Systematic Review

Long-Term Diets and Changes in Body Composition and Bone Mineral Density: A Systematic Review and Meta-analysis

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Context: *The long-term effects of diets on body composition (BC) and bone mineral density (BMD) remain unclear.*
Objective: *To examine the effect of weight-loss inducing dietary interventions on BC and BMD at ≥12 months.*
Data Sources: *We conducted a systematic search on Medline, Embase, PubMed, and the Cochrane Library databases from inception until March 2025.*
Data Extraction: *We included randomized controlled trials (RCTs) of ≥12 months evaluating dietary interventions in adults (body mass index [BMI] ≥25 kg/m^2) on BC and BMD. We categorized diets into moderate macronutrients (MM), low-fat/high-carbohydrate (LFHC), high-fat/low-carbohydrate (HFLC), and usual diet (UD). We completed data screening/extraction in duplicate and independently. We used RevMan 5.3 for pooling and the Cochrane tool for risk of bias (ROB) assessment.*
Results: *Of 34 382 records, we included 23 trials reporting on BC and BMD. Most RCTs had high or unclear ROB. Baseline BMI was 28.6-37.7 kg/m^2 and most interventions lasted 12 months. Dual-energy X-ray absorptiometry was the primary BC assessement tool used (72%). Nine trials compared MM with HFLC diets and 5 trials compared MM diets with UDs. HFLC diets reduced fat mass (FM) compared with MM diets (2 trials; mean difference [MD], −2.88 kg; 95% CI, −5.41 to −0.34). Compared with a UD, the MM diet did not reduce FM (2 trials; MD, −11.36 kg; 95% CI, −26.36 to 3.63). There was no difference in the FM change between HFLC and LFHC diets. Similalry, there was no difference in the visceral adipose tissue and the subcutaneous adipose tissue parameters across different diets, with only few exceptions. Four RCTs evaluated BMD parameters, and one trial only showed a possible reduction in bone loss with a high-protein compared to a low-protein diet.*
Conclusion: *HFLC diets modestly reduced FM when compared to MM diets. Conversely, FM did not differ between MM diets and UDs. The impact of diets on other BC parameters did not differ. Data on BMD parameters are very scarce, with a possible benefit from a high-protein diet. More high-quality trials are needed.*
Systematic Review Registration: *PROSPERO no. CRD42018103116.*

Key words: public health, maternal health, child health, supplementation, health disparities, micronutrients, malnutrition, diet, epidemiology.

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INTRODUCTION

Obesity, a growing public health challenge, has been initially defined by the World Health Organization based on body mass index (BMI) cutoff points.[1] With time, the limitations of BMI emerged due to its inability to detect differences in muscle, bone, and adipose tissues, and its limited consideration for gender and age groups.[1] While several organizations advocated for the use of body composition (BC) methodologies, such as bioelectrical impedance analysis (BIA) and dual-energy X-ray absorptiometry (DXA) to evaluate obesity and excess adiposity,[2,3] many scientific bodies have not yet comprehensively integrated evaluation of BC in their recommendations (**Table S1**).[4–16]

Identifying the "best" dietary approach for weight management is an important debate among patients, healthcare providers, and researchers.[17] In addition to weight loss, changes in BC and bone loss are important considerations with long-term diets. Several previous systematic reviews and meta-analyses assessed the impact of a weight-loss–inducing diet on BC changes (**Table S2**). While some revealed a reduction in body fat percentage with lower-carbohydrate diets (relative to their comparator diets)[18–20] and low-fat diets (compared with high-fat or other weight-reducing diets),[21,22] others found no superiority of an individual diet on fat mass (FM)[23] and lean mass[19] compared with other diets. These systematic reviews included trials with a high dropout rate and a high heterogeneity in interventions and durations (**Table S2**). We aimed to review the impact of long-term (≥12 months) dietary interventions, classified according to Acceptable Macronutrient Distribution Range (AMDR), on BC and bone mineral density (BMD) parameters.

METHODS

The protocol of this systematic review is registered on PROSPERO (CRD42018103116)[24] and followed the Preferred Reporting Guidelines for Systematic Reviews and Meta-Analyses (PRISMA 2020) (**Table S3**).[25] PICO (Participants, Interventions, Comparators, Outcomes) elements are summarized in **Table 1**.

Study Inclusion

We included randomized controlled trials (RCTs) of active dietary interventions with a duration of 12 months or more, conducted on adults with overweight or obesity (identified using a mean sample BMI of ≥25 kg/m^2), as compared with another dietary intervention or with a usual diet (UD). We excluded studies with the majority of participants being pregnant, those with chronic diseases, those receiving pharmacotherapy associated with weight changes, as well as trials providing the interventions based on genetic profiles, or providing individual specific nutrient, meal replacement, or very-low-calorie diets (<800 kcal/d).

Outcomes of Interest

The outcomes of interest were BC—namely, fat mass (FM), lean mass, appendicular lean mass, fat-free mass (FFM), skeletal muscle index, muscle mass, as well as subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT) and total adipose tissue areas, mass and volume, and BMD at any site. We aimed to include all outcome measures being expressed as achieved level, absolute change or percentage change.

Search Strategy, Article Screening, and Data Extraction

We conducted a systematic search in 4 databases: Cochrane, Embase, PubMed, and Medline. The search strategy combined key words and Medical Subject Heading (MeSH) terms related to overweight and obesity, diet therapy, and RCTs.[26] The search period extended until March 2025 and is available online.[26]

Table 1. PICO Criteria for Inclusion of Studies

Parameter	Criteria
Participants	Randomized controlled trials (RCTs) conducted on adults with overweight or obesity (identified using a mean sample body mass index [BMI] of ≥25 kg/m^2)
Interventions	Active dietary interventions of ≥12 months total duration, classified by the Acceptable Macronutrient Distribution Range (AMDR) into (1) moderate macronutrients (MM): carbohydrates 45%–65%, protein 10%–35%, fat 20%–35%; (2) high-fat/low-carbohydrate (HFLC): fat above and/or carbohydrates below the AMDR; (3) low-fat/high-carbohydrate (LFHC): fat below and/or carbohydrates above the AMDR
Comparators	Another eligible dietary intervention (eg, HFLC vs LFHC or MM) or a usual diet (UD) control where participants were encouraged to maintain their usual lifestyle
Outcomes	Body composition (BC): fat mass, lean/appendicular lean mass, fat-free mass, skeletal muscle index, total/muscle mass; adipose depots: visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), total adipose (area/mass/volume); bone mineral density (BMD) at any site; outcomes accepted as achieved level, absolute change, or % change.

Pairs of reviewers conducted the screening of titles, abstracts, and full texts as well as data extraction, in duplicate and independently. Reviewers used standardized sheets for data screening and extraction. Reviewers were cross-trained on the screening and data extraction process to ensure a low discrepancy rate (≤5%). In case of disagreement, content experts (M.C. and J.J.) intervened for conflict resolution.

Risk-of-Bias Assessment

We used the 2011 Cochrane tool to evaluate the risk of bias (ROB) in duplicate and independently.[27] We planned to assess publication bias through funnel plots. However, this assessment was not feasible as none of the comparisons included 10 or more studies.

Diet Classification

We used the AMDR[28] to classify dietary interventions into a moderate macronutrients (MM) diet for those that had all macronutrients within the National Academy of Sciences recommendations (carbohydrate, protein, and fat composition constituting 45%–65%, 10%–35%, and 20%–35% of advised energy intake, respectively). A high-fat/low-carbohydrate (HFLC) diet was defined as having a content of fat and/or carbohydrate percentages that exceeded and/or were below the AMDR ranges for fats and carbohydrates, respectively. A low-fat/high-carbohydrate (LFHC) diet was defined with a fat composition below the AMDR and/or carbohydrate composition exceeding the AMDR.[28] A UD included control diets, where participants were encouraged to maintain their usual lifestyle during the study.

