of participants ranged from 65.9 to 184.9 kg (median: 92.5 kg), with 1 RCT conducted in Chinese women<sup>23</sup> and another evaluating the efficacy of SB in severely obese subjects postgastric bypass surgery. Dropouts ≥20% were reported in 13 included RCTs. Finally, the majority of studies were conducted in young, white, obese women, with few data available on their use in men and in individuals whose body mass index <30 kg/m² (Table II in the Data Supplement; Table 1).

# Weight Loss and Change in Other Anthropometric Measures

Short-term RCTs revealed generally greater weight loss and improvements in other anthropometric measures with popular diets, with some heterogeneity on Zone.<sup>24,25</sup> Findings from the 2 head-to-head RCTs suggest that Atkins, WW, and Zone achieved similar short-term weight loss and improvements in other anthropometric measures<sup>25,26</sup> (Table III in the Data Supplement).

There was also heterogeneous reporting of changes in weight and other anthropometric measures in long-term RCTs (Table 2). At 12 months, the 10 RCTs comparing popular diets to usual care showed that only WW was consistently more efficacious at reducing weight (range of mean changes: –3.5 to –6.0 kg versus –0.8 to –5.4 kg; *P*<0.05 for 3/4 RCTs; Table 2; Figure 3). This reduction was accompanied by statistically significant improvements in other anthropometric measures in the 3 WW RCTs reporting these outcomes. Atkins' efficacy was inconsistent at 12 and 24 months, whereas the single SB RCT<sup>16</sup> found no difference versus usual care among severely obese patients postgastric



**Figure 2.** Risk of bias of included trials as per the Cochrane Risk of Bias Tool.

Table 2. Change in Body Weight and Other Anthropometric Measures in Long-Term (≥12 mo) Trials\*

						•					
			Weight			Body Mass Index		Waist Ci	Waist Circumference		Body Fat
Study	Follow-Up, mo	Baseline, kg	Mean Change, kg	% Change	Baseline, kg/m²	Mean Change, kg/m²	% Change	Baseline, cm	Mean Change, cm	Baseline, kg or %	Mean Change, kg or %
Atkins											
Foster (2003) <sup>11</sup>											
Control	12	$98.3\pm16.4$	NR	$-2.5\pm6.3$	$34.4\pm3.1$	N R	R	N	Æ	NR	N R N
Intervention		98.7±19.5		-4.4±6.7	$33.9 \pm 3.8$						
Davis (2009) 12											
Control	12	101±19	-3.1±5.8	NR	37±6	N R	N	NR	RN	NR	N
Intervention		93.6±18	-3.1±4.8		35∓6						
Goldstein (2011) <sup>13</sup>											
Control	12	92.2±13.7	$-5.4\pm5.7$	NR	$33.3\pm3.0$	N	M	113±10	R	NR	NR
Intervention		91.7±10.2	$-3.4\pm4.0$		$33.1 \pm 3.6$			112±8			
Shai (2008) <sup>14</sup> †											
Control	12	91.3±12.3	NR		$30.6 \pm 3.2$	N R		$105.3\pm9.2$	Æ		
Intervention		91.8±14.3		N	$30.8 \pm 3.5$		N	$106.3\pm9.1$		N	N N
Control	24	91.3±12.3	-2.9±4.2		$30.6 \pm 3.2$	-1.0±1.4		$105.3\pm9.2$	$-2.8\pm4.3$		
Intervention		91.8±14.3	-4.7±6.5‡		$30.8 \pm 3.5$	-1.5±2.1		$106.3\pm9.1$	$-3.8\pm5.2$		
Foster (2010) <sup>15</sup>											
Control	12	$103.5\pm14.4$	-10.81 (-12.4, -9.28)		$36.1 \pm 3.46$					40.4±7.8 kg	-7.29 kg (-8.55, -6.03)
Intervention		$103.3\pm15.5$	-10.87 (-12.1, -9.67)	NR	$36.1 \pm 3.59$	N	NR	NR	R	40±7.6 kg	-7.83 kg (-7.89, -6.14)
Control	24	$103.5\pm14.4$	-7.4 (-9.1, -5.63)		$36.1 \pm 3.46$					40.4±7.8 kg	-3.84 kg (-5.03, -2.64)
Intervention		$103.3\pm15.5$	-6.3 (-8.06, -4.63)		$36.1 \pm 3.59$					40±7.6 kg	-3.99 kg (-5.50, -2.79)
South Beach											
Swenson (2007) <sup>16</sup>											
Control	12	166.5±71	NR	$-60.3\pm15.3$ §	46.3 <del>±</del> 9.4	N R	$-14.0\pm5.5$	140±25	R	58.4±14 kg	N
Intervention		197.5±85		$-59.6\pm13.0$ §	50.7±8.7		$-17.0\pm4.5$	145±16		70.5±21 kg	
Weight Watchers											
Pinto (2013) <sup>17</sup>											
Control	12	97.3±17.1	-5.4 (SE: 0.8)	NR	$36.4\pm5.0$	N R	M	NR	R	NR	N
Intervention		$98.9\pm19.1$	-6.0 (SE: 0.8)		$35.5 \pm 5.3$						
Jebb (2011) <sup>18</sup>											
Control	12	86.5±11.5	-2.25 (SE: 0.21)	NR	31.3±2.6	NR	NR	$99.9 \pm 9.3$	-3.16 (SE: 0.28)	32.9±7.4 kg	-1.85 (SE: 0.19) kg
Intervention		86.9±11.6	-5.06 (SE: 0.31)‡		31.5±2.6			100±9.2	-5.6 (SE: 0.37)‡	33.3±7.0 kg	-4.23 (SE: 0.28) kg‡
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			Weight			Body Mass Index		Waist Cl	Waist Circumference		Body Fat
Study	Follow-Up, mo	Baseline, kg	Mean Change, kg	% Change	Baseline, kg/m²	Mean Change, kg/m²	% Change	Baseline, cm	Mean Change, cm	Baseline, kg or %	Mean Change, kg or %
Jolly (2011) <sup>19</sup> †											
Control	12	92.04±14.75	-0.8(-2.0, 0.4)	NB	$33.06 \pm 3.5$	-0.32 (-0.7, 0.1)	NB	N	NB	N	N
Intervention	!	93.47±14.15	-3.5 (-4.8, -2.1)		$33.96 \pm 3.9$	-1.17 (-1.7, -0.7)		į	į	į	
Heshka (2003) <sup>20</sup>											
Control	12	93.1±14.4	-1.3 (SE: 0.4)		$33.6 \pm 3.7$	-0.5 (SE: 0.2)		99±12	-1.6 (SE: 0.6)	42 <del>+</del> 9%	
Intervention	!	94.2±13.1	-4.3 (SE: 0.4)#	NB	$33.8 \pm 3.4$	-1.6 (SE: 0.2)#	NB	101±12	-4.1 (SE: 0.6)‡	44±8%	N
Control	24	93.1±14.4	-0.2 (SE: 0.4)		$33.6 \pm 3.7$	-0.2 (SE: 0.2)		99±12	-0.6 (SE: 0.6)	45±9%	
Intervention	I	94.2±13.1	-2.9 (SE: 0.5)#		$33.8 \pm 3.4$	-1.1 (SE: 0.2)#		101±12	-2.4 (SE: 0.6)‡	44±8%	
Head-to-Head											
Dansinger (2005) <sup>21</sup> †											
Atkins		100±14	-2.1±4.8		$35 \pm 3.5$	-0.7±1.6		109±11	$-2.5\pm4.5$		
Weight Watchers	12	97±14	$-3.0\pm4.9$	N	$35\pm 3.8$	-1.1±1.7	N	108±11	$-3.3\pm5.4$	R	NR
Zone		99±18	$-3.2\pm6.0$		$34\pm4.5$	$-1.1\pm2.0$		108±13	$-2.9\pm5.3$		
Gardner (2007) <sup>22</sup> †											
Control		85±14	-2.2(-3.6, -0.8)		31±4	$-0.9\pm2.0$				38∓6%	$-1.0\pm3.4\%$
Atkins	12	86±13	-4.7 (-6.3, -3.1)¶	NR	32±4	-1.7±2.5¶	NR	NR	NR	41±6%	$-2.9\pm4.8\%$
Zone		84±12	-1.6(-2.8, -0.4)		31±3	$-0.5\pm2.0$				40 <del>±</del> 6%	$-1.3\pm3.4\%$

All values are mean±SD or mean (95% CI) unless otherwise indicated. NR indicates not reported; and SE, standard error.

\* Only long-term follow-up data from these studies are presented in this table.

Only long-term lonow-up data nom tress studies are pres Trial had other arms that were not included.

‡P<0.05 for difference between groups.

SLoss of excess body weight.  $\|P<0.05$  for difference between groups; calculated using data presented in the original article.  $\PP<0.05$  vs. Zone.

