Diabetology & Metabolic Syndrome

REVIEW

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Low fat-diet and circulating adipokines concentrations: a systematic review and meta-analysis of randomized controlled trials

Sepideh Soltani[1], Fatemeh Meshkini[2], Kimia Torabinasab[3], Elham Razmpoosh[4], Omid Toupchian[5], Sheida Zeraattalab-Motlagh[6], Amirhossein Hemmati[7], Zohreh Sadat Sangsefidi[5] and Shima Abdollahi[5*]

Abstract

Background Low-fat diets have gained considerable attention in the management of obesity. The present meta-analysis evaluated randomized controlled trials (RCTs) to determine whether adults adhering to low-fat diets (≤ 30% of total energy intake) experience more significant changes in serum adipokine levels compared to those following high-fat diets.

Main text : A comprehensive search was conducted in PubMed, Scopus, Web of Science, and CENTRAL for eligible RCTs up to February 4, 2025. Weighted mean differences (WMD) were calculated and pooled using a random-effects model. Forty-eight trials were included in this study. The meta-analysis found no significant effects of low-fat diets on serum leptin (WMD = 0.06 ng/ml; 95% CI: -0.33, 0.45; $P = 0.76$; $I^2 = 64.57\%$), resistin (WMD = -0.67 ng/ml; 95% CI: -1.52, 0.17; $P = 0.12$; $I^2 = 86.53\%$), or adiponectin (WMD = 0.07 ng/ml; 95% CI: -0.29, 0.43; $P = 0.76$; $I^2 = 90.29\%$). Subgroup analysis showed a significant decrease in adiponectin levels among females ($n = 4$; WMD = -0.47 ng/ml; $P = 0.02$; $I^2 = 0\%$). However, low-fat diets with higher protein content increased adiponectin levels ($n = 3$; WMD = 1.78 ng/ml; $P < 0.001$; $I^2 = 0\%$). Sensitivity analysis revealed that excluding the study by Heggen et al. (2012) resulted in a significant reduction in serum resistin levels (WMD = -0.93 ng/ml; $P = 0.04$; $I^2 = 86.9\%$).

Conclusions Low-fat diets may have beneficial effects on resistin levels. Additionally, low-fat diets with higher protein content may increase adiponectin levels. However, due to the uncertainty of the available evidence, firm conclusions cannot be drawn. Further high-quality research is needed to confirm these findings.

Keywords Adipokines, Leptin, Low-fat diet, Restricted fat diet, Adiponectin, Meta-analysis

*Correspondence:
Shima Abdollahi
sh.abd6864@yahoo.com
[1]Yazd Cardiovascular Research Center, Non-communicable Diseases Research Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[2]Department of Cardiovascular Sciences, Aging + Cardiovascular Discovery Center, Lewis Katz School of Medicine, Temple University, Philadelphia, PA, USA
[3]Student Research Committee, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Department of Health Research Methods, Evidence, and Impact (HEI), McMaster University, Hamilton, ON, Canada
[5]Department of Nutrition, School of Public Health, North Khorasan University of Medical Sciences, Bojnurd, Iran
[6]Department of Health and Human Performance, University of Houston, Houston, TX, USA
[7]Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran

Introduction

Obesity has emerged as a global epidemic, presenting a significant public health challenges [1]. The World Health Organization (WHO) defines it as the excessive fat accumulation that presents a risk to health [2]. Adipokines, bioactive molecules secreted by adipose tissue, play a cnetral role in regulating key physiological processes, including energy balance, inflammation, insulin sensitivity, and lipid metabolism [3]. These molecules act as crucial signaling mediators, enabling communication between adipose tissue and other organs to maintain metabolic homeostasis [4]. In the context of obesity, adipose tissue hypertrophy and hyperplasia alter adipokine secretion patterns, contributing to insulin resistance, chronic low-grade inflammation, and disruptions in lipid metabolism [3]. The pathophysiology of obesity multifactorial, involving complex interactions among genetic, environmental, and lifestyle factors [5]. Among these, dietary habits play a critical role in both the onset and management of obesity [6]. Various dietary strategies have been proposed to combat obesity, with low-fat diets being one of the most commonly adopted approaches [7]. The underlying rationale is that reducing dietary fat can help lower overall energy intake, promote weight loss, and improve obesity-related metabolic markers [8]. However, the effects of different dietary compositions on metabolic outcomes remain inconsistent. For instance, a systematic review of randomized controlled trials (RCTs) found that high-protein, low-fat diets did not significantly affect anthropometric measurements in overweight and obese individuals compared to low-protein, high-fat diets [9].