Statistical Considerations

We used counts (percentages) and means (ranges or SDs) to describe discrete and continuous variables, respectively. When 2 or more RCTs assessed the same intervention and outcome measure, and using the same machine and software (in the case of DXA), we pooled their results in a meta-analysis. We calculated the mean difference (MD) and 95% CI of continuous variables using a random-effects model. The meta-analysis was computed using Review Manager (RevMan, version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, 2014; Copenhagen, Denmark).[29]

RESULTS

The search strategy yielded 34 382 records. After duplicate removal and screening of citations and full-text articles, we included 23 original trials providing data on BC and 4 trials on BMD (**Figure 1**). **Table 2** summarizes the included trials' characteristics, diet categories and co-interventions, and the outcomes assessed. Half of the included trials were conducted in the United States, followed by Australia (18%) and several European countries (32%), including Spain, Sweden, Denmark, Norway, Israel, and Portugal. Sixty-four percent of the studies recruited both men and women, with women generally being predominant in the enrolled population, while a smaller proportion included only 1 gender (∼9% of trials included men only and 27% included women only). The mean age of participants ranged from 22.4 to 70.6 years, with approximately two-thirds of studies reporting a mean age below 50 years. The mean baseline BMI ranged between 28.6 and 37.7 kg/m^2. The number of participants per arm varied widely, from as few as 7 to as many as 318, and dropout rates ranged from 0% to 69.2%. Most interventions (72%) lasted 12 months, while 14% extended over 18 months and another 14% extended over 24 months. The most common dietary intervention was an MM diet, with co-interventions frequently including physical activity (31%) and behavioral support (24%). Fat mass–related outcomes were the most frequently assessed, most often measured using DXA (72%), using devices such as the Hologic QDR-4500 (Hologic, Inc., Marlborough, MA, USA), Lunar Prodigy, and GE Lunar (GE Healthcare, Madison, WI, USA), followed by BIA (14%).

Body Composition Parameters

Table 3 describes the results on BC parameters featured by diet group comparisons. The achieved FM was the most reported parameter, followed by fat-free and lean masses.

Fat Mass Parameters. A total of 21 trials evaluated FM parameters (achieved [kg], change [kg], or percent change [%]) in response to various diets.

MM vs HFLC diets. Eight trials evaluated FM parameters in response to an HFLC diet compared with an MM diet, over a duration of 12–24 months[30–37] **Table 3**). Six studies assessed the achieved FM (kg or %) at the end of the study; none of them showed any significant differences between HFLC and MM diets, and for some, the assessment of the statistical significance between arms was not provided.[30–34,37] We pooled the data of trials reporting on FM change in kilograms and FM % change.[30,31,37] Two trials were included in each meta-analysis. The forest plots show an MD in absolute FM change (kg) of −2.88 (−5.41 to −0.34), I^2 of 0% (**Figure 2A**), and an MD in %FM change of −1.12 (−2.51 to 0.27), I^2 of 31% (**Figure 2B**), favoring the HFLC arm over the MM

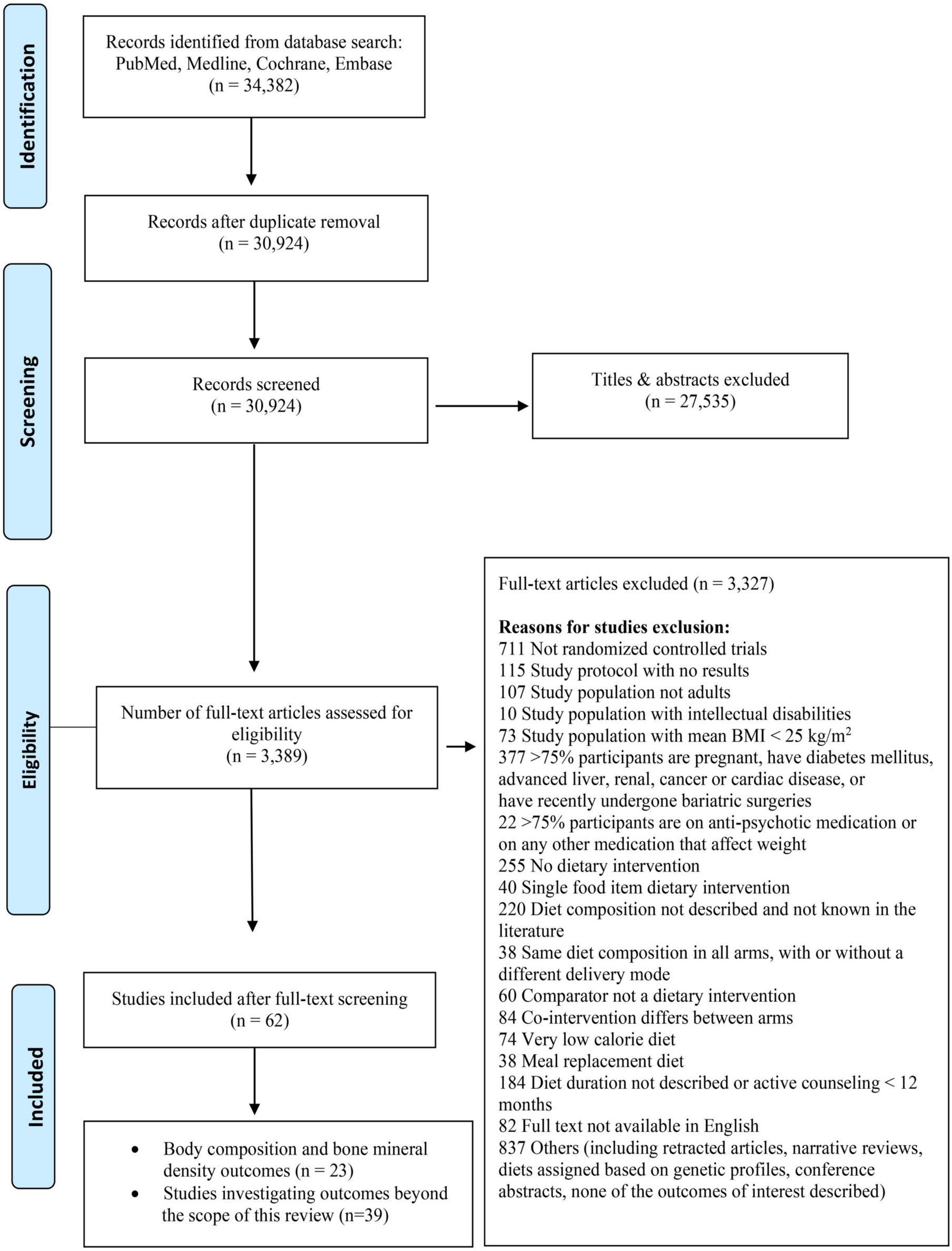

Figure 1. Flow Diagram Based on PRISMA 2020. Abbreviations: BMI, body mass index; PRISMA, Preferred Reporting Guidelines for Systematic Reviews and Meta-Analyses.

arm. A third trial reporting on the absolute FM change was not included in the meta-analysis as the SDs for this parameter were not available. It showed less reduction in FM (kg) with HFLC (–2.9 kg) compared with MM (–4.6 kg); the *P* value for the comparison was not available.[32] Bazzano et al[35] evaluated the %FM change and showed a significant reduction only in the HFLC diet (–1.2; –2.0 to –0.4), but not in the MM diet (0.3; –0.5 to

Table 2. Summary of the Included Trials Reporting on Body Composition and Bone Mineral Density