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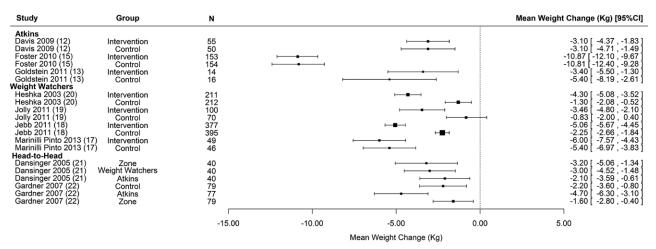


Figure 3. Forest plot for mean weight change from baseline to 12 months among long-term trials. N is the number of patients included in the 12-month analysis. CI indicates confidence interval.

bypass surgery (Table 2; Figure 3). Head-to-head comparisons of Atkins, WW, and Zone, as well as of Atkins, Zone, and control, suggest that at 12 months, Atkins (range: -2.1 to -4.7 kg), WW (-3.0 kg), Zone (-1.6 to -3.2 kg), and control (-2.2 kg) all achieved modest weight loss. 21,22 The only statistically significant comparisons from these head-to-head RCTs were reported by Gardner et al<sup>22</sup> for Atkins versus Zone for weight loss and body mass index (Table 2; Figure 3). Overall, much of the weight loss achieved early in follow-up (eg, <6 months) was regained over time such that these diets were generally similar in efficacy relative to control by 12 months (data not shown). This trend was particularly prominent with the Atkins diet. Similarly, 24-month data suggest that the weight lost with Atkins or WW at 12 months is partially regained over time (Table 2).

### **Lipid Levels**

Of the 14 short-term RCTs, 3 examined the effect of SB, WW, and Zone on lipid profiles. Eight RCTs provided data on Atkins and suggest a favorable impact on high-density lipoprotein cholesterol and triglycerides relative to usual care, WW, and Zone. However, Atkins may have an adverse effect on low-density lipoprotein cholesterol levels, with unchanged or increased levels observed in 5 RCTs (Table IV in the Data Supplement). Long-term RCTs comparing Atkins to usual care showed significant improvements in high-density lipoprotein cholesterol and, to a lesser extent, triglyceride levels at 12 and 24 months; there was no evidence of a low-density lipoprotein cholesterol increase (Table 3). There were no or limited data on the effect of SB and WW on lipid profiles versus usual care at ≥12 months. Finally, results from the 2 long-term head-tohead RCTs found no marked differences between the Atkins, WW, and Zone diets in improving lipid levels at 12 months, with only a significant improvement in triglyceride levels for Atkins versus Zone reported by Gardner et al<sup>22</sup> (Table 3).

## **Blood Pressure**

Findings from short-term RCTs showed that Atkins and WW had favorable effects on SBP and DBP, with benefits being greatest with the Atkins diet. No blood pressure data were available regarding SB, and only 1 RCT provided such data regarding Zone (Table V in the Data Supplement). Atkins and

WW had inconsistent long-term effects on SBP and DBP versus usual care, with only a significant improvement in DBP at 12 months with WW reported by Heshka et al<sup>20</sup> and at 24 months with Atkins reported by Foster et al.<sup>15</sup> There were no blood pressure data for SB (Table 4). Findings from the 2 head-to-head RCTs indicated that Zone was less effective than Atkins and WW and similar to usual care at improving SBP and DBP, even increasing SBP in 1 RCT. There were no statistically significant comparisons in these 2 trials, with the exception of Atkins being more effective than Zone and control at improving SBP in the study by Gardner et al<sup>22</sup> (Table 4).

#### **Glycemic Control Measures**

Overall, there were no major differences in glycemic control measures between popular diets in short-term RCTs. Atkins showed a trend toward worsened fasting glucose, but improved fasting insulin. There was limited evidence available on WW and Zone (1 RCT each) (Table VI in the Data Supplement). Limited long-term evidence was also available on the impact of popular diets on glycemic control measures versus usual care (Atkins: 1 RCT; WW: 2 RCTs) (Table VII in the Data Supplement). Findings from head-to-head RCTs suggest that Atkins, WW, Zone, and control were similar at improving fasting glucose and insulin at 12 months, with no statistically significant difference between groups (Table VII in the Data Supplement).

#### Discussion

Our systematic review was designed to examine the currently available evidence on the efficacy of the Atkins, SB, WW, and Zone diets at promoting weight loss and improving cardiovascular risk factors, with a particular focus on sustained weight loss at ≥12 months. We found a small number of heterogeneous RCTs. Although this heterogeneity prevented quantitative synthesis of our findings,<sup>8,9</sup> qualitative synthesis of this limited body of evidence was nevertheless informative.

Our results suggest that all 4 diets are modestly efficacious for short-term weight loss, but that these benefits are not sustained long-term. Long-term RCTs comparing popular diets to usual care suggested that WW might be more efficacious than Atkins and SB at 12 months, as it was the only diet achieving consistent weight loss across trials. These findings were

Table 3. Change in Lipid Levels in Long-Term (≥12 mo) Trials\*

			Total Cholesterol		Low-[	Low-Density Lipoprotein Cholesterol	lesterol	High-De	High-Density Lipoprotein Cholesterol	olesterol		Triglycerides	
Study	Follow-Up, mo	Baseline, mmol/L	Mean Change, mmol/L	% Change	Baseline, mmol/L	Mean Change, mmol/L	% Change	Baseline, mmol/L	Mean Change, mmol/L	% Change	Baseline, mmol/L	Mean Change, mmol/L	% Change
Atkins													
Foster (2003) <sup>11</sup>													
Control	12	2±0.8	NR	$-0.075\pm0.21$	$3.1\pm0.8$	NR	$-0.08\pm0.31$	$1.3\pm0.3$	NR	$0.041\pm0.29$	$1.4\pm0.9$	N	$0.008\pm0.04$
Intervention		$5.2\pm0.9$		$0.003\pm0.25$	3.4±0.8		$0.008\pm0.43$	$1.2\pm0.3$		0.28±0.50† 1.5±1.3	1.5±1.3		$-0.19\pm0.26$ †
Davis (2009) <sup>12</sup>													
Control	12	$4.3\pm0.9$	-0.1±0.7	N	2.4±0.7	$-0.2\pm0.7$	R	$1.2\pm0.3$	$0.1\pm0.2$	NR	$1.4\pm0.7$	0.0±0.0	NR
Intervention		4.4±0.8	0.1±0.8		$2.5\pm0.7$	$-0.04\pm0.6$		$1.3\pm0.2$	$0.2\pm0.3$ †		1.4±0.8	$-0.2\pm0.9$	
Goldstein (2011) <sup>13</sup>													
Control	12	$5.17\pm0.96$	$-0.05\pm0.54$	N	N.	NR	M	$1.1\pm0.3$	$0.14\pm0.23$	NR	$2.21\pm0.97$	$-0.045\pm0.62$	NR
Intervention		$5.02\pm0.65$	$-0.2\pm0.7$					$1.14\pm0.34$	$0.11\pm0.2$		2.31±1.12	$-0.45\pm0.76$	
Shai (2008) <sup>14</sup> ‡													
Control	12	M	NR	NR	$3.0\pm0.9$	NR	M	1±0.3	NR	NR	1.8±0.7	NR	NR
Intervention					$3.0\pm0.9$			1±0.2			2.1±1.3		
Control	24				$3.0\pm0.9$	-0.001		1±0.3	0.17		1.8±0.7	-0.032	
Intervention					$3.0\pm0.9$	-0.078		1±0.2	0.22†		2.1±1.3	-0.27†	
Foster (2010) <sup>15</sup>													
Control		$5.0\pm0.9$			$3.2\pm0.8$	$-0.22\ (-0.33, -0.12)$		$1.2\pm0.3$	0.10 (0.065, 0.14)		1.4±0.8	-0.36 (-0.45, -0.27)	
Intervention	12	4.9±0.8	NR	NB	$3.1\pm0.7$	$-0.22\ (-0.33, -0.11)$	M	$1.2\pm0.4$	0.21 (0.16, 0.25)†	NR	1.3±0.6	-0.20 (-0.32, -0.09)†	NR
Control	24	$5.0\pm0.9$			$3.2\pm0.8$	-0.21 (-0.3, -0.12)		$1.2\pm0.3$	0.12 (0.07, 0.14)		1.4±0.8	-0.16 (-0.29, -0.04)	
Intervention		4.9±0.8			$3.1\pm0.7$	$-0.12\ (-0.24,\ -0.01)$		$1.2\pm0.4$	0.2 (0.16, 0.25)†		1.3±0.6	$-0.14 \; (-0.26,  -0.02)$	
South Beach													
Swenson (2007) <sup>16</sup>													
Control	12	NR	NR	NR	NR	NR	M	NR	NR	NR	NR	NR	NR
Intervention													
Weight Watchers													
Pinto (2013) <sup>17</sup>													
Control	12	M	NR	NR	R	NR	M	NR	NR	NR	NR	N	NR
Intervention													
Jebb (2011) <sup>18</sup>													
Control	12	NR	0.03 (SE: 0.03)	N	NR	0.02 (SE: 0.03)	NR	NR	0.04 (SE: 0.01)	NR	NR	-0.06 (SE: 0.03)	NR
Intervention			0.00 (SE: 0.04)			-0.01 (SE: 0.03)			0.06 (SE: 0.01)			-0.09 (SE: 0.03)	:
													(conunuea)

Continued Table 3.