In contrast, low-fat diets have demonstrated potential in modulating inflammation and improving insulin sensitivity in individuals with overweight and obesity. Adipokines are considered potential mediators in the complex interplay between dietary intake and metabolic disorders. Several clinical trials have examined the relationship between low-fat diets and adipokine levels. For example, a study by Arvidsson et al. reported that a low-calorie, low-fat diet significantly increased circulating adiponectin levels in adults with overweight and obesity, indicating a possible reduction in chronic inflammation [10]. However, not all findings are consistent. Research by Cornier et al. found that leptin levels decreased in both low-fat and high-fat diet groups during weight loss, regardless of macronutrient composition [11].

Although low-fat diets are commonly recommended for weight loss and improving metabolic outcomes, inconsistencies in the literature underscore the need for further investigations, particularly regarding their influence on adipokines. To address these gaps, we conducted a systematic review and meta-analysis of RCTs to evaluate the effects of low-fat diets compared to high-fat diets on adipokine levels. This analysis aims to enhance our understanding of the potential role of low-fat diets in managing obesity and associated metabolic disorders.

Methods

This systematic review and meta-analysis were conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions guideline [12]. The results are reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. The review protocol was registered with PROSPERO (CRD42020188745).

Literature search

We conducted a comprehensive search of electronic databases including PubMed, Scopus, Web of Science, and CENTRAL from inception to February 4, 2025. Advanced search strategies were employed using various combinations of free-text terms and Medical Subject Headings (MeSH) related to both low-fat diets and circulatory adipokines. No restrictions were applied regarding publication year or language. The detailed search strategies are provided in Supplementary Table 1. In addition, the reference lists of previously published relevant meta-analyses were manually screened to identify any trials that may have been missed during the electronic search.

Eligibility criteria

Articles were independently assessed for eligibility by three reviewers (FM, KT and AH). Any discrepancies were resolved by the chief investigator.

Randomized controlled trials (parallel or cross-over design) conducted in adults were included if they compared the effects of a low-fat diet—defined as providing ≤ 30% total energy intake from fat or less than 67 g of fat per 2000 kcal—with a control diet providing > 31% total energy intake from fat, on serum or plasma levels of leptin, adiponectin, resistin and other circulatory adipokines. Studies were excluded if they had a follow-up duration of less than one month, lacked sufficient data to estimate mean changes in outcomes, or exhibited a clear deviation from the intervention (defined as a follow-up rate below 70%). Trials in which co-interventions (e.g., lifestyle modifications) were not balanced between groups were also excluded. Inter-reviewer agreement was assessed using Cohen's kappa statistic, with values > 0.90 considered acceptable. To evaluate concordance, half of the eligible publications were randomly selected, and rankings from both abstract and full-text screening stages were compared, yielding a kappa coefficient of 0.90.

Data extraction, study quality, and certainty of evidence

Data were extracted independently by three authors (SS, OT, and ZS) and included the following: [1] study

information (first author, study location, year of publication, RCT design, and intervention duration); [2] participant characteristic (age, sex, health status, and number of participants per group); [3] detailed descriptions of the intervention and control diet prescriptions; [5] co-interventions (such as calorie restriction or physical activity programs); and [6] serum adipokine levels—mean and standard deviation (SD) at baseline and at the end of the intervention, or mean change and SD. Serum adipokine concentrations were analyzed in mg/dL; data reported in other units was converted accordingly using appropriate conversion factors. In cases where multiple publications reported on the same study, the version with the largest sample size was included. When studies reported outcomes at multiple time points, the data from the longest follow-up period were selected. For studies with more than one eligible intervention arm (e.g., two types of low-fat diets), the arms were combined and treated as a single intervention group.

The methodological quality of included RCTs was assessed using the Revised Cochrane Risk-of-Bias Tool for Randomized Trials (RoB 2) [14]. This assessment evaluated five key domains:

bias arising from the randomization process, deviations from intended interventions, incomplete outcome data, measurement of outcomes, and selection of the reported results. Due to the nature of dietary interventions, most trials did not blind participants or investigators. However, this lack of blinding was considered unlikely to affect the measurement of laboratory outcomes.