Study (year), country	Age, mean (SD or range), y	Men, %	Baseline BMI, mean (SD or range), kg/m^2	No. randomized/No. completed	Diet duration, mo	Diet types (as per authors) (diet categories)	Physical activity/ behavioral support	Outcomes assessed	Assessment technique
Williams et al (1994), USA[68]	N/A	100	30.7 (2.1)	45/39	12	Diet (MM)	None	FM change (%)	Hydrostatic weighing, and maximal oxygen uptake (VO_2max)
	N/A	100	30.7 (2.2)	44/40		Control (UD)			
Pritchard et al (1997), Australia[40]	43.6 (6.0)	100	29.0 (2.8)	22/18	12	Low-fat diet (MM)	None	FM achieved (kg), FM change (%), LM achieved (kg), LM change (%)	DXA, Hologic 1000/W, software, version 5.47. Hologic, Inc., MA, USA
	44.9 (6.5)	100	29.2 (2.8)	24/21		Exercise (UD)			
	42.3 (4.5)	100	28.6 (2.8)	20/19		Control (UD)			
Due et al (2004), Denmark[43]	39.4 (35.3-43.6)	24	30.8 (29.9-31.6)	25/18	12	Medium-protein (MM)	Behavioral support	Change in FM (kg), LM (kg)	DXA, Hologic 1000/W, software, version 5.61. Hologic, Inc., MA, USA
	39.8 (35.8-43.8)	24	30.0 (29.1-30.9)	25/23		High-protein (MM)			
Ebbeling et al (2005), USA[44]	29.8 (1.7)	12	N/A	17/11	12	Low glycemic load (MM)	Both	Change in FM (%), LM (%)	DXA, Hologic model QDR 4500. Hologic, Inc., MA, USA
	27.2 (1.3)	12	N/A	17/12		Low-fat (MM)			
Gardner et al (2007), USA[36]	42.0 (5.0)	0	32.0 (4.0)	77/68	12	Atkins (HFLC)	Behavioral support	FM change (%)	DXA, Hologic QDR-2000, QDR 4500. Hologic, Inc., MA, USA
	40.0 (6.0)	0	31.0 (3.0)	79/61		Zone (HFLC)			
	40.0 (7.0)	0	31.0 (4.0)	79/61		Learn (MM)			
	42.0 (6.0)	0	32.0 (3.0)	76/59		Ornish (LFHC)			
Tanumihardjo et al (2009), USA[47]	30.7 (6.6)	27	33.7 (3.8)	30/14	18	High vegetable (MM)	Physical activity	FM change (kg)	ADP
	36.4 (9.4)	27	33.3 (3.5)	30/18		Energy- and fat-reducing diet (MM)			
Sukumar et al (2010), USA[46]	58.5 (4.1)	0	32.1 (4.6)	29/26	12	High-protein (MM)	Physical activity	FM achieved (kg), FM change (%), LM achieved (kg), LM change (%)	DXA, Lunar Prodigy Advanced. GE Healthcare, Madison, WI, USA
	57.4 (4.7)	0		31/21		Normal-protein (MM)			
Foster-Schubert et al (2012), USA[39]	57.4 (4.4)	0	30.7 (3.9)	87/80	12	Control diet (MM)	None	LM achieved (kg), LM change (kg), LM change (%)	DXA, GE Lunar, GE Healthcare, Madison, WI, USA
	58.1 (6.0)	0	31.1 (3.9)	118/105		Diet (UD)			
	58.1 (5.0)	0	30.7 (3.7)	117/106		Control diet (MM)	Physical activity		
	58.0 (4.5)	0	31.0 (4.3)	117/108		Diet (UD)			
Fernandez et al (2012), Spain[33]	35.9 (12.4)	46	31.2 (2.7)	13/4	12	Insulin-resistant, "diet A" (HFLC)	None	FM achieved (%)	BIA, Holtain BC Analyzer, UK Omron BF 300, Tanita Corporation, Kyoto, Japan
	42.2 (15.1)	25	32.0 (2.0)	12/4		Insulin-resistant, "diet B" (MM)			
	47.3 (11.8)	13	33.0 (2.5)	8/4		Insulin-sensitive, "diet A" (HFLC)			
	40.6 (14.6)	43	31.4 (2.2)	7/4		Insulin-sensitive, "diet B" (MM)			

(continued)

Table 2. Continued

Study (year), country	Age, mean (SD or range), y	Men, %	Baseline BMI, mean (SD or range), kg/m²	No. randomized/No. completed	Diet duration, mo	Diet types (as per authors) (diet categories)	Physical activity/ behavioral support	Outcomes assessed	Assessment technique
Wycherley et al (2012), Australia[30]	51.3 (9.4) 50.2 (9.3)	100 100	33.0 (3.9) collectively	58/33 62/35	12	High-protein (HFLC) High-carbohydrate (MM)	None	FM achieved (kg), FM change (kg), FFM achieved (kg), FFM change (kg)	DXA, Lunar Prodigy; General Electric.
Griffin et al (2013), Australia[31]	22.4 (21.6-23.2) 22.5 (21.7-23.3)	0 0	34.1 (32.7-35.5) 33.8 (32.1-35.5)	36/21 35/15	12	Higher-protein (HFLC) Higher-carbohydrate (MM)	None	FM achieved (kg), FM change (kg), LM change (kg)	DXA, Lunar Prodigy GE Healthcare, Giles, UK
Jesudason et al (2013), USA[45]	59.5 (0.4) (5.38) 59.4 (0.4)(5.04)	0 0	34.0 (0.4) 33.4 (0.4)	164/69 159/67	24	High-protein (MM) High normal-protein (MM)	None	FM achieved (kg), FM change (%), LM achieved (kg), LM change (%)	DXA, Norland XR-800 machine (Siemens Medical)
Bazzano et al (2014), USA[35]	47.8 (10.4) 45.8 (9.9)	11 12	35.6 (4.5) 35.2 (3.8)	73/60 75/59	12	Low-fat (MM) Low-carbohydrate (HFLC)	Behavioral support	Change in FM (%), LM (%)	BIA, RJL Systems
Mellberg et al (2014), Sweden[32]	60.3 (5.9) 59.5 (5.5)	0 0	32.6 (3.3) 32.7 (3.6)	35/22 35/27	24	Low-carbohydrate (HFLC) Paleolithic diet (MM)	None	FM achieved (kg), FM change (kg)	DXA, Lunar Prodigy. GE healthcare
de Souza et al (2012), USA[48]	53(9.0) 49 (9.0) 55 (7.0) 49 (9.0)	25 18 0 0	33.1 (3.4) 33.9 (3.3) 31.6 (4.2) 32.5 (3.8)	104/182 104/182 122/242 122/242	24	Low-fat, average protein (LFHC) Low-fat, high protein (LFHC) High-fat, average protein (HFLC) High-fat, high protein (HFLC)	Both	Change in FM (kg), LM (kg), VAT (kg), SAT (kg)	DXA on a Hologic QDR 4500A (GE Healthcare, Madison, WI, USA) and CT (General Electric High-Light or LightSpeed volume)
Santanasto et al (2015), USA[41]	70.6 (5.9) 69.9 (6.2)	19 14	33.6 (3.3) 32.0 (3.1)	21/18 15/14	12	Diabetes Prevention Program (MM) Control (UD)	Physical activity	Change in FM (%), LM (%), muscle area (cm^2), VAT area (cm^2), SAT area (cm^2)	DXA, Hologic QDR 4500. Hologic Inc., USA
Brinkworth et al (2016), Australia[34]	51.6 (7.8) 51.0 (6.5)	31 39	33.7 (4.0) 33.2 (4.0)	57/32 61/33	12	Very low carbohydrate, high-fat (HFLC) Higher carbohydrate, low-fat (MM)	None	FM achieved (kg), FM achieved (%)	DXA, Lunar Prodigy. GE Heathcare

(continued)