			Total Cholesterol	_	Low-De	Low-Density Lipoprotein Cholesterol	olesterol	High-De	High-Density Lipoprotein Cholesterol	olesterol		Triglycerides	
Study	Follow-Up, Baseline, mo mmol/L	Baseline, mmol/L	Mean Change, mmol/L	% Change	Baseline, mmol/L	Mean Change, mmol/L	% Change	Baseline, mmol/L	Mean Change, mmol/L	% Change	Baseline, mmol/L	Mean Change, mmol/L	% Change
Jolly (2011) <sup>19</sup> ‡													
Control	12	N	Æ	NR	NR	NR	M	R	NR	NR	N	NR	NR
Intervention													
Heshka (2003) <sup>20</sup>													
Control	12	5.4±0.92	5.4±0.92 -0.25 (SE: 0.04)					$1.26\pm0.33$	0.021 (SE: 0.02)		$1.59\pm0.93$	0.017 (SE: 0.043)	
Intervention		$5.54\pm0.98$	5.54±0.98 -0.23 (SE: 0.04)	NB	N	N	R	$1.29\pm0.31$	0.052 (SE: 0.02)	N	1.75±1.12	-0.088 (SE: 0.042)	NB
Control	24	$5.4\pm0.92$	5.4±0.92 -0.3 (SE: 0.05)					$1.26\pm0.33$	0.0 (SE: 0.02)		$1.59\pm0.93$	-0.0 (SE: 0.04)	
Intervention		$5.54\pm0.98$	5.54±0.98 -0.3 (SE: 0.05)					$1.29\pm0.31$	0.0 (SE: 0.02)		1.75±1.12	-0.0 (SE: 0.05)	
Head-to-Head													
Dansinger (2005) <sup>21</sup> †‡	<u></u>												
Atkins		$5.53\pm0.8$	$-0.1\pm0.6$		$3.52\pm0.8$	$-0.2\pm0.6$		$1.24\pm0.41$	0.1±0.2		1.72±1.12	0.0±0.9	
Weight Watchers	12	5.72±1.19	$-0.2\pm0.6$	NR	3.67±1	$-0.2\pm0.7$	Æ	$1.22\pm0.06$	$0.1\pm0.3$	N	$1.74\pm0.98$	$-0.1\pm0.7$	NR
Zone		5.74±1.19	$-0.3\pm0.9$		$3.57\pm1.16$	$-0.3\pm0.9$		$1.24\pm0.34$	$0.1\pm0.3$		$2.19\pm1.39$	0.0±1.7	
Gardner (2007) <sup>22</sup> ‡													
Control					$2.69\pm0.75$	0.0±0.4		$1.31\pm0.28$	0.1±0.2		1.34±0.82	$-0.2\pm0.7$	
Atkins	12	NR	R	NR	$2.82\pm0.75$	9.0∓0.0	NR	$1.37 \pm 0.36$	0.1±0.2	NR	1.4±0.88	$-0.3\pm0.7$ §	NR
Zone					$2.95\pm0.83$	$0.0\pm0.5$		$1.34\pm0.28$	0.1±0.2		1.39±1.11	$0.0\pm0.5$	

All values are mean±SD or mean (95% CI) unless otherwise indicated. NR indicates not reported; and SE, standard error. \*Only long-term follow-up data from these studies are presented in this table.

†P<0.05 for difference between groups.

‡Trial had other arms that were not included.

§P<0.05 vs. Zone.

Table 4. Change in Blood Pressure in Long-Term (≥12 mo) Trials\*

		S	ystolic Blood Pressure		D	iastolic Blood Pressure	
Study	Follow-Up, mo	Baseline, mm Hg	Mean Change, mm Hg	% Change	Baseline, mm Hg	Mean Change, mm Hg	% Change
Atkins							
Foster (2003)11							
Control	10	123.3±14.1	ND	1.7±11.8	77.6±10.8	ND	-3.8±13.2
Intervention	12	120.5±11.0	NR	-1.0±9.4	74.6±8.5	NR	-3.7±12.4
Davis (2009) <sup>12</sup>		120.0±11.0		-1.0±3.4	74.0±0.5		-0.7 ± 12.4
Control		130±17	-1.8±22.6		77±10	-2.2±11.6	
Intervention	12	125±18	2.0±15.6	NR	77±10 73±9	-2.2±11.0 -2.9±9.4	NR
Goldstein (2011) <sup>13</sup>		125±10	2.0±13.0		73±9	-2.5±5.4	
Control		100.14	E . 10		00.0	20.7	
	12	136±14	-5±12	NR	80±9	-3.8±7	NR
Intervention		140±17	-14±38		79±10	-8.3±19	
Shai (2008) <sup>14</sup> †		1000 100			70.1.0.1		
Control	12	129.6±13.2	NR		79.1±9.1	NR	
Intervention		130.8±15.1		NR	79.4±9.1		NR
Control	24	129.6±13.2	-4.3±11.8		79.1±9.1	$-0.9\pm8.1$	
Intervention		130.8±15.1	-3.9±12.8		79.4±9.1	$-0.8\pm8.7$	
Foster (2010) <sup>15</sup>							
Control	12	124.6±15.8	-4.06 (-6.07, -2.05)		76±9.7	-2.19 (-3.58, -0.79)	
Intervention		124.3±14.1	-5.64 (-7.62, -3.67)	NR	73.9±9.4	-3.25 (-4.74, -1.76)	NR
Control	24	124.6±15.8	-2.6 (-5.07, -0.12)		76±9.7	-0.5 (-2.13, 1.13)	
Intervention		124.3±14.1	-2.7 (-5.08, -0.27)		73.9±9.4	-3.2 (-4.66, -1.73)‡	
South Beach							
Swenson (2007) <sup>16</sup>							
Control	12	NR	NR	NR	NR	NR	NR
Intervention		1111	1411	1411		1411	1411
Weight Watchers							
Pinto (2013) <sup>17</sup>							
Control	12	NR	NR	NR	NR	NR	NR
Intervention	12	INU	INU	INIT	INIT	INIT	INIT
Jebb (2011) <sup>18</sup>							
Control	10	124.2±14.7	-1.50 (SE: 0.64)	ND	79.1±9.0	-1.29 (SE: 0.41)	ND
Intervention	12	124.7±17.1	-2.37 (SE: 0.67)	NR	78.2±9.8	-1.61 (SE: 0.44)	NR
Jolly (2011) <sup>19</sup> †		12111 = 1711	2.07 (02. 0.07)		70.2_0.0	1.01 (02. 0.11)	
Control	40	ND	ND	ND	ND	ND	ND
Intervention	12	NR	NR	NR	NR	NR	NR
Heshka (2003) <sup>20</sup>							
Control		121±12	0.2 (SE: 0.8)		79±9	1.4 (SE: 0.6)	
Intervention	12	123±14	-0.6 (SE: 0.9)		79±8	-0.4 (SE: 0.6)‡	
Control		123±14 121±12	-0.0 (SE: 0.9) -2.4 (SE: 1.0)	NR	79±9	0.0 (SE: 0.6)	NR
Intervention	24					, ,	
		123±14	-2.2 (SE: 1.1)		79±8	-0.6 (SE: 0.7)	
Head-to-Head							
Dansinger (2005) <sup>21</sup> †		100 17	0.0.10		77 0	4.4.7.5	
Atkins	12	129±17	0.2±12	NR	77±9	-1.4±7.5	NR
Weight Watchers	1.4	133±17	-2.7±13.0	1411	74±11	-1.7±6.4	1411
Zone		130±16	1.4±15.0		77±10	-1.2±9.5	
Gardner (2007) <sup>22</sup> †							
Control		116±12	-3.1±9.3		75±9	$-2.2\pm6.7$	ND
Atkins	12	118±11	−7.6±11.0§∥	NR	75±8	$-4.4\pm8.4$	NR
Zone		115±13	$-3.3\pm8.1$		74±9	-2.1±5.8	

All values are mean ±SD or mean (95% CI) unless otherwise indicated. NR indicates not reported; and SE, standard error.

<sup>\*</sup>Only long-term follow-up data from these studies are presented in this table.

<sup>†</sup>Trial had other arms that were not included.

<sup>‡</sup>*P*<0.05 for difference between groups.

<sup>§</sup>P<0.05 vs. Zone.

<sup>||</sup> P<0.05 vs. Control.

not replicated in head-to-head RCTs, the most robust evidence available. Rather, head-to-head RCTs suggest that at 12 months, Atkins, WW, and Zone all achieved modest and similar weight loss. Moreover, 24-month data suggest that the modest weight losses achieved with Atkins or WW are partially regained over time. Moreover, there were more limited data on the long-term effects of the 4 popular diets on other cardiovascular risk factors, with Atkins and WW being the most studied. Overall, results from the 2 long-term head-to-head RCTs showed no marked differences among Atkins, WW, and Zone at improving cardiovascular risk factor levels. Although North Americans spend millions of dollars in the weight loss industry, available data are conflicting and insufficient to identify one popular diet as being more beneficial than the others.