The certainty of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework [15], which reflects the degree of confidence that the estimated effect is close to the true effect. The certainty was downgraded if serious concerns were identified in any of the following domains: risk of bias (defined as ≥ 50% of contributing studies having a serious risk of bias), inconsistency (substantial heterogeneity across studies, indicated by I^2 ≥50%), imprecision (assessed using a minimally contextualized approach, with the null value as the decision threshold), and publication bias (evidence of small study effects). Downgrading for indirectness was not applied, as the populations, interventions, and comparators were considered sufficiently comparable across the included studies.

Statistical analysis

The primary effect size was calculated as the mean difference in serum adipokine levels (follow-up minus baseline) between participants assigned to low-fat versus high-fat diets. When the variance of paired differences was not reported, the SD of the mean difference was imputed using correlation coefficients, as recommended by the Cochrane Handbook for Systemic Review [16]. Correlation coefficients were derived from studies that reported SDs for baseline, final, and net changes: 0.75 for leptin, 0.82 for adiponectin, and 0.63 for resistin. Given the potential variation in study design and methodology, pooled estimates were calculated using a random-effects model (DerSimonian and Laird method) [12]. We assessed the presence of heterogeneity using the Cochran Q test, and I^2 statistic was used to quantify the extent of heterogeneity. Predefined subgroup analyses were planned based on sex, study duration, study design, geographical location, macronutrient composition (protein and carbohydrate content), health status, study quality, and the presence of calorie restriction or physical activity programs. However, some subgroup analyses could not be conducted due to insufficient data. Sensitivity analyses were performed by sequentially removing individual studies from the main analysis to assess their influence on the overall effect size. Publication bias was evaluated visually using funnel plots and statistically using Egger's and Begg's tests. All analyses were conducted using Stata software 17.0 (StataCorp).

Results

The initial search strategy identified 1127 publications, of which 518 were removed as duplicates (Fig. 1). After screening the titles and abstracts, 211 articles were selected for full text review. Following this evaluation, 171 studies were excluded for the following reasons:

Animal study ($n = 1$), both groups were low-fat ($n = 9$), both groups were high-fat ($n = 2$), conducted in athletes ($n = 1$), duplicate population ($n = 9$), inappropriate study design ($n = 10$), meal pattern study ($n = 1$), conference abstract ($n = 1$), irrelevant outcome ($n = 111$), deviation from the intervention ($n = 4$), short duration of intervention ($n = 5$), absence of the intended intervention ($n = 7$), insufficient data for analysis ($n = 8$), and lack of a washout period in cross-over design ($n = 2$).

Moreover, four publications from the PRIDIMED study were excluded due to a high deviation from the intervention protocol (greater than 40%) (Supplementary Table 2). An additional eight papers were identified and included after updating the search strategy. In total, 48 eligible RCTs met the eligibility criteria and were included in the meta-analysis to assess the effects of low-fat versus high-fat diets on serum adipokine levels: adiponectin ($n = 34$) [10, 17–48], leptin ($n = 39$) [10, 11, 17–21, 25–29, 33–37, 39–46, 48–61], and resistin ($n = 11$) [17, 19–21, 26, 27, 35, 37, 42, 43, 62]. The inter-reviewer reliability, assessed using Cohen's kappa statistic, was 0.95, indicating an excellent level of agreement during both the abstract and full-text screening stages.

The characteristics of the included studies are summarized in Table 1. The included studies were published