Table 2. Continued

Study (year), country	Age, mean (SD or range), y	Men, %	Baseline BMI, mean (SD or range), kg/m^2	No. randomized/No. completed	Diet duration, mo	Diet types (as per authors) (diet categories)	Physical activity/behavioral support	Outcomes assessed	Assessment technique
Gepner et al (2017), Israel[51]	47.2 (9.0)	86	30.3 (3.4)	138/60	18	Low-fat (MM)	Physical activity	Change in VAT area (cm^2), deep and superficial SAT area (cm^2)	MRI, Ingenia 3.0 T, Philips Healthcare, Netherlands
	47.8 (9.8)		30.9 (3.3)	139/66		Mediterranean (HFLC)			
	49.5 (9.2)		31.1 (3.9)	138/57		Low-fat (MM)	None		
	47.0 (8.8)		30.9 (4.4)	139/56		Mediterranean (HFLC)			
Gardner et al (2018), USA[38]	39.3 (6.8)	45	33.4 (3.4)	314/241	12	Low-fat (MM)	None	FM change (%)	DXA, Hologic QDR 4500. Hologic Inc., USA
	40.2 (6.7)	41	33.3 (3.4)	318/238		Low-carbohydrate (HFLC)			
Boutelle et al (2022), USA[42]	46.4 (12.4)	17	35.2 (5.6)	69/56	12	Regulation of Cues (ROC) (UD)	Both	FM change (%)	DXA, software not specified
	48.2 (11.1)	19	34.2 (5.6)	67/55		ROC + weight loss (MM)			
Sommersten et al (2022), Norway[50]	41.6 (8.8)	47	36.4 (4.3)	68/14	12	Acellular HCLF (HFLC)	Physical activity	Change in VAT area (cm^3), SAT area (cm^3), TAT area (cm^3)	CT, SOMATOM Force, Siemens, Germany
			37.7 (5.1)	62/22		Cellular HCLF (HFLC)			
			35.9 (4.8)	63/21		LCHF (HFLC)			
Mogna-Peláez et al (2024), Spain[37]	51.1 (9.8)	58	33.7 (4.0)	48/32	24	American Heart Association diet (MM)	Behavioral support	Change in FM (%), VAT area (kg), LM (kg)	DXA, Lunar iDXA, enCORE 14.5, Madison, WI, USA
	49.2 (8.9)	54	33.3 (4.0)	50/26		Fatty Liver in Obesity (HFLC)			
Pereira et al (2024), Portugal[49]	44.0 (8.8)	29	33.9 (2.6)	59/40	18	WLM3P (HFLC)	Both	Change in FM (kg), VAT area (cm^2)	BIA, InBody model 770, Seoul, Korea
	46.2 (8.4)	26	34.1 (2.2)	53/37		LCD (HFLC)			

Abbreviations: ADP, air displacement plethysmography; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass; HCLF, high-carbohydrate low-fat; HFLC, high-fat/low-carbohydrate; LFHC, low-fat/high-carbohydrate; LM, lean mass; MM, moderate macronutrients; MRI, magnetic resonance imaging; N/A, not available; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; UD, usual diet; VAT, visceral adipose tissue; VO_2 max, hydrostatic weighing and maximal oxygen uptake; WLM3P, Weight Loss Maintenance 3-Phase Program.

Table 3. Summary of the Change in Fat Mass by Diet Group Comparisons

Diet categories	MM vs HFLC	HFLC vs LFCH	MM vs UD	MM vs MM[a]	HFLC vs HFLC
Achieved (kg) at study end	Wycherley et al[30]: HFLC: 26.2 (8.3) MM: 26.3 (7.9), P[b] = .11 Griffin et al[31]: HFLC: 47.6 (44.8; 50.4) MM: 44.4 (39.8; 49.0), $P = 0.19$ Mellberg et al[33,b]: MM: 33.9 (3.3) HFLC: 37.8 (2.7), P = NS	—	Pritchard et al[40]: MM: 16.1 (4.4) kg UD: 19.3 (3.9) kg $P < .05$ Foster-Schubert et al[39]: MM: 31.2 (9.5) kg UD: 37.8 (8.7) kg $P < .01$	Sukumar et al[46]: MM (HP): 35.4 (10.6) MM (NP): 32.4 (8.3), $P = .321$[c] Jesudason et al[45]: MM (HP): 40.5 (1.4) MM (NP): 39.9 (1.6), $P = .47$	—
Achieved (%) at study end	Fernandez et al[33]: HFLC: 35.3 (8.2) MM: 35.0 (10.8), P = NA Brinkworth et al[34]: HFLC: 36.1 (9.8) MM: 35.8 (8.5), P[d] = NA Mogna-Peláez et al[37]: HFLC: 39.2 (8) MM: 40.1 (7), $P = .803$	—	Boutelle et al[42]: UD: 45.48% MM: 43.36%, P = N/A	—	—
Absolute change (kg)	**Pooled estimate[30,31]** **MD -2.88 kg (-5.41; -0.34), I^2 = 0% favoring HFLC diet** Mellberg et al[32]: MM: -4.6 (NA) HFLC: -2.9 (NA), P = NA	de Souza et al[48]: HFLC: -5.3 (0.4) LFHC: -5.6 (0.4), $P = .63$	Foster-Schubert et al[39]: MM: -20.8 UD: -5.3, $P = .006$	Due et al[43]: MM (MP): -3.1 (-1.4; -4.7) MM (HP): -4.6 (-2.7; -6.6), P = NS **Tanumihardjo et al[47,e]:** **MM (HV): 0.5** **MM (EFR): -4.5, $P < .001$**	Pereira et al[49]: HFLC (WLM3P): -11.2 (7.4) HFLC (LCD): -6.7 (7.2), $P = .009$
Percent change (%)	**Pooled estimate[30,37]** MD -1.12 (-2.51; 0.27), I^2 = 31% favoring HFLC diet **Bazzano et al[35]:** **MM: 0.3 (-0.5 to 1.1)** **HFLC: -1.2 (-2.0; -0.4), $P = .011$** Gardner et al[36,f]: MM: -1.97 (3.2) HFLC: -2.15 (3.1), P = NS Mogna-Peláez et al[37]: HFLC: -1.85 (4.13) MM: -1.55 (3.24), P = NS	—	Pooled estimate[40,41] -11.36 (-26.36; 3.63), I^2 = 99% favoring MM diet	Ebbeling et al[44]: MM (LGL): -16.5 MM (LF): -15.7, $P = .97$ Sukumar et al[46]: MM (HP): 11.7 (10.1) MM (NP): 11.7 (10.1), P = NS Jesudason et al[45]: MM (HP): 12.9 (1.8) MM (NP): 14.3 (1.9), P = NS	Pereira et al[49]: HFLC (WLM3P): -6.6 (6.2) HFLC (LCD): -3.6 (5.0), $P = .023$

Fat mass values are shown as mean (SD or 95% CI). Significant results are shown in bold.
[a]Diets that fall under MM diet as per Acceptable Macronutrient Distribution Range but differ in their composition
[b]P value for the treatment effect between groups for the change from weeks 0, 12, and 52 (repeated-measures ANOVA)
[c]P for diet × time = .834
[d]P for time × diet = .41
[e]Estimated from figure.
[f]Gardner et al compared MM vs HFLC vs LFHC.
Abbreviations: EFR, energy- and fat-reducing; HFLC, high-fat/low-carbohydrate; HP, high-protein; HV, high-vegetables; LCD, low-carbohydrate diet; LF, low-fat; LFHC, low-fat/high-carbohydrate; LGL, low glycemic load; MM, moderate macronutrients; MP, moderate protein; N/A, not applicable; NA, not available; NP, normal protein; NS, nonsignificant; UD, usual diet; WLM3P, Weight Loss Maintenance 3 Phases Program.