The prevalence of overweight and obesity has risen steadily over the past few decades worldwide, with nearly 1.5 billion adults estimated to be overweight or obese as of 2008.27 In the United States, the prevalence of overweight and obesity reaches 69.2% and 35.9%, respectively.<sup>28</sup> The health consequences of this trend are well-established and include increased prevalences of cardiovascular disease, metabolic syndrome, and type 2 diabetes mellitus.<sup>29</sup> Consequently, effective prevention and management strategies are needed to reduce the burdens of overweight, obesity, and their associated comorbidities.<sup>30,31</sup> Despite their popularity, 1-4 the Atkins, SB, WW, and Zone diets seem to only achieve modest sustained weight loss. Comprehensive lifestyle interventions aimed at curbing both adult and childhood obesity are urgently needed. Interventions that include dietary, behavioral, and exercise components, as well as legislative measures and industry regulations, may be better suited to the multifaceted obesity epidemic.<sup>32</sup>

Our results stem from the review of RCTs that predominantly enrolled young, white, obese women. Few data were available in other ethnic groups or in individuals who were overweight but not obese. The paucity of data available in men is also concerning. Pagoto et al.<sup>33</sup> previously highlighted this underrepresentation in their systematic review of RCTs investigating different lifestyle interventions for weight loss, where the average proportions of men and women were 27% versus 73%, respectively.<sup>33</sup> Thus, our findings regarding study populations in RCTs in this area are not an isolated occurrence.

The generalizability of the weight loss observed with these popular diets in RCTs to a real-world setting remains unclear. We found that 12-month mean weight loss with WW ranged from 3.0 to 6.0 kg.<sup>17–22</sup> In a recent observational study of individuals prescribed a 12-month WW diet by health-care professionals through the UK's WW National Health Service Referral Scheme, median weight loss was 2.8 kg at 12 months.<sup>34</sup> Thus, the weight loss achieved in the ideal conditions of RCTs likely overestimates that achieved by patients seen as part of everyday clinical practice.

To our knowledge, our study is the first systematic review of RCTs to specifically focus on the Atkins, SB, WW, and Zone diets. A previous systematic review of major commercial weight loss programs in the United States examined the 3 major nonmedical weight loss programs at the time (WW, Jenny Craig, LA Weight loss), as well as medically supervised proprietary programs, online programs, and organized self-help programs, but excluded book-based diets.<sup>35</sup> This previous

review included case series in addition to RCTs. Similar to our findings, the authors concluded that: "With the exception of 1 trial of WW, the evidence to support the use of major commercial and self-help weight loss programs is suboptimal." <sup>35</sup>

#### Limitations

First, our review focused on the Atkins, SB, Zone, and WW popular diets. To ensure this, only RCTs clearly referencing or mentioning the diet name were included, which could have resulted in fewer included studies. Moreover, other commercial diets are available that were not studied here; such diets deserve to be the object of additional studies. However, the 4 included diets constitute a representative sample of commercial North American popular diets. Second, some of the included RCTs were limited by relatively small sample sizes and may have been underpowered. Third, a key principle of RCTs is the use of intention-to-treat analysis in which all patients are included. Included studies had high attrition rates, and studies varied in their statistical approach to address this limitation, each of which rests on a given set of assumptions: completers' analysis assumes participants completing the trial are similar to those who do not, resulting in potential selection bias, whereas the last-observation-carried-forward method assumes that participants' subsequent outcomes are the same as the last one available, underestimating the data's true variability. 36 Although using missing data techniques such as multiple imputation can help reduce the bias because of incomplete follow-up, every effort must be made to ensure complete followup to ensure the validity of trials. Fourth, inclusion was restricted to published data. We reviewed a large number of RCTs during the conduct of our systematic review, and only a small number of the published RCTs were well-designed. Thus, the probability that there are well-designed RCTs that are unpublished is low, limiting the potential contribution of these unpublished data. Nonetheless, the presence of publication bias, a potential limitation of all systematic reviews, cannot be excluded. Finally, all included trials were open-label, a limitation inherent to trials examining dietary interventions.

### **Conclusions**

Our study was designed to examine the evidence currently available from the literature to examine the efficacy of 4 commercial, popular diets on weight loss and improving cardiovascular risk factors, with a particular focus on sustained weight loss at ≥12 months. Our results suggest that all 4 diets are modestly efficacious at decreasing weight in the short-term, but that these benefits are not sustained long-term. RCTs comparing popular diets to usual care showed that only WW consistently demonstrated greater efficacy at reducing weight at 12 months. Head-to-head RCTs demonstrated that Atkins, WW, and Zone are all modestly and similarly efficacious at achieving sustained weight loss at ≥12 months. Finally, while North Americans spend millions of dollars in the weight loss industry, available data are conflicting and insufficient to identify one popular diet as being more beneficial than the others.

### Acknowledgments

We thank Yevgeniya Mizina, Anna Eisenberg, and Tara Dourian for their help with data abstraction, and Maria Eberg for generating the forest plot.

### **Sources of Funding**

This work was supported by the Canadian Institutes of Health Research (CIHR; grant number MOP-87343). Dr. Wakil was supported by a Canadian Cardiovascular Outcomes Research Team summer studentship funded through a CIHR Team Grant in Cardiovascular Outcomes Research. Dr. Filion is a CIHR New Investigator. Dr. Poirier is a Senior Clinician-Research Scholar from the Fonds de recherche du Québec-Santé. Dr. Schiffrin holds a Canada Research Chair (CRC) on Hypertension and Vascular Research from CIHR/Government of Canada CRC Program.

#### **Disclosures**

None.

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# SUPPLEMENTAL MATERIAL

# 1. Supplemental Tables

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# Supplemental Table 1. Overview of the five popular diets

Diet	Duration of	Energy Intake		Protein		Carbohydrates		Fat	Low	Low	Alcohol Intake	Caffeine
	Treatment		%	Type of Protein	%	Type of Carbohydrate	%	Type of Fat	Carb	Fat		Intake
Atkins <sup>1</sup>	Phase 1: 2 weeks. Phase 2: Ongoing weight loss Phase 3: Until target weight is maintained. Phase 4: Lifelong maintenance	Not specified	10	Not Specified	30	Strict Rules	60	Not specified	Yes	No	Phase 1: none After: in moderation (counted as a carbohydrate)	Avoid caffeine
Ornish <sup>2</sup>	Indefinite	Not specified	20	Lean proteins	70	Whole grains, fruits, vegetables	10	Not specified	No	Yes	None	Avoid caffeine
South Beach <sup>3</sup>	Phase 1: 2 weeks Phase 2: Until target weight is achieved. Phase 3: Lifelong maintenance	Not specified	30	Lean Proteins	20	Phase 1: very limited Phase 2 and 3: Moderate limitations on processed carbs	50	Poly- or mono- unsaturated	Yes	Yes	Wine is allowed (especially red wine). About a glass/day.	No restriction
Weight Watchers <sup>4</sup>	Plan is until healthy weight is maintained. After: maintenance plan.	Points based on caloric content, fiber and fat content. Min: 1050 Max: 2350	20 - 25	Lean Proteins	45 - 55	Whole Grains, Fruits, Vegetables	20 - 35	Recommend 2 tablespoons of healthy oil (mono- unsaturated, vitamin E)	No	Yes	Based on point system. 1 cup/day for women. 2 cups/day for men.	No restriction
Zone <sup>5</sup>	Indefinite	Men: 1400-1500 calories Women: 1100- 1200 calories	30	Not specified	40	Low glycemic load	30	Plan approved fats: e.g. Almonds, olive oil, avocado.	Yes	Yes	Treated as a carbohydrate. 1 serving of alcohol = 10g of carbohydrates	Avoid caffeine

# Supplemental Table 2. Baseline characteristics of participants in short-term (4 to 24 weeks) trials.

C. 1	Particip	pants	Duration	D 1.			Nutritional	Exercise	Age	Female	Caucasian	Weight	BMI
Study	Randomized	Analyzed	(Weeks)	Population		arms	Counseling	Prescription	(y)	(%)	(%)	(kg)	$(kg/m^2)$
Atkins													
Rankin 2007 <sup>6</sup>	32*	29*,†	4	BMI > 24.5, premenopausal, otherwise healthy	Atkins	HC/LP/LFD with CR	No	No	39.5*	100	87.5	83.3*	32.1
Nickols- Richardson 2005 <sup>7</sup>	28	28	6	BMI: 25-40, premenopausal, otherwise healthy	Atkins	NCEP HC/LFD with CR	Yes	No	39.5	100	NR	82.0	30.7
Phillips 2008 <sup>8</sup>	28	20†	6‡	BMI: 29-39, otherwise healthy	Atkins minus 750 calories for 4 weeks	AHA LFD minus 750 calories for 4 weeks	No	No	35.5†	75.0†	70.0†	97.8†	33.9†
Hernandez 2010 <sup>9</sup> §	32	32	6	BMI: 30-40, otherwise healthy		HC/US Food Guide Pyramid LFD with CR ensive behavioral gram	Yes	No	43.1	68.8	NR	102	NR
Liu <sup>10</sup> 2013	50	49#	12	BMI ≥ 24**, aged 30-65	Atkins	Traditional Chinese diet design with CR††	No	No	47.9	100	0	65.9	26.7
Brehm 2005 <sup>11</sup>	50	40†	16	BMI: 30-35, otherwise healthy	Atkins	AHA LFD with CR	Yes	No	43.0†	100	80.0	90.8†	33.2†
Brehm 2003 <sup>12</sup>	53	42†	24	BMI: 30-35, otherwise healthy	Atkins	AHA LFD with CR	Yes	No	43.7†	100	75.5	91.7†	33.6†
Yancy 2004 <sup>13</sup>	120	119#	24	BMI: 30-60, hyperlipidemic, generally healthy	Atkins + Daily Supplements	LFD with CR	Yes	Yes	44.9#	76.5#	76.5#	97.3#	34.3‡‡
South Beach													
Aude 2004 <sup>14</sup>	60	54†	12	BMI $\geq$ 27, otherwise healthy	South Beach with CR	NCEP diet with CR	Yes	No	45.1†	51.9†	NR	99.5†	35.2†
Weight Watch	hers			·									
Rippe 1998 <sup>15</sup>	80	44†	12	Overweight/obese, otherwise healthy§§	WW	Maintenance of current diet/exercise	No	No	36.8†	100	NR	81.5†	NR
Johnston 2013 <sup>16</sup>	292	257†	24	BMI: 27-40, aged ≥ 18	WW	Self-help	No	No	46.6	89.7	90.7	90.1	33.0
Zone				•									
Landers 2002 <sup>17</sup>	91##	33†,##	12	BMI > 27, otherwise healthy	Zone	Hypocaloric diabetic exchange diet	Yes	No	NR	NR	NR	NR	NR
Head-to-Head	l												
McAuley $2005^{18}$ ,	96***	93†††	24	BMI > 27, insulin-resistant, otherwise healthy	Atkins Zor	HC/high-fibre diet	No	Yes	45.6†††	100	100	95.8†††	35.7†††
Truby 2006, 2009 <sup>19, 20</sup> ,      , ;;;	176	176§§§	24	BMI: 27-40, otherwise healthy	Atkins WV	Maintenance V Of current diet/exercise	No	Yes	40.5	73.9	NR	89.0	31.5