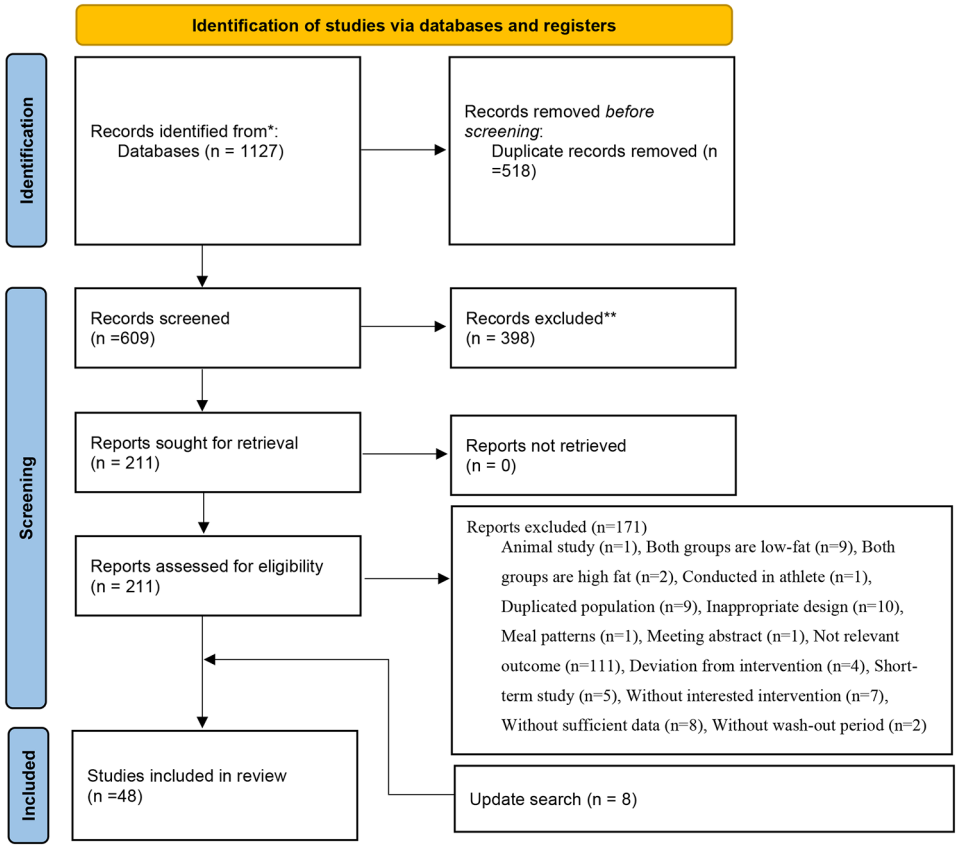

Fig. 1 PRISMA Flow Diagram of Study Selection

between 2000 and 2023. Most were conducted in European countries ($n=20$) [10, 11, 19–26, 31, 36, 37, 39, 42, 49, 52, 53, 58, 59], and the United States ($n=16$) [18, 27, 29, 38, 40, 43–45, 50, 51, 55–57, 60–62]. Others were carried out in Asian countries ($n=7$), and Australia ($n=5$). The majority of the trials used a parallel-group design ($n=41$) [10, 11, 17–33, 35, 37–44, 46–50, 52, 53, 55, 56, 59–62], while the remaining employed a crossover design. Participants included both sexes in most studies ($n=37$) [10, 18–32, 35–40, 42–47, 49, 51–54, 57, 59–65], with a smaller number of studies conducted exclusively females ($n=7$) [10, 11, 34, 41, 48, 50, 56, 66, 67], or males ($n=4$) [17, 33, 55, 58]. The intervention durations varied widely, ranging from 4 to 416 weeks. Regarding participant health status, most studies included overweight or obese individuals without other health conditions ($n=31$) [18–23, 25, 27, 29, 30, 32, 36–39, 43, 45–47, 49, 51, 57, 59, 62]; others involved obese individuals with metabolic disorders ($n=9$) [17, 24, 26, 34, 35, 41, 44, 53, 61], or patients with metabolic syndrome or/and diabetes ($n=4$) [31, 42, 52, 54]. Two studies included healthy normal-weight participants ($n=2$) [28, 40, 46, 66], while one study was conducted in patients with knee osteoarthritis and another in those with dyslipidemia.

Methodological quality and certainty of evidence

Of the 48 included studies, six were assessed as having a low risk of bias [24, 31, 35, 43, 46, 53], while 28 studies were rated as having some concerns [10, 11, 17–21, 23, 26, 28–30, 33, 36, 39–41, 47, 49, 51, 52, 54, 56–58, 60–62] and 14 studies were deemed to have a high risk of bias [22, 25, 27, 32, 34, 37, 38, 42, 44, 45, 48, 50, 55, 59] (Supplementary Table 3). The primary sources of bias weredeviation from intended interventions and missing outcomes, which are common challenges in dietary intervention studies due to the impossibility of participant blinding. Six studies were specifically rated as high risk of bias for incomplete outcome data [22, 25, 38, 45, 50], due to imbalanced missing data between groups and the absence of intention-to-treat analyses. Additionally, many studies did not report details on random sequence generation or allocation concealment, contributing to concerns about selection bias. According to the GRADE assessment (Supplementary Table 4), the overall certainty of the evidence was rated as low for serum adiponectin and leptin, and very low for serum resistin. These ratings reflect downgrades due to concerns related to risk of bias, imprecision, or inconsistency.