1.1; $P = .011$). Two additional trials compared HFLC with MM diets on FM percent change and did not report a significant difference between arms.[37,38]

HFLC vs MM vs LFHC. One trial, the A-to-Z weight-loss study, compared 3 diets and showed that participants on the HFLC diet had a mean percent FM reduction of –1.9% (SD, 4.2%), while those on the MM diet had a reduction of –1.0% (SD, 3.4%), and those on the LFHC diet had a reduction of –1.5% (SD, 4.0%). However, the P value for statistical significance was not reported.[36]

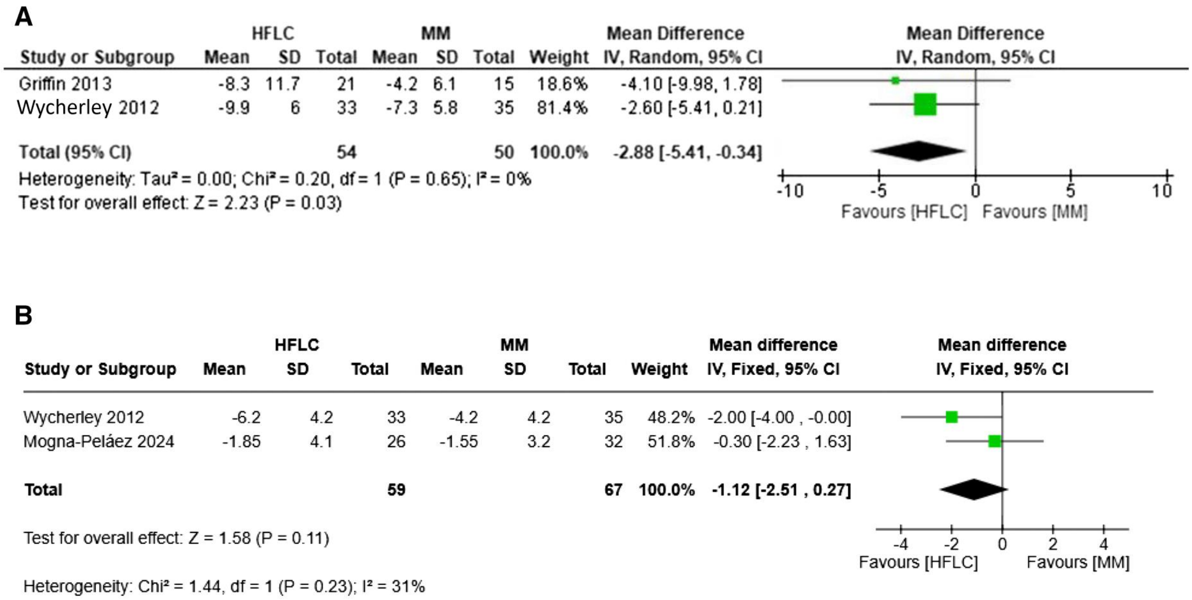

Figure 2. Forest Plots Comparing Fat Mass Parameters Between a High-Fat/Low-Carbohydrate Diet and a Moderate Macronutrients Diet. Fat mass change (kg) (A) and fat mass change (%) (B) between an HFLC diet and MM diet are shown. Abbreviations: HFLC, high-fat/low-carbohydrate; IV, inverse variance; MM, moderate macronutrients.

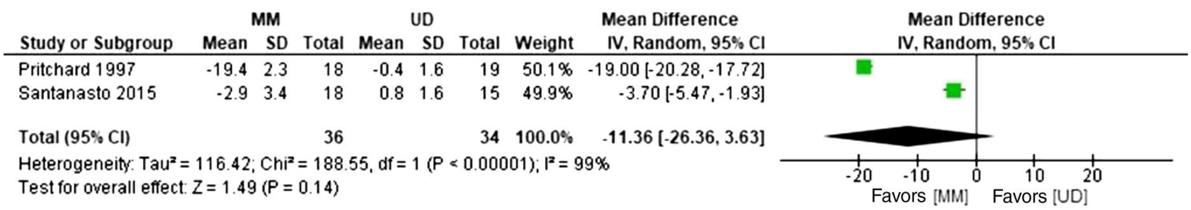

Figure 3. Forest Plot Comparing Fat Mass Change (%) Between a Moderate Macronutrient Diet and Usual Diet. Abbreviations: IV, inverse variance; MM, moderate macronutrients; UD, usual diet.

MM vs UD. Four studies evaluated FM parameters in response to an MM diet compared with a UD[39–42] (**Table 3**). In 2 studies, the FM achieved at study end was significantly lower in the moderate MM group compared with the UD group.[39,40] The meta-analyses of 2 trials[40,41] showed an MD in the percentage FM change of −11.36% (−26.36 to 3.63), I^2 of 99% (**Figure 3**).[40,41] The Foster-Schubert et al study[39] showed that participants on the MM diet with exercise had an absolute FM change of −20.8 kg, while those on the UD had a change of −5.3 kg ($P = .006$). In Boutelle et al,[42] the UD group (Regulation of Cues [ROC]) %FM at 12 months was 45.48% compared with 43.36% in the ROC with weight-loss (MM) group, indicating a reduction of approximately 2.1 percentage points in favor of the MM intervention (*P* value not available).

MM vs MM. We identified 5 studies comparing diets with different distributions of protein, fat, or glycemic load, but falling under the same category, MM diet, according to the AMDR classification[43–47] (**Table 3**). Two RCTs assessed the achieved FM (kg) and showed no differences between 2 groups receiving MM diets, even if the protein content differed within this category. Sukumar et al[46] showed a mean (SD) achieved FM of 35.4 (10.6) kg in the high-protein diet group and 32.4 (8.3) kg in the normal-protein diet group (*P* for diet = .321 and *P* for diet × time = .834). Similarly, Jesudason et al[45] reported a mean (SE) achieved FM of 40.5 (1.4) kg in the MM high-protein diet group and 39.9 (1.6) kg in the MM normal-protein diet group (*P* for diet= 0.47 and diet × time = .59) . Two studies assessed the absolute FM change.[43,47] One of them showed no difference between a medium- and a high-protein MM diet (−3.1 kg; 95% CI, −1.4 to −4.7; and −4.6 kg; 95% CI, −2.7 to −6.6, respectively).[43] Conversely, Tanumihardjo et al[47] reported a significant difference in absolute FM change, with the high-vegetable MM diet group showing a change of 0.5 kg compared with the energy- and fat-reduction MM diet group with -4.5 kg ($P < .001$). Three studies assessed the FM change (%) and showed no differences between arms.[44–46]

HFLC vs LFHC. De Souza et al[48] reported no significant difference in FM reduction between HFLC and LFHC diets, with changes of –5.3 (0.4) kg and –5.6 (0.4) kg, respectively ($P = 0.63$).

HFLC and HFLC. Pereira et al[49] found that, within HFLC diets, the Weight Loss Maintenance 3-Phase Program (WLM3P) achieved a greater absolute FM reduction compared with a low-carbohydrate diet (–11.2 (7.4) kg vs –6.7 (7.2) kg; $P = .009$), and similarly for percentage change [–6.6% (6.2%) vs –3.6% (5.0%); $P = .023$]. The diets differed in their introduction of carbohydrates and intensity of behavioral support. The WLM3P diet featured a gradual increase in carbohydrate intake and more intensive support than the low-carbohydrate diet.

VAT and SAT Parameters. Six studies evaluated visceral[31,37,41,49,50] or subcutaneous fat[48,50] (**Table 4**). Two trials compared HFLC with MM diets on absolute VAT area change (cm^2)[51] and on absolute VAT mass change (kg).[37] In the former, patients on the HFLC diet lost –39.9 (34.9) cm^2 VAT, while those on the MM diet lost –41.0 (38.6) cm^2 (P value not available).[51] In the latter, VAT mass at study end was 2.2 kg in the MM group vs 1.7 kg in the HFLC group, with reductions of −0.39 (0.65) kg and −0.38 (0.57) kg (P = not significant [NS]).[37] One study reported a decrease in the absolute change in VAT area (cm^2) that was larger with an MM diet compared with a UD (MM, –34.8 [40.4]; UD, –1.0 [29.3]; $P < .05$).[41]

Two trials assessed the effects HFLC diets on VAT parameters.[49,50] In Sommersten et al,[50] 2 HFLC diets were used: the acellular diet and the cellular diet constituted diet category 1 and the low-carbohydrate/very-high-fat diet constituted the second diet category. The VAT area decreased by 667 cm^2 in the acellular and cellular higher-carbohydrate, low-fat diet and by 926 cm^3 (95% CI, −1321 to −530) in the LCHF diet (P = NS). In Pereira et al,[49] the VAT area decreased by 53.1 cm^2 (SD, 38.1) in the HFLC WLM3P and by −29.8 cm^2 (SD, 34.6) in the HFLC ($P = .01$).