AHA indicates American Heart Association; BMI, body mass index; CR, calorie restriction; HC, High-carbohydrate; LP, Low-protein; LFD, low-fat diet; NCEP, National Cholesterol Education Program; NR, not reported; WW, Weight Watchers.

<sup>\*</sup> The number of participants in each arm of the study is not reported. Baseline characteristics were averaged across groups assuming an equal sample size in each treatment group. † Completers analysis. ‡ The dietary

intervention involved a 4-week weight loss phase and a 2-week weight maintenance phase. Except for fasting glucose and insulin outcomes reported at 4 and 6 weeks, all other outcomes of interest were reported at 2 and 6 weeks of follow-up, hence 6-week outcomes were included in our systematic review. § Substudy of Foster et. al<sup>21</sup> with independent measurements except for those assessing weight. || Delivered in-person to participants through group sessions held throughout the study follow-up, and comprising topics on behavioural skills (e.g., self-monitoring, stimulus control, relapse management); an exercise prescription; and daily multivitamin supplements. # Intention-to-treat analysis (ITT). \*\* Overweight for the Chinese people is defined as BMI  $\geq$  24. †† Daily CR to 65% on average of usual intake, with calories from carbohydrates, protein and fat being 50-55%, 17-19% and 26-33%, respectively. ‡‡ Linear mixed-effects model analysis which assumes non-informative dropouts. §§ Study participants' weight exceeded the 1983 Metropolitan Life Insurance Table of desirable weight for height by 20 to 50%. || || Trial had other arms that were not included. ## A total of 91 participants were randomized to 1 of 3 dietary interventions. The results presented are that of the 33 study completers in the Zone or usual care arms only. \*\*\* Of the 96 participants randomized, 3 withdrew before the start of their assigned diet intervention and were excluded from analyses. ††† ITT analysis, with mixed-models comprising a random effect for each participant and assuming an underlying variance-covariance structure. ‡‡‡ Lipid and glycemic control measures data for the Truby et al. \*\* trial were reported in a secondary paper by Morgan et al. \*\* trial were reported in a secondary paper by Morgan et al. \*\* trial were reported in a secondary paper by Morgan et al. \*\* trial were reported in a secondary paper by Morgan et al. \*\* trial were reported in a secondary paper by Morgan et al. \*\* trial were reported in a secondary paper by Morgan et

# $Supplemental\ Table\ 3.\ Change\ in\ body\ weight\ and\ other\ anthropometric\ measures\ in\ short-term\ (4\ to\ 24\ weeks)\ trials.$

	Follow-		We	eight		I	Body Mass Index		W	aist Circumference			Body Fat	
Study	up (Weeks)	Baseline (kg)	Follow- Up (kg)	Mean Change (kg)	% Change	Baseline (kg/m²)	Follow-Up (kg/m <sup>2</sup> )	Mean Change (kg/m²)	Baseline (cm)	Follow-Up (cm)	Mean Change (cm)	Baseline (kg or %)	Follow-Up (kg or %)	Mean Change (kg or %)
Atkins			_	_				_						
Rankin 2007 <sup>6</sup> Control Intervention	4	79.2±16.0 87.3±15.2	76.6±15.7 83.5±14.8	-2.6±1.7 -3.8±1.2	NR	31.4±5.4 32.7±5.5	NR	NR	NR	NR	NR	NR	NR	NR
Nickols-	-													
Richardson 2005 Control Intervention	6	79.8±12.1 84.6±12.7	75.6±15.4 78.2±15.9	-4.2† -6.4 <b>†,</b> §	NR	30.3±5.5 31.1±4.9	29.0±5.3 29.3±4.6	-1.3† -1.8†	NR	NR	NR	NR	NR	NR
Phillips 2008 <sup>8</sup>		04.0±12.7	76.2±13.7	-0.41,8		31.1±4.7	27.5±4.0	-1.0						
Control Intervention	6	100.2 (SE: 3.7) 95.4 (SE: 4.1)	96.1 (SE: 4.0) 89.9 (SE: 3.8)	-4.0 (SE: 0.5) -5.2 (SE: 0.6)	NR	33.8 (SE: 1.1) 34.0 (SE: 0.9)	32.3 (SE: 1.2) 32.0 (SE: 0.8)	-1.5† -2.0†	NR	NR	NR	NR	NR	NR
Hernandez 2010 <sup>6</sup> Control Intervention	6	103±11 101±13	95.4±11.3 97.3±12.9	-6.0±3.5 -6.2±4.8	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR NR
Liu 2013 <sup>10</sup>		101213	)1.5±12.7	0.2_4.0										1110
Control	12	67.0 (SE: 1.3)	61.2 (SE: 1.1)	-5.1 (-5.5, -4.7)	NR	26.9 (SE: 0.4)	24.5 (SE: 0.4)	-2.1 (-2.2, -1.9)	91.0 (SE: 1.1)	84.2 (SE: 1.3)	-6.5 (-8.3, -4.7)	23.1 (SE: 0.8) kg	20.1 (SE: 0.7) kg	-2.59 (-3.02, -2.15) kg
Intervention	12	64.8 (SE: 1.3)	59.5 (SE: 1.2)	-5.3 (-6.1, -4.5)	112	26.6 (SE: 0.5)	24.4 (SE: 0.4)	-2.2 (-2.6, -1.8)	90.2 (SE: 1.1)	82.4 (SE: 1.4)	-7.9 (-9.2, -6.5)	22.6 (SE: 0.8) kg	20.1 (SE: 0.8) kg	-2.48 (-3.10, -1.85) kg
Brehm 2005 <sup>11</sup>				(-0.1, -4.3)				(-2.0, -1.8)			(-9.2, -0.3)			(-3.10, -1.63) kg
Control	16	90.9 (SE: 2.1)	NR	-6.14 (SE: 0.91)	NR	33.5 (SE: 0.5)	NR	NR	NR	NR	NR	37.15 (SE: 0.92) kg	33.91 (SE: 1.29) kg	-3.2 (SE: 0.67) kg
Intervention	10	90.6 (SE: 2.4)	NIX	-9.79 (SE:	NK	32.8 (SE: 0.5)	TVIC	THE	TVIC	NIX	NK	37.89 (SE: 1.27)	31.70 (SE: 1.41)	-6.2 (SE: 0.67)§
Brehm 2003 <sup>12</sup>				0.71)§								kg	kg	kg
Control Intervention	24	92.31±6.0 91.2±8.4	NR	-3.9 (SE: 1.0) -8.5 (SE: 1.0)§	NR	34.04±1.83 33.17±1.83	NR	NR	NR	NR	NR	37.83±2.65 kg 37.33±4.79 kg	35.85±4.13 kg 32.55±5.17 kg	-2.0 (SE: 0.75) kg -4.8 (SE: 0.67)§
		91.2±8.4		-8.5 (SE: 1.0)§		33.17±1.83						37.33±4.79 kg	32.33±3.17 kg	kg
Yancy 2004 <sup>13</sup>				-6.5	-6.7									-2.8
Control	24	96.8±19.2	NR	(-8.4, -4.6) -12.0§	(-8.7, -4.8) -12.9§	34.0±5.2	NR	NR	NR	NR	NR	41.1±NR %	38.3±NR %	(-3.9, -1.9) % -5.8§
Intervention		97.8±15.0		(-13.8, -10.2)	(-14.8, -10.9)	34.6±4.9						41.0±NR %	35.2±NR %	(-6.7, -4.8) %
South Beach														
Aude 2004 <sup>14</sup> Control Intervention	12	99.9±21.1 99.1±31.9	NR	-3.4±2.0 -6.2±1.8§	NR	35.5±6.0 34.9±4.0	NR	NR	NR	NR	NR	NR	NR	NR
Weight Watcher	S	)).1±31.)		0.221.03		54.924.0								
Rippe 1998 <sup>15</sup> Control	12	82.1±5.3	NR	1.3±1.3	NR	NR	NR	NR	NR	NR	NR	36.2±2.7%	36.0±NR %	-0.2†
Intervention  Johnston 2013 <sup>16</sup>		81.2±7.6		-6.1±4.0§								36.8±2.6 %	32.5±NR %	-4.8 <b>†,</b> §
Control Intervention	24	90.0±12.7 90.2±14.1	NR	-0.6±NR -4.6±NR§	NR	32.8±3.6 33.1±3.7	NR	NR	NR	NR	NR	NR	NR	NR
Zone														
Landers 2002 <sup>17</sup> *														
Control Intervention	12	NR	NR	-5.4±2.8 -4.4±3.2	NR	NR	NR	NR	NR	NR	NR	NR	NR	-3.52±2.62 kg -3.62±2.28 kg
Head-to-Head McAuley 2005 <sup>18</sup>	. +													
Control	•	98.0±15.1	93.7±14.6	-4.3†		36.6±5.6	35.2±5.6	-1.4†	109.1±11.6	104.3±10.9	-4.8†	46.1±9.9 kg	42.7±9.7 kg	-3.4†
Atkins Zone	8	96.0±10.8 93.2±14.5	89.4±10.3 87.8±13.7	-6.6†,§ -5.4†,§	NR	36.0±3.9 34.5±5.3	33.5±3.7 32.4±4.8	-2.5†,§ -2.1†,§	108.9±9.9 108.0±11.5	100.6±9.6 100.3±9.6	-8.3† <b>,</b> § -7.7† <b>,</b> §	44.2±6.9 kg 42.1±8.0 kg	39.8±7.1 kg 39.0±7.8 kg	-4.4†,§ -3.1†,§
Truby 2006, 2009	9 <sup>19, 20</sup> ,*													
Control Atkins	24	87.9±13.5 90.3±12.7	NR	0.6±2.2 -6.0±6.4	0.6±2.7 -6.2±6.2	31.5±2.9 31.9±2.2	NR	NR	100±10.1 102±10.6	NR	-0.8±3.8 -8.1±7.4	33.4±6.5 kg 35.7±6.0 kg	NR	0.3±4.4 kg -4.6±4.8 kg
WW		88.8±13.3		-6.6±5.4	-7.3±6.1	31.2±2.7			100±10.3		-8.3±7.0	34.2±6.9 kg		-5.0±4.3 kg