Table 1 Characteristic of trials that investigated the effect of low-fat *versus* high-fat diets on serum level of adipokines in adults that were eligible for inclusion in the meta-analysis

Author, Year/ Country	Sex/ (Mean age int/cont)	Health status, Number of participants	Study design/ duration (week)	Prescribe diet (% per calorie)						Co-intervention	Results
				Low fat diet			High fat diet			Calorie restriction (kcal/d)/ Exercise (yes/no)	
				CHO	Protein	Fat	CHO	Protein	Fat		
Arvidsson, 2004/ Europe [10]	F [35.1/ 35.3]	Healthy obese [20/ 20]	P/ 10	60–65	15–20	20–25	40–45	15–20	40–45	Yes (Deficit of 500 kcal/d of TEE)/Yes	Adiponectin, Leptin,
Bradley, 2009/ UK [49]	B [40.5/ 37.1]	Healthy obese [12/ 12]	P/ 8	60	20	20	20	20	60	Yes (Deficit of 500 kcal/d of TEE)/No	Leptin,
Brehm, 2003/ US [50]	F [43.1/ 44.2]	Healthy obese [20/ 22]	P/ 24	55	15	30	-	-	> 31	Yes (Not mentioned)/No	Leptin,
Cardillo, 2006/ US [18]	B [55/ 54]	Healthy obese [26/ 27]	P/ 144	47	20	< 30	51	17	32	Yes (Deficit of 500 kcal/d of TEE)/No	Adiponectin, Leptin
Cornier, 2005/ Sweden [11]	F [36.8/ 43.6]	Healthy obese [4/5]	P/16	60	20	20	40	20	40	Yes (Deficit of 400 kcal/d of TEE)/No	Leptin,
de Luis, 2008/ Spain [19]	B [46.5/ 46.5]	Healthy obese [99/105]	P/ 8	52	20	27	38	26	36	Yes (Not mentioned)/ Yes	Adiponectin, Leptin, Resistin
de Luis, 2012/ Spain [20]	B [43.3/ 43.3]	Healthy obese [158/ 147]	P/ 12	53	20	27	38	26	36	Yes (Not mentioned)/ Yes	Adiponectin, Leptin, Resistin
de Luis, 2016/ Spain [21]	B [52.9/ 52.9]	Healthy obese [194/ 198]	P/ 36	52.5	18.4	29.1	30.9	36.3	32.8	Yes (Deficit of 500 kcal/d of TEE)/No	Adiponectin, Leptin, Resistin
Due, 2008/ Denmark [22]	B [28.2/ 27.8]	Healthy obese [18/ 28]	P/24	60	15	25	45	15	40	No/ No	Adiponectin,
							50	15	35		
Ebbeling, 2012/ US [51]	B [30.3/ 30.3]	Healthy obese [21/ 42]	C/ 4	60	20	20	40	20	40	No/ No	Leptin,
							10	30	60		
Fava, 2013/ Italy [52]	B [30/ 58]	Metabolic syndrome [38/ 50]	P/ 24	55		28	45		38	No/ No	Leptin,
Frisch, 2009/ Germany [23]	B [47/ 47]	Healthy obese [100/ 100]	P/ 48	> 55	15	< 30	< 40	25	> 35	Yes (Deficit of 500 kcal/d of TEE)/No	Adiponectin,
Gepner, 2017/ Israel [53]	B [48.4/ 47.4]	Metabolic obese [118/ 122]	P/ 72			30			> 35	No/ Yes (each diet group was further randomized into added PA groups (LF^{PA+}, MED/ LC^{PA+}) or no added PA groups)	Leptin,
Goldenshluger, 2021/ Isreal [24]	B [48.4/ 47.4]	Metabolic obese [79/ 80]	P/ 24			30			> 35	No/ Yes (each diet group was further randomized into added PA groups (LF^{PA+}, MED/ LC^{PA+}) or no added PA groups)	Adiponectin,
Haufe, 2011/ Germany [25]	B [45/ 43.5]	Healthy obese [50/ 52]	P/ 24		0.8 gr/kg	≤ 20	≤ 90 gr/dy	0.8 gr/kg	≥ 30	Yes (Deficit of 30% energy intake)/No	Adiponectin, Leptin
Heggen, 2012/ Norway [26]	B [49.8/ 50.3]	Metabolic obese [88/ 93]	P/ 12	55–60	15	< 30	30–35	25–30	35–40	Yes (Deficit of 500 kcal/d of TEE)/No	Adiponectin, Leptin, Resistin
Hu, 2015/ US [27]	B [47.8/ 45.8]	Healthy obese [73/ 75]	P/ 48			30	< 40gr			No/Yes	Adiponectin, Leptin, Resistin
Iqbal, 2005/ US [62]	B [54/ 55]	Healthy obese [32/ 39]	P/ 26			< 30			> 30	Yes (Deficit of 500 kcal/d of TEE)/No	Resistin