An HFLC diet resulted in similar absolute change in deep and superficial SAT area compared with the MM diet (–58.5 vs –55.9 cm^2; $P = .78$; and –25.5 vs –27.0 cm^2; $P = .45$, respectively).[51] Similarly, the change in SAT mass (kg) was not significantly different when an HFLC diet was compared with an LFHC diet.[48] Comparing the MM diet to a UD, the decrease in the overall SAT area (cm^2) was –46.7 (SD, 62.8) in the former and –24.8 (SD, 63.8) cm^2 in the latter (P value not available).[41] Finally, in the 12-month trial by Sommersten et al,[50] all 3 HFLC diets—acellular (−1056 cm^2), cellular (−1204 cm^2), and low-carbohydrate/high-fat (−1598 cm^2)—produced reductions in SAT, with no available data whether there were significant differences between arms.

Fat-Free, Lean, and Muscle Masses. Two RCTs assessed FFM[30,47] (**Table 5**). Participants on the HFLC diet achieved a significantly higher mean FFM of 65.6 (SD, 5.9) kg compared with those on the MM diet, who achieved 64.3 (7.8) kg ($P < .01$), with a smaller absolute reduction in FFM with the HFLC diet of –2.6 (SD, 3.7) kg, compared with the MM diet of –3.8 (SD, 4.7) kg ($P < .05$).[30] Conversely, Tanumihardjo et al[47] found no significant differences in the absolute change in FFM between the 2 MM diet groups (high-vegetable diet vs kcal-reduction diet).

Eleven studies assessed lean mass parameters[31,35,37,39–41,43–46,48] (**Table 5**). Three studies compared MM with HFLC diets.[31,35,37] There was no difference in the achieved and absolute change in lean mass (kg),[31,37] but there was a significant difference in lean mass percent change with the MM diet (–0.4%; 95% CI, –1.2% to 0.4%) compared with the HFLC diet (1.3%; 95% CI, 0.5% to 2.0%; $P = .01$).[35] De Souza et al[48] showed that the HFLC diet decreased lean mass significantly more than the LFHC diet (absolute change HFLC vs LFHC, –2.9 [1.9] vs –2.2 [0.3]; $P = .04$). Three studies compared the MM diet with the UD, and found no significant difference in the achieved or the absolute change in lean mass.[39–41] Yet, the percentage change in lean mass was significantly greater in the MM diet group compared with the UD in the 2 studies, but in opposite directions.[39,40]

Four RCTs compared diets that fall under the MM category of the AMDR classification. There was no difference in the achieved, absolute, and percent change in lean mass between arms, except in Sukumar et al,[46] which reported a significant difference in the achieved lean mass between the MM high-protein diet group (44.0 [5.8] kg) and the MM normal-protein diet group (40.3 [4.6] kg) ($P = .034$ for diet and $P = .504$ for diet × time).

BMD Parameters

We included a total of 4 studies (3 trials reported on BC and BMD and 1 trial reported only on BMD).[34,45,46,52] The changes in BMD parameters in various diet group comparisons are shown in **Table 6**. Two trials compared the HFLC diet with the LFHC diet. Brinkworth et al[34]

Table 4. Summary of the Change in Adipose Tissue Components (Visceral, Subcutaneous, and Total Adipose Tissues) by Diet Category Comparisons

Diet categories	MM vs HFLC	HFLC vs LFCH	MM vs UD	MM vs MM[a]	HFLC vs HFLC[a]
VAT area					
Absolute change (cm^2)	Gepner et al[51]: MM: -41.0 (38.6) HFLC: -39.9 (34.9), $P = $ NA	—	**Santanasto et al[41]: MM: -34.8 (40.4) UD: -1.0 (29.3), $P < .05$**	N/A	• **Pereira et al[49]:** • **HFLC (WLM3P): -53.1 (38.1)** • **HFLC (LCD): -29.8 (34.6), $P = .010$** • Sommersten et al[50]: • HFLC (acellular and cellular higher carbohydrate, low-fat): -667 ($P < .05$) • HFLC (LCHF): -926 (-1321, -530), $P = $ NA
Percent change (%)	N/A	—	N/A	N/A	Sommersten et al[50]: HFLC (acellular and cellular higher carbohydrate, low-fat): -0.40 HFLC: -0.35, $P = $ NA
Absolute change (kg)	Mogna-Peláez et al[37]: MM: -0.39 (0.65) HFLC: -0.38 (0.57), $P = $ NS	de Souza et al[48]: HFLC: -1.1 (0.2) LFHC: -1.3 (0.2), $P = .32$	—	—	—
SAT area					
Absolute change (cm^2)	Gepner et al, deep[51]: MM: -55.9 (42.0) HFLC: -58.5 (44.7), $P = .78$ Gepner et al, superficial[51]: MM: -27.0 (25.0) HFLC: -25.5 (24.9), $P = .45$	—	Santanasto et al[41]: MM: -46.7 (62.8) UD: -24.8 (63.8), $P = $ NA	N/A	Sommersten et al[50]: HFLC (acellular and cellular higher carbohydrate, low-fat): -1127 HFLC (LCHF): -1598, $P = $ NA
Absolute change (kg)	—	de Souza et al[48]: HFLC: -1.9 (0.4) LFHC: -2.4 (0.4), $P = .32$	—	—	—
SAT volume					
Change (cm^3)	—	—	—	—	**Sommersten et al[50]: HFLC (acellular and cellular higher carbohydrate, low-fat): -1127 HFLC (LCHF): −1598, $P < .001$**
TAT volume					
Absolute change (cm^3)	—	—	—	—	**Sommersten et al[50]: HFLC (acellular and cellular higher carbohydrate, low-fat): -1777 HFLC (LCHF): -2583, $P < .001$**

Values are mean (SD). Significant results are shown in bold.
[a]Diets that fall under MM as per the Acceptable Macronutrient Distribution Range differ in their composition. Their diet brands are defined within parentheses.
Abbreviations: HFLC, high-fat/low-carbohydrate; LCD, low-carbohydrate diet; LFHC, low-fat/high-carbohydrate; MM, Moderate Macronutrients; N/A, not applicable; NA, not available; NS, nonsignificant; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; UD, usual diet; VAT, visceral adipose tissue; WLM3P, Weight Loss Maintenance 3 Phases Program.

Table 5. Summary of the Change in Lean and Fat-Free Mass by Diet Group Comparisons

Diet categories	MM vs HFLC	HFLC vs LFCH	MM vs UD	MM vs MM[a]
Fat-free mass, mean (SD)				
Achieved (kg)	**Wycherley et al[30]: MM: 64.3 (7.8) HFLC: 65.6 (5.9), $P < .01$**	—	N/A	N/A
Absolute change (kg)	**Wycherley et al[30]: MM: -3.8 (4.7) HFLC: -2.6 (3.7), $P < .05$**	—	N/A	• Tanuamihardjo et al[47]: • MM (HV): -0.5 • MM (EFR): -0.75, $P =$ NS
Lean mass, mean (SD or 95% CI)				
Achieved (kg)	Mogna-Peláez et al[37]: MM: 51.9 (10) HFLC: 52.4 (8), $P = .984$	—	Pritchard et al[40]: MM: 64.2 (6.6) UD: 65.7 (7.0), $P =$ NS Foster-Schuber et al[39]: MM: 39.2 (3.9) UD: 40.5 (5.1), $P = .15$	**Sukumar et al[46]: MM (HP): 44.0 (5.8) MM (NP): 40.3 (4.6), $P = .034$** Jesudason et al[45]: MM (HP): 37.7 (0.6) MM (NP): 37.1 (0.7), $P = .34$
Absolute change (kg)	Griffin et al[31]: MM: -0.3 (-0.6; 1.1) HFLC: -0.9 (-0.2; 2.1), $P = .22$	**de Souza et al[48]: HFLC: -2.9 (1.9) LFHC: -2.2 (0.3), $P = .04$**	Foster-Schubert et al[39]: MM: -1.1 UD: 0.7, $P = .15$ Santanasto et al[41]: MM: -1.2 (1.7) UD: -0.1 (1.2), $P =$ NS	Due et al[43]: MM (MP): -0.4 (-1.2 to 0.4) MM (HP): -0.9 (-1.8 to 0.0), $P =$ NS
Percent change (%)	**Bazzano et al[35]: MM: -0.4 (-1.2; 0.4) HFLC: 1.3 (0.5; 2.0), $P = .01$**	—	• **Pritchard et al[39,40]:** • **MM: -3.9 (0.5)** • **UD: 0.2 (0.4) $P < .05$** • **Foster-Schubert et al[39]:** • **MM: 11.8** • **UD: 3.5, $P = .008$**	Ebbeling et al[44]: MM (LGL): -1.1 MM (LF): -1.5, $P = .92$ Sukumar et al[46]: MM (HP): 2.7 (4.0) MM (NP): 2.7 (4.0), $P =$ NS Jesudason et al[45]: MM (HP): 4.6 (0.6) MM (NP): 4.6 (0.8), $P =$ NS
Muscle mass (cm^2), mean (SD)				
Absolute change (cm^2)	N/A		Santanasto et al[41]: MM: -5.0 (6.4) UD: -2.1 (5.7), $P =$ NA	N/A