All values are mean±SD or mean (95% CI) unless otherwise indicated. NR indicates not reported; SE, standard error; WW, Weight Watchers.

* Trial had other arms that were not included. † Calculated from data in the publication. ‡ Data at the end of the 8-week intervention period, not including weight maintenance period (the study's maximum duration of follow-up is 24 weeks). § p<0.05 vs. Control.

# Supplemental Table 4. Change in lipid levels in short-term (4 to 24 weeks) trials.

		Total Cholesterol			Low-Density Lipoprotein Cholesterol			High-Density Lipoprotein Cholesterol			Triglycerides		
Study	Follow-up (Weeks)	Baseline TC (mmol/L)	TC at Follow-Up (mmol/L)	TC Mean Change (mmol/L)	Baseline (mmol/L)	Follow-Up (mmol/L)	Mean Change (mmol/L)	Baseline (mmol/L)	Follow-Up (mmol/L)	Mean Change (mmol/L)	Baseline (mmol/L)	Follow-Up (mmol/L)	Mean Change (mmol/L)
Atkins		(IIIIIOL/L)	(mmor E)	(IIIIIOI/E)									
Rankin 2007 <sup>6</sup>													
Control	4	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Intervention	4	NK	NK	NK	NK	NK	NK	NK	NK	NK	NK	NK	NK
Nickols-													
Richardson 2005 <sup>7</sup>													
Control	6	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Intervention Phillips 2008 <sup>8</sup>													
Control		3.95 (SE: 0.22)	3.76 (SE: 0.22)	-0.19‡	2.43 (SE: 0.18)	2.18 (SE: 0.24)	-0.25‡	1.29 (SE: 0.11)	1.15 (SE: 0.12)	-0.14‡	0.68 (SE: 0.08)	0.78 (SE: 0.27)	0.10‡
Intervention	6	4.08 (SE: 0.11)	4.22 (SE: 0.16)	0.14‡	2.13 (SE: 0.37)	2.47 (SE: 0.35)	0.341	1.41 (SE: 0.14)	1.41 (SE: 0.13)	0.01	0.88 (SE: 0.16)	0.65 (SE: 0.05)	-0.23‡
Hernandez 2010 <sup>9</sup>		(BE: 0.11)	1.22 (52: 6:16)	0.114	2.13 (02. 0.57)	2.17 (82. 0.88)	0.5 14	1111 (021 0111)	1111 (82. 0.15)	0.04	0.00 (BE: 0.10)	0.05 (52. 0.05)	0.20 +
					2.6†	2.4†	02.02	1.2†	1.1†	0.1.02	1.2.0.62	1.02.0.55	02.05
Control	6	NR	NR	NR	(IQR: 2.4, 3.0)	(IQR: 2.2, 2.9)	-0.2±0.2	(IQR: 1.1, 1.5)	(IQR: 1.0, 1.2)	-0.1±0.2	1.3±0.62	1.02±0.55	-0.3±0.5
Intervention	U	INK	INK	INK	2.8†	3.1†	0.3±0.7#	1.1†	1.1†	0.0±0.3	1.4±0.66	0.91±0.33	-0.5±0.7
					(IQR: 2.0, 3.3)	(IQR: 2.5, 3.4)	0.5±0.7#	(IQR: 0.9, 1.6)	(IQR: 0.9, 1.5)	0.0±0.3	1.4±0.00	0.91±0.55	-0.5±0.7
Liu 2013 <sup>10</sup>				0.10						0.4.4			0.45
Control		5.19 (SE: 0.24)	4.55 (SE: 0.16)	-0.68	3.44 (SE: 0.20)	2.99 (SE: 0.13)	-0.5	1.44 (SE: 0.08)	1.31 (SE: 0.07)	-0.14	1.33 (SE: 0.12)	0.90 (SE: 0.11)	-0.45
	12			(-1.11, -0.26)			(-0.84, -0.17) 0.05			(-0.27, -0.00)			(-0.57, -0.33) -0.88
Intervention		5.01 (SE: 0.21)	5.00 (SE: 0.25)	0.01 (-0.61, 0.62)	3.30 (SE: 0.16)	3.35 (SE: 0.23)	(-0.40, 0.50)	1.30 (SE: 0.07)	1.45 (SE: 0.07)	0.16 (-0.02, 0.34)#	1.69 (SE: 0.26)	0.79 (SE: 0.07)	(-1.37, -0.41)
Brehm 2005 <sup>11</sup>				(-0.01, 0.02)			(-0.40, 0.50)			(-0.02, 0.54)#			(-1.57, -0.41)
Control		5.08 (SE: 0.21)	4.89 (SE: 0.25)	-0.19‡	3.24 (SE: 0.15)	3.02 (SE: 0.21)	-0.22‡	1.15 (SE: 0.04)	1.2 (SE: 0.05)	0.05‡	1.65 (SE: 0.23)	1.48 (SE: 0.15)	-0.17‡
Intervention	16	5.31 (SE: 0.25)	5.17 (SE: 0.27)	-0.14‡	3.49 (SE: 0.21)	3.42 (SE: 0.26)	-0.07‡	1.15 (SE: 0.05)	1.34 (SE: 0.07)	0.19‡,#	1.46 (SE: 0.15)	0.91 (SE: 0.07)	-0.55‡
Brehm 2003 <sup>12</sup>		, ,		•			•	, ,			` `	, ,	•
Control	24	4.78 (SE: 0.16)	4.74 (SE: 0.16)	-0.04‡	2.95 (SE: 0.16)	2.79 (SE: 0.15)	-0.16‡	1.26 (SE: 0.06)	1.37 (SE: 0.07)	0.11‡	1.23 (SE: 0.11)	1.25 (SE: 0.14)	0.02‡
Intervention	24	5.34 (SE: 0.17)	5.32 (SE: 0.18)	-0.02‡	3.23 (SE: 0.14)	3.21 (SE: 0.15)	-0.02‡	1.34 (SE: 0.07)	1.52 (SE: 0.07)	0.16‡	1.68 (SE: 0.15)	1.29 (SE: 0.17)	-0.39‡
Yancy 2004 <sup>13</sup>													
Control	24	6.20±NR	5.85±NR	-0.35 (NR)	3.83±NR	3.64±NR	-0.19 (NR)	1.40±NR	1.36±NR	-0.04 (NR)	2.15±NR	1.84±NR	-0.3 (NR)
Intervention		6.32±NR	6.11±NR	-0.21 (NR)	4.07±NR	4.11±NR	0.04 (NR)	1.43±NR	1.57±NR	0.14 (NR)#	1.78±NR	0.94±NR	-0.8 (NR)#
South Beach Aude 2004 <sup>14</sup>													
Control		5.33±0.95		-0.3±0.5	3.17±0.69		-0.2±0.4	1.41±0.48		-0.1±0.2	1.64±0.899		-0.2±0.5
Intervention	12	5.51±1.2	NR	-0.3±0.5	3.32±1.16	NR	-0.2±0.4 -0.1±0.7	1.3±0.37	NR	-0.1±0.2 -0.0±0.2	2.05±1.51	NR	-0.5±1.1
Weight Watchers		3.31±1.2		-0.3±0.6	3.32±1.10		-0.1±0.7	1.5±0.57		-0.0±0.2	2.03±1.31		-0.5±1.1
Rippe 1998 <sup>15</sup>													
Control	10	N.T.	N.T.	MD	MD	MD	N.D.	MD	NTD.	N.T.	N.T.	N.T.	MD
Intervention	12	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Johnston 2013 <sup>16</sup>													
Control	24	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Intervention					1110	1110							
Zone													
Landers 2002 <sup>17</sup> *	10												
Control Intervention	12 12	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Head-to-Head	12												
McAuley 2005 <sup>18</sup> *,§													
Control	8	5.9±0.9	5.3±0.9	-0.6‡	3.9±0.8	3.6±0.9	-0.3‡	1.16±0.21	1.09±0.25	-0.07‡	1.77±0.57	1.46±0.51	-0.31‡
Atkins	8	5.8±1.0	5.5±1.2	-0.3‡,††	3.8±0.9	3.8±1.0	0.0‡	1.17±0.28	1.18±0.29	0.01‡,#	1.78±0.76	1.09±0.25	-0.69‡,#
Zone	8	5.7±1.0	5.0±0.8	-0.7‡	3.7±0.8	3.3±0.7	-0.4‡,**	1.21±0.23	1.16±0.24	-0.05‡	1.86±0.66	1.23±0.43	-0.63‡,#
Truby 2006, 2009 <sup>1</sup>													
Control	24	$5.80 \pm 1.1$	NR	-0.5±0.2	$3.64\pm0.84  $	$3.55\pm0.73  $	-0.09‡	1.19±0.22	$1.04\pm0.20  $	-0.15‡	$1.40\pm0.65  $	1.38±0.65	-0.02‡
Atkins	24	5.77±0.9	NR	-0.3±0.8	3.72±0.52	3.56±0.76	-0.16‡	1.22±0.23	1.14±0.32	-0.08‡	1.65±0.70	1.01±0.33	-0.64‡
Weight	24	5.58±1.1	NR	-0.6±0.7#	3.56±0.81	3.13±0.58	-0.43‡	1.16±0.24	0.98±0.15	-0.18‡	1.55±0.77	1.20±0.47	-0.35‡
Watchers							•			•			