Table 1 (continued)

Author, Year/ Country	Sex/ (Mean age int/cont)	Health status, Number of participants	Study design/ duration (week)	Prescribe diet (% per calorie)						Co-intervention	Results
				Low fat diet			High fat diet			Calorie restriction (kcal/d)/ Exercise (yes/no)	
				CHO	Protein	Fat	CHO	Protein	Fat		
Izadi, 2018/ Iran [28]	B [42.4/ 41]	Healthy normal weight [60/ 30]	P/ 12	58 59	15 15	26 25	54	15	31	No/ No	Adiponectin, Leptin
Juanola-Falgarona, 2013/ US [29]	B [44.1/ 43.2]	Healthy obese [40/ 81]	P/ 24	51.4	31.4	17.2	41.8 42.2	18.6 18.6	39.6 40.2	Yes (Deficit of 500 kcal/d of TEE)/No	Adiponectin, Leptin
Keogh, 2008/ Australia [30]	B [49.4/ 50.5]	Healthy obese [47/ 52]	P/ 8	46	24	30	4	35	61	Yes (Deficit of 30% energy intake)/No	Adiponectin,
Komiyama, 2003/ Japan [54]	B [55.6/ 55.6]	Diabetes and with or without impaired glucose tolerance [53/ 53]	C/ 4	70	15	15	55	15	30	No/ No	Leptin,
Lovejoy, 2003/ US [55]	M [36.7/ 36.7]	Healthy obese [30/ 15]	P/ 36	58	17	25	52	15	33	No/ No	Leptin,
Maiorino, 2016/ Italy [31]	B [51.9/ 52.4]	Diabetes[107/ 108]	P/ 416			<30	< 50		>30	No/ Yes	Adiponectin,
Mayr, 2019/ Australia [32]	B [61.8/ 61.8]	Healthy obese [31/ 34]	P/ 26	45–65	15–25	< 30	35	15	42	No/ No	Adiponectin,
Miller, 2008/ US [56]	F [39.4/ 39.4]	Healthy obese [12/ 13]	P/ 12	60	15	25	60 g /day			No/ No	Leptin,
Mohammadi Zadeh, 2018/ Iran [17]	M [49.3/ 45.5]	Diabetes and obese [11/ 31]	P/ 24	50	20	30	50 20 30	15 35 10	35 45 60	No/ No	Adiponectin, Leptin, Resistin
Petrisko, 2020/ US [57]	B [43.2/ 43.2]	Healthy obese [17/ 34]	C/ 4	61	18	21	10 10	40 30	50 60	Yes (Not mentioned)/ No	Leptin,
Pieke, 2000/ Germany [58]	M [39.2/ 39.2]	Dyslipidemia [19/ 19]	C/ 6	54	18.2	28	40.5	19.8	39	No/ No	Leptin,
Rajaie, 2013/ Iran [34]	F [42.4/ 42.4]	Metabolic syndrome and obese [30/ 30]	C/ 6	60–65	15–17	20–25	43–47	15–17	36–40	Yes (Deficit of 350–750 kcal/d of TEE)/No	Adiponectin, Leptin,
Reddy, 2023/ Australia [35]	B [52.1/ 52.6]	Metabolic obese [19/ 18]	P/ 12	50	20	30	33	15–20	44	No/ No	Adiponectin, Leptin, Resistin
Rolland, 2011/ UK [37]	B [41.9/ 45.8]	Healthy obese [14/ 17]	P/ 36	36	36	28	20	40	40	Yes (Deficit of 600 kcal/d of TEE)/No	Adiponectin, Leptin, Resistin
Ruth, 2013/ US [38]	B [41.5/ 43.5]	Healthy obese [15/ 18]	P/ 12	60	15	25	< 40gr	35	60	Yes (Deficit of 500 kcal/d of TEE)/No	Adiponectin,
Salwa, 2012/ France [36]	B [45/ 45]	Healthy obese [13/ 13]	C/ 4	40	35	25	44	25	31	Yes (Deficit of 30% energy intake)/No	Adiponectin, Leptin
Saris, 2000/ Europe countries* [59]	B [39.5/ 38]	Healthy obese [159/ 77]	P/ 24			10		32		No/ No	Leptin,
Shai, 2008/ Israel [39]	B [51/ 52.5]	Healthy obese [104/ 218]	P/ 96	50.7	19	30	40.4 50.2	21.8 18.8	39.1 33.1	Yes (Not mentioned)/ No	Adiponectin, Leptin,
Song, 2016/ US [40]	B [36.6/ 36.1]	Normal weight [62/ 30]	P/ 6	64	18	18	46	18	36	Yes (Deficit of 33% energy intake)/No	Adiponectin, Leptin,