Significant results are shown in bold.
[a]When comparing the same categories, diet types are defined within parentheses.
Abbreviations: EFR, energy- and fat-reducing; HFLC, high-fat/low-carbohydrate; HP, high-protein; HV, high-vegetables; LF, low-fat; LFHC, low-fat/high-carbohydrate; LGL, low glycemic load; MM, moderate macronutrients; MP, moderate-protein; N/A, not applicable; NA, not available; NP, normal protein; NS, nonsignificant; UD, usual diet.

compared a an HFLC diet with an LFHC diet for a period of 12 months. Weight, total bone mineral content, and total BMD remained unchanged in both diet groups. In Tirosh et al[52] the diets differed in the macronutrient composition, such as fat (20% vs 40%), protein (15% vs 25%) and carbohydrate percentage (ranging from 35 to 65%). At 2 years, there was a significant drop in BMD at all sites, but there were no significant differences between study arms.[52]

Two studies compared MM diets, differing in protein composition.[45,46] Sukumar et al[46] compared a high-protein MM diet with a normal-protein MM diet over a 1-year period. There was no significant difference between the 2 groups in weight-loss percentage; participants in the high-protein group lost 6.6% (4.0%) of their weight, while those in the normal-protein group lost 7.4% (5.2%) (P = NS). Participants in the normal-protein group experienced significantly greater BMD loss compared with the high-protein group at the ultra-distal radius (−3.3% [4.2%] vs −0.9% [3.2%]; $P < .05$), lumbar spine (−1.4% [3.6%] vs 0.2% [3.4%]; $P < .05$), and total hip (−1.2% [1.8%] vs −0.4% [1.3%]; $P < .05$).[46] Jesudason et al[45] compared a high-protein MM diet with a high-normal-protein MM diet (≤80 vs ≥90 g/d) in postmenopausal women over a 1-year duration. The study found that neither the "high protein" nor the "high normal protein" diet had any significant effect on weight or bone density, and there was no interaction between diet and time at any of the 4 measured sites. After 2 years, a higher percentage of bone loss was observed at all sites in the "high normal protein" group compared with the "high protein" group, but this difference was not significant.[45] Tirosh et al[52] compared an HFLC diet with an LFHC diet.[52] The diets differed in the macronutrient composition, such as fat (20% vs 40%), protein (15% vs 25%), and carbohydrate

Table 6. Summary of the Achieved BMD (g/cm^2) by Site in Different Diet Group Comparisons

Study, year	Diet category	Weight loss (kg)	Total BMD (g/cm^2)	Lumbar spine (g/cm^2)	Total hip (g/cm^2)	Femoral neck (g/cm^2)	Forearm (g/cm^2)
Sukumar et al,[46] 2010	MM (HP) vs MM (NP)	MM (HP) -6.6% ± 4.0% MM (NP) -7.4% ± 5.2% *P*: NS	MM: 1.19 (0.09) MM: 1.12 (0.10) *P* for diet: .023 *P* for diet × time: .951	MM: 1.25 (0.18) MM: 1.12 (0.17) *P* for diet: .063 *P* for diet × time: .028	MM: 1.01 (0.12) MM: 0.93 (0.10) *P* for diet: .020 *P* for diet × time: .050	MM: 0.94 (0.11) MM: 0.89 (0.10) *P* for diet: .085 *P* for diet × time: .884	MM: 0.68 (0.06) MM: 0.67 (0.08) *P* for diet: .419 *P* for diet × time: .490
Jesudason et al,[45] 2013	MM (HP) vs MM (HNP)	MM (HP) 9.0%±1.0% MM (HNP) 10.1%±1.0% *P*: NS	—	High-protein (MM): 1 y: 1.17 (0.02) 2 y: 1.15 (0.02) High-normal protein (MM): 1 y: 1.18 (0.02) 2 y: 1.15 (0.02) *P* for diet: .603 *P* for diet × time: .239	High-protein (MM): 1 y: 0.98 (0.01) 2 y:s 0.96 (0.02) High-normal protein (MM): 1 y: 0.98 (0.01) 2 y: 0.97 (0.02) *P* for diet: .985 *P* for diet × time: .540	High-protein (MM): 1 y: 0.92 (0.01) 2 y: 0.9 (0.02) High-normal protein (MM): 1 y: 0.92 (0.01) 2 y: 0.91 (0.02) *P* for diet: .814 *P* for diet × time: .176	High-protein (MM): 1 y: 0.35 (0.01) 2 y: 0.36 (0.01) High-normal protein (MM): 1 y: 0.36 (0.01) 2 y: 0.37 (0.01) *P* for diet: .152 *P* for diet × time: .239
Brinkworth et al,[34] 2016	HFLC vs LFHC	HFLC (kg): 79.2 ± 13.7 (-15%) LFHC (kg) 83.4 ± 13.1 (-12%) *P*: .18	HFLC: 1.22 (0.09) LFHC: 1.23 (0.08) *P* for time × diet: .25	—	—	—	—
Tirosh et al,[52] 2015	HFLC vs LFHC	No significant differences among diet groups (6.4% of initial body weight), $P = .34$	N/A	High-protein vs average-protein: $P = .4215$ High-fat vs low-fat: $P = .1242$ High-carbohydrate vs low-carbohydrate: $P = .6507$	High-protein vs average-protein: $P = .3446$ High-fat vs low-fat: $P = .4402$ High-carbohydrate vs low-carbohydrate: $P = .9219$	High-protein vs average-protein: $P = .8026$ High-fat vs low-fat: $P = .4672$ High-carbohydrate vs low-carbohydrate: $P = .4932$	—

Abbreviations: BMD, bone mineral density; HFLC, high-fat/low-carbohydrate; HNP, high-normal protein; HP, high-protein; LFHC, low-fat/high-carbohydrate, MM, moderate macronutrients; N/A, not applicable; NP, normal-protein; NS, nonsignificant.

percentage (ranging from 35% to 65%). At 2 years, there was a significant decrease in BMD at all sites, but there was no significant differences between study arms.[52]

Table S4 and **Figure S1** present the ROB assessment of the included trials. Most of the RCTs had "high" or "unclear" ROB. Common biases were related to the lack or inadequate reporting of allocation concealment as well as blinding of participants, personnel, and outcome assessment. High ROB was mostly related to incomplete outcome reporting. Other biases consisted of imbalances in baseline characteristics, industrial sponsorship, conflict of interest, and lack of description of funding sources.