All values are mean  $\pm$ SD or mean (95% CI) unless otherwise indicated. IQR indicates interquartile range; NR, not reported; SE, standard error.

\* Trial had other arms that were not included.  $\dagger$  Median (IQR).  $\ddagger$  Calculated from data in the publication. \$ Data at the end of the 8-week intervention period, not including weight maintenance period (the study's maximum duration of follow-up is 24 weeks).  $\parallel$  Lipid data for the Truby et al. trial were reported in a secondary paper by Morgan et al.  $^{20}$  # p<0.05 vs. Control. \*\* p<0.05 vs. Atkins.  $\dagger$ † p<0.05 vs. Zone.

# Supplemental Table 5. Change in blood pressure in short-term (4 to 24 weeks) trials.

	Follow-up		Systolic Blood	Pressure	Diastolic Blood Pressure				
Study	(Weeks)	Baseline (mm Hg)	Follow-Up (mm Hg)	Mean Change (mm Hg)	% Change	Baseline (mm Hg)	Follow-Up (mm Hg)	Mean Change (mm Hg)	% Change
Atkins									
Rankin 2007 <sup>6</sup>									
Control	4	NR	NR	NR	NR	NR	NR	NR	NR
Intervention									
Nickols-	-								
Richardson 2005	,								
Control	6	NR	NR	NR	NR	NR	NR	NR	NR
Intervention									
Phillips 2008 <sup>8</sup>		104.1 (CE: 4.0)	115.2 (CE, 2.0)	0.04		72.2 (SE. 2.6)	(( 0 (GE, 2 2)	C 44	
Control	6	124.1 (SE: 4.0)	115.2 (SE: 3.0)	-8.9†	NR	73.2 (SE: 3.6)	66.8 (SE: 3.3)	-6.4†	NR
Intervention	1	123.3 (SE: 3.1)	112.6 (SE: 2.7)	-10.7†		70.0 (SE: 3.5)	65.8 (SE: 2.6)	-4.2†	
Hernandez 2010 <sup>9</sup>									
Control	6	NR	NR	NR	NR	NR	NR	NR	NR
Intervention									
Liu 2013 <sup>10</sup>				15.7				0.1	
Control		131.4 (SE: 3.4)	116.4 (SE: 2.6)	-15.7		85.5 (SE: 2.0)	77.7 (SE: 2.0)	-8.1	NR
	12	ŕ	ŕ	(-20.4, -11.0)	NR	ŕ		(-11.3, -4.8)	
Intervention		134.0 (SE: 3.4)	113.7 (SE: 2.0)	-20.3		86.5 (SE: 1.6)	75.7 (SE: 1.5)	-10.8	
Brehm 2005 <sup>11</sup>				(-24.8, -15.8)				(-13.0, -8.7)	
Control		119 (SE: 2.9)	116 (SE: 3.5)	-3†		77 (SE: 1.7)	75 (SE: 2.8)	-2†	
	16		, ,	-3† -9†	NR	, ,			NR
Intervention Brehm 2003 <sup>12</sup>		119 (SE: 3.5)	110 (SE: 3.4)	-91		76 (SE: 1.7)	71 (SE: 2.1)	-5†	
		115 (SE, 2.47)	112 (SE, 2.41)	24		75 (SE: 1.99)	74 (CE, 1.62)	1.4	
Control Intervention	24	115 (SE: 2.47)	113 (SE: 2.41)	-2† -2†	NR	` /	74 (SE: 1.62)	-1† 5÷	NR
Yancy 2004 <sup>13</sup>		116 (SE: 3.23)	114 (SE: 2.82)	-21		79 (SE: 2.69)	74 (SE: 2.23)	-5†	
Yancy 2004				75				5.0	
Control		NR	NR	-7.5 (-11.6, -3.5)	NR	NR	NR	-5.2	NR
	24			-9.6				(-7.5, -2.9) -6.0	
Intervention		NR	NR	(-13.3, -6.0)	NR	NR	NR	(-8.0, -3.9)	NR
South Beach				( 15.5, 0.0)				( 0.0, 3.7)	
Aude 2004 <sup>14</sup>									
Control									
Intervention	12	NR	NR	NR	NR	NR	NR	NR	NR
Weight Watchers	e e								
Rippe 1998 <sup>15</sup>	3								
Control		117.4±8.8	114.5±9.6	-3.2±11.8		81.1±6.5	79.0±6.7	-2.1±7.9	
Intervention	12	117.2±13.8	110.7±13.1	-6.5±13.1	NR	81.0±7.0	76.7±8.8	-4.3±9.6§	NR
Johnston 2013 <sup>16</sup>		117.2:15.0	110.7=15.1	0.5±15.1		01.0=7.0	70.7=0.0	1.527.08	
Control									
Intervention	24	NR	NR	NR	NR	NR	NR	NR	NR
Zone									
Landers 2002 <sup>17</sup> *									
Control									
Intervention	12	NR	NR	NR	NR	NR	NR	NR	NR
Head-to-Head									
McAuley 2005 <sup>18</sup> *,	'i								
Control	•	126±11	122±13	-4†		81±10	80±9	-1†	
Atkins*	8	130±14	118±14	-12†	NR	83±10	76±10	-7†	NR
		124±13	122±14	-2†		80±9	76±7	-4†	
Zone*							– .		
Zone* Truby 2006, 2009	9 <sup>19, 20</sup> *								
Zone* Truby 2006, 2009 Control	<b>9</b> <sup>19, 20</sup> *	130±16.1		-2.8±11.8		81±9.6		-1.6±7.4	
Truby 2006, 2009 Control			<b>.</b>						,
Truby 2006, 2009	9 <sup>19, 20</sup> *	130±16.1 135±15.1 127±15.1	NR	-2.8±11.8 -7.2±11.6 -4.1±11.7	NR	81±9.6 83±10.7 80±10.7	NR	-1.6±7.4 -4.9±8.1 -4.4±8.6	NR

All values are mean±SD or mean (95% CI) unless otherwise indicated. NR indicates not reported; SE, standard error.

<sup>\*</sup> Trial had other arms that were not included.  $\dagger$  Calculated from data in the publication.  $\ddagger$  Data at the end of the 8-week intervention period, not including weight maintenance period (the study's maximum duration of follow-up is 24 weeks). \$ p<0.05 vs. Control.

Supplemental Table 6. Change in glycemic control outcomes in short-term (4 to 24 weeks) trials.

			Fasting Glucose		Fasting Insulin			
Study	Follow-up (Weeks)	Baseline (mmol/L)	Follow-Up (mmol/L)	Mean Change (mmol/L)	Baseline (pmol/L)	Follow-Up (pmol/L)	Mean Change (pmol/L)	
Atkins								
Rankin 2007 <sup>6</sup>								
Control	4	4.71±0.59	4.63±0.26	-0.08†	ND	NID	NID	
Intervention	4	4.76±0.31	4.53±0.42	-0.23†	NR	NR	NR	
Nickols-								
Richardson 20057								
Control	_	N.D.	N.D.	N.D.		N.T.		
Intervention	6	NR	NR	NR	NR	NR	NR	
Phillips 2008 <sup>8</sup> *,†								
Control		4.99 (SE: 0.11)	5.07 (SE: 0.09)	0.08†	118.4#	100.4#	-18†	
Intervention	6	5.09 (SE: 0.06)	5.33 (SE: 0.12)	0.24†	126.4#	87.5#	-38.9†	
Hernandez 2010 <sup>9</sup>		**** (*********************************	*****	**=*				
Control		4.76±0.46	4.75±0.36	-0.0±0.3	74.3±42.4	54.87±39.59	-19.5±36.8	
Intervention	6	4.75±0.61	4.8±0.42	0.1±0.6	78.48±50.7	45.84±25	-32.6±55.6	
Liu 2013 <sup>10</sup>		1.75±0.01	1.0=0.12	0.1=0.0	70.10_50.7	13.01=23	32.0233.0	
				-0.32				
Control		6.15 (SE: 0.24)	5.86 (SE: 0.19)	(-0.83, 0.20)				
	12			0.12	NR	NR	NR	
Intervention		6.01 (SE: 0.18)	6.11 (SE: 0.24)	(-0.52, 0.76)				
Brehm 2005 <sup>11</sup>				(-0.32, 0.70)				
Control					151 (SE: 22)	133 (SE: 18)	-18†	
	16	5 (SE: 0.01)	NR	NR		, ,		
Intervention Brehm 2003 <sup>12</sup>		· · · · ·			135 (SE: 12)	86 (SE: 10)	-49†	
		5.06 (SE 0.10)	4.06 (GE 0.11)		166 (GE 1605)	105 7 (CF 14 C)	40.21	
Control	24	5.06 (SE: 0.12)	4.86 (SE: 0.11)	NR	166 (SE: 16.25)	125.7 (SE: 14.6)	-40.3†	
Intervention		5.5 (SE: 0.14)	5.00 (SE: 0.12)		117.37 (SE: 12.50)	100 (SE: 9.72)	-17.37†	
Yancy 2004 <sup>13</sup>								
Control	24	NR	NR	NR	NR	NR	NR	
Intervention								
South Beach								
Aude 2004 <sup>14</sup>								
Control	12	NR	NR	NR	NR	NR	NR	
Intervention		1,11	1111	1111		- 112	- 1,21	
Weight Watchers								
Rippe 1998 <sup>15</sup>								
Control	12	NR	NR	NR	NR	NR	NR	
Intervention	12	1117	1414	INIX	1417	1417	1117	
Johnston 2013 <sup>16</sup>	-			_				
Control	24	ND	ND	ND	ND	ND	ND	
Intervention	24	NR	NR	NR	NR	NR	NR	
Zone								
Landers 200217*								
Control	10	ND	NE	NE	ND	370	170	
Intervention	12	NR	NR	NR	NR	NR	NR	
Head-to-Head								
McAuley 2005 <sup>18</sup> *,:	+							
	•	- 0 -			102.79§	73.6§		
Control		5.0±0.6	$4.8\pm0.4$	-0.2†	(84.7, 123.6)	(52.8, 77.1)	-29.2†	
	_				104.18§	60.4§		
Atkins	8	5.1±0.6	$4.8\pm0.4$	-0.3†	(84.7, 127.8)	(7.4,10.2)	-43.8†	
					82.65§	46.5§		
Zone		5.1±0.5	$5.0\pm0.6$	-0.1†	(70.84, 95.8)	(39.58, 54.2)	-36.2†	
Truby 2006, 2009 <sup>1</sup>	9, 20*				(10.04, 75.0)	(37.30, 34.2)		
Control		5.48±0.5		-0.1±0.5	68.1±35.6	75.9±45.0	7.8†	
					"	"		
Atkins	24	5.47±0.5	NR	-0.2±0.5	73.2±35.1	54.8±32.4	-18.4†	
Weight		5.46±0.5		-0.5±0.6**	62.2±32.4	52.9±30.2	-9.3†	
Watchers					02.2_02.1	22.7_30.2	01	

All values are mean  $\pm$ SD or mean (95% CI) unless otherwise indicated. NR indicates not reported; SE, standard error.

<sup>\*</sup> Trial had other arms that were not included. † Calculated from data in the publication. ‡ Data at the end of the 8-week intervention period, not including weight maintenance period (the study's maximum duration of follow-up is 24 weeks). § Geometric mean. || Glycemic control measures data for the Truby et al. trial were reported in a secondary paper by Morgan et al. \*\*Publication\*\* Values reported in mg/dL in the publication are: Baseline: Atkins: 18.2 (SE: 3), Control: 17.05 (SE: 3.92); 6 weeks: Atkins: 12.6 (SE: 1.2), Control: 14.46 (SE: 2.09). \*\* p<0.05 vs. Control.

Supplemental Table 7. Change in glycemic control in long-term (≥12 months) trials.\*

		Fasti	ng Glucose	Fasting Insulin		
Study	Follow-up (Months)	Baseline Mean Change (mmol/L) (mmol/L)		Baseline (pmol/L)	Mean Change (pmol/L)	
Atkins						
Foster 2003 <sup>22</sup>						
Control	10	NID	ND	ND	ND	
Intervention	12	NR	NR	NR	NR	
Davis 2009 <sup>23</sup>						
Control	10	NID	ND	ND	ND	
Intervention	12	NR	NR	NR	NR	
Goldstein 2011 <sup>24</sup>						
Control	10	10.4±1.9	2.1±1.3	ND	ND	
Intervention	12	10.5±2.6	1.8±0.9	NR	NR	
Shai 2008 <sup>25‡</sup>						
Control	10	$2.3\pm0.7$		92.4±47.2		
Intervention	12	5.1±1.6		97.9±70.8		
Control	2.	2.3±0.7	NR	92.4±47.2	NR	
Intervention	24	5.1±1.6		97.9±70.8		
Foster 2010 <sup>21</sup>						
Control						
Intervention	12			NR	NR	
Control		NR	NR			
Intervention	24					
South Beach						
Swenson 2007 <sup>26</sup>						
Control						
Intervention	12	NR	NR	NR	NR	
Weight Watchers						
Marinilli Pinto 2013 <sup>27</sup>						
Control						
Intervention	12	NR	NR	NR	NR	
Jebb 2011 <sup>28</sup>						
Control			0.01 (SE: 0.03)		-0.65 (SE: 0.95)	
Intervention	12	NR	-0.06 (SE: 0.02)†	NR	-3.89 (SE: 0.97)†	
Jolly 2011 <sup>29</sup> ‡			-0.00 (SE. 0.02)		-3.67 (SE. 0.71)	
Control						
Intervention	12	NR	NR	NR	NR	
Heshka 2003 <sup>30</sup>						
Control		4.94±0.67	0.20 (SE: 0.03)	125.01±69.45	-2.1 (SE: 3.5)	
Intervention	12		0.20 (SE: 0.03) 0.19 (SE: 0.03)		-2.1 (SE: 3.5) -13.9 (SE: 3.5)†	
Control		5.11±0.78 4.94±0.67	0.19 (SE: 0.03) 0.3 (SE: 0.04)	125.01±62.51 125.01±69.45	16.0 (SE: 4.2)	
Intervention	24		0.3 (SE: 0.04) 0.3 (SE: 0.04)		4.2 (SE: 4.2)†	
Head-to-Head		5.11±0.78	0.5 (SE: 0.04)	125.01±62.51	4.2 (SE. 4.2)	
Dansinger 2005 <sup>31</sup> ‡						
Atkins		7.06±2.44	0.1+1.7	152.8±111.1	9 2±16 5	
	10	7.06±3.44	0.1±1.7		-8.3±46.5	
Weight Watchers	12	6.44±2.94	-0.3±1.1	138.9±69.45	-18.1±42.4	
Zone		6.44±2.67	-0.2±1.0	215.3±256.97	-37.5±97.2	
Gardner 2007 <sup>32‡</sup>		52.00	0.0±0.5	CO 45:55 C	10.5:25.4	
Control	10	5.3±0.9	$0.0^{\pm}0.5$	69.45±55.6	-12.5±35.4	
Atkins	12	5.1±0.5	-0.1±0.7	69.45±48.62	-12.5±33.3	
Zone		5.2±1.1	-0.1±0.4	69.45±48.62	-10.4±34.0	

All values are mean±SD or mean (95% CI) unless otherwise indicated. NR indicates not reported; SE, standard error.

<sup>\*</sup> Only long-term follow-up data from these studies are presented in this table.  $\dagger$  p<0.05 for difference between groups. ‡ Trial had other arms that were not included.

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