DISCUSSION

In this systematic review, long-term (≥12 months) dietary interventions encompassing different macronutrient compositions were evaluated in relation to BC and BMD outcomes. Our findings on 23 original trials suggest that, for individuals with overweight and/or obesity, HFLC diets may be associated with modest reductions of 1%–2% in FM compared with MM diets. The clinical significance of these reductions remain questionable, since a minimum 5% decrease in FM might be needed for improvement in metabolic parameters.[53] The MM diets did not significantly reduce FM when compared with UDs. The data on adipose tissue components are inconclusive. With regard to lean and FFM, the data are suggestive of a possible protective effect of an HFLC diet compared with an MM diet.

Given the limitations of BMI measurement, particularly its inability to reflect lean mass and FM accurately, understanding the effect of weight-loss diets on BC parameters using reference methods, such as DXA and BIA, has a direct clinical implication. Body composition, particularly the distribution between FM and FFM, is closely linked to cardiovascular outcomes.[54] Excess adiposity, especially VAT, is associated with increased risks of hypertension, dyslipidemia, and insulin resistance, all of which are significant risk factors for cardiovascular diseases.[54,55] Given the complex interrelationship between obesity and other chronic diseases, such as cardiovascular diseases,[56,57] an HFLC diet could be integral to a holistic approach to address multiple adverse obesity-related health outcomes. The possible superiority of an HFLC diet in attaining FM reduction is supported by several previous systematic reviews on the topic. A meta-analysis by Chawla et al[58] demonstrated the effectiveness of low-carbohydrate diets in improving many cardiovascular risk factors. Hashimoto et al[20] described the effectiveness of both the low-carbohydrate and control diets in reducing body FM (2–24 months) and found that the reduction was higher in the low-carbohydrate group, with a mean difference in the change in FM of 0.82 kg. Similarly, Clifton et al[19] found that high-protein diets over a duration of 1–4 years were associated with a slightly larger FM loss (equivalent to 0.44 kg loss at study end) and participants who had 5% or greater increased protein intake at study end had 3-fold more FM loss compared with their counterparts with lower intake. Such potential modest benefit of an HFLC diet on BC is in line with our findings in a previous network meta-analysis on the long-term effects of diets on weight.[26]

Hall[59] proposed the carbohydrate–insulin model of obesity that extends beyond caloric intake and energy expenditure. The model suggests that diets high in carbohydrates induce insulin secretion which "directs the partitioning of energy toward storage as fat in adipose tissue," and in turn, increases feelings of hunger and appetite and therefore promotes obesity.[59] In addition, dietary fat is important for the regulation of neuropeptide Y, cholecystokinin, and corticotropin-releasing hormone, which are essential for the regulation of digestion and sensations of satiety.[60] AMP-activated protein kinase, pertinent to insulin, glucose, and fatty acid metabolism, has also shown favorable responses to dietary fat.[60] Furthermore, our aforementioned findings are bolstered by previous findings of reviews that favor an HFLC diet over other diets in relation to several chronic conditions. A review by Noakes and Windt[61] has shown that HFLC diets are effective at regulating glycemia, reducing hyperinsulinemia in individuals with type 2 diabetes, and improving most of the cardiometabolic profile (eg, decreased triglycerides, increased high-density-lipoprotein cholesterol).

This review also assessed the effects of different diets on BMD; there was no effect of different diets on BMD except for 1 study.[46] The latter trial compared 2 MM diets, high-protein (MM) diet with a normal-protein (MM) diet over 1 year and found that participants in the normal-protein group experienced significantly greater BMD loss at different sites, weight-bearing and peripheral sites, compared with the high-protein diet, while there was no difference in weight loss between arms.[46] Previous systematic reviews exploring bone loss in response to diet-induced weight loss showed heterogeneous results. Wright et al[62] conducted a systematic review looking at the effect of higher-protein vs normal-protein diets on BMD and bone mineral content. Participants lost an average of 7.0 (2.6) kg of body weight following the weight-loss intervention; 54.5% of those in the high-protein group and 32.6% in the normal-protein group achieved a reduction of 10% or more from their baseline body weight. The systematic review revealed that most studies (59%) reported a reduction in bone parameters during weight loss, regardless of protein intake, although a high-protein diet slightly mitigated the loss of total BMD compared with a normal-protein diet.[62] Soltani et al[63] also performed a systematic review and meta-analysis and reported that weight-loss interventions (calorie restriction and exercise), compared with no interventions, reduced BMD at the hip and lumbar spine, particularly in individuals with obesity and after more than 4 months of intervention. While the weight loss attributed to exercise alone was relatively small in comparison to the greater weight reduction achieved through diet alone, there was no comparison between different diets to assess their impact on BMD.[63] The systematic review and meta-analysis by Zibellini et al,[64] which included 41 publications, showed that diet-induced weight loss was associated with significant decreases in total hip BMD (decrease of 0.010 to 0.015 g/cm^2) for interventions lasting 6, 12, or 24 months, but not for shorter durations. Conversely, there was no significant effect on lumbar spine or whole-body BMD, except for a small decrease in total body BMD after 6 months. When subgroup analyses were conducted by degree of dietary intervention, there was a significant reduction in total hip BMD with moderate energy restriction but not with severe energy restriction using very-low-energy diets or low-energy diets. In contrast, lumbar spine BMD significantly decreased with interventions involving very-low-energy diets or low-energy diets, but not with moderate energy restriction.[64]

We aimed to compare the impact of diets administered at least 1 year on BC and BMD parameters in order to assess the sustainability of the effect of weight-loss diets among individuals with a BMI of 25 kg/m^2 or greater. We considered the AMDR classification, which is widely used and standardized, allowing for ease of cross-comparison across studies. The limitations of this review relate to the participants in the RCTs, mostly belonging to the Western population, which limits the generalizability of the findings to populations from non-Western countries. In addition, many included trials excluded individuals with chronic comorbidities or those taking medications that influence weight or metabolism, such as corticosteroids or antidiabetics. This restricts the applicability of our findings to more medically complex, real-world populations. Our analysis was also limited by the small number of studies evaluating the same dietary interventions. Moreover, most of the included trials were rated as having high or unclear ROB, particularly in domains such as allocation concealment, blinding, and attrition. These risks may introduce systematic error and limit the internal validity of the findings. While we attempted to assess the robustness of results, the small number of included trials (only 2 per comparison) precluded formal sensitivity analyses, as removing 1 study would eliminate the possibility of meta-analytic synthesis altogether. Similarly, although we observed high heterogeneity in certain outcomes (eg, %FM change), I^2 estimates derived from only 2 studies are statistically unstable and should be interpreted cautiously. Subgroup analyses and meta-regression, which are commonly used to explore heterogeneity, could not be conducted due to the very limited number of trials. Furthermore, a few studies did not report a clinical trial registration number despite multiple journals requiring that number for publication as of the early–mid 2000s.[65,66] Additional limitations of this study include the small number of studies that could be meta-analyzed due to differences in the collection, analysis, and reporting of parameters of interest across the studies. Finally, the lack of quantitative and rigorous collection of dietary adherence data limits our ability to assess the accurate effectiveness of the dietary interventions,[67] which affects the validity and reliability of the findings.

CONCLUSION

This systematic review highlights the wide heterogeneity in BC outcomes assessed with long-term weight-loss diets. Results suggest that HFLC diets may be associated with modest reductions in FM compared with MM diets, whereas MM diets compared with UDs, and HFLC compared with LFHC diets did not yield significant results. Although high-protein diets may help attenuate bone loss associated with weight reduction, this finding was largely influenced by a single trial and should therefore be interpreted with caution. Additional high-quality, long-term studies are needed to confirm these observations. Furthermore, standardized methods for reporting BC and bone parameters are essential to enhance comparability across studies and generate more conclusive evidence.

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Supplementary Material

Supplementary Material is available at *Nutrition Reviews* online.

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Conflicts of Interest

None declared.

Data Availability

The authors will make the template data collection forms, extracted data from included studies, and aggregated data used in analyses publicly available as supplementary material. Any additional methodological documents will be accessible upon request or linked in the manuscript, ensuring transparency and reproducibility of their findings.

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Nutrition Reviews, 2026, 00, 1–17
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