Table 1 (continued)

Author, Year/ Country	Sex/ (Mean age int/cont)	Health status, Number of participants	Study design/ duration (week)	Prescribe diet (% per calorie)						Co-intervention	Results
				Low fat diet			High fat diet			Calorie restriction (kcal/d)/ Exercise (yes/no)	
				CHO	Protein	Fat	CHO	Protein	Fat		
Strath, 2019/ US [60]	B [72.3/ 69.2]	Knee osteoarthritis [6/ 15]	P/ 12	60	20	20	≤ 20 gr/d		Unlimited Unlimited	Yes (Deficit of 500 kcal/ day in male and 250–300 kcal/day in female)/ No	Leptin,
Tabesh, 2013/ Iran [41]	F [50/ 50.4]	Metabolic obese [34/ 19]	P/ 8	64.8 57.1	12.92 16.2	25.5 < 30	55.1	13.5	33.2	Yes (Deficit of 200 to 500 kcal/ day)/ No	Adiponectin, Leptin
Theodore, 2007/ Australia [33]	M [Middle age]	Healthy obese [20/ 15]	P/ 16	55	20	25	40	20	35	Yes (Not mentioned)/ No	Adiponectin, Leptin
Tierney, 2011/ 8 European counties [42]	B [55.4/ 54.6]	Metabolic syndrome [206/ 211]	P/ 12			28 28			38 38	No/ No	Adiponectin, Leptin, Resistin
Varady, 2011/ US [43]	B [36/ 35]	Healthy obese [8/ 9]	P/ 6	55	20	25	5	35	60	Yes (Deficit of 25% energy intake)/No	Adiponectin, Leptin, Resistin
Vetter, 2010/ US [44]	B [58.6/ 60.8]	Diabetes and obese [42/ 37]	P/ 24			≤30	< 30gr			Yes (Deficit of 500 kcal/ day)/ No	Adiponectin, Leptin,
von Frankenberg, 2017/ US [45]	B [18–55]	Healthy obese [10/ 10]	C/ 4	62	18	20	27	18	55	No/ No	Adiponectin,
Volek, 2009/ US [61]	B [36.9/ 32.6]	Metabolic obese [20/ 20]	P/ 12	56	20	24	12	28	59	Yes (Deficit of 500 kcal/ day)/ No	Leptin,
Wan, 2017/ China [46]	B [23.4/ 23.5]	Healthy [101/ 206]	P/ 24	66	14	20	56 46	14 14	30 40	No/ No	Adiponectin, Leptin
Wycherley, 2010/ Australia [47]	B [50.2/ 49.9]	Healthy obese [23/ 26]	P/ 52	46	24	30	4	35	61	Yes (Not mentioned)/ No	Adiponectin
Youssef, 2015/ Saudi Arabia [48]	F [20–22]	Healthy obese [6/ 12]	P/ 6	55 60	30 15	15 25	30	30	40	Yes (Not mentioned)/ No	Adiponectin,

Meta-analysis

Adiponectin

A total of 34 trials (comprising 3,793 participants) reported the effects of a low-fat diet on serum adiponectin levels compared with a high-fat diet [10, 17–48]. Pooled analysis showed no significant overall effect (WMD = 0.07 ng/ml; 95% CI: -0.29,0.43; $I^2 = 90.29\%$; P-heterogeneity < 0.001), indicating substantial between-study variability (Fig. 2).

Subgroup analysis based on the study location and the protein content of the low-fat diet significantly reduced heterogeneity (Supplementary Table 5). Specifically, studies conducted in females, showed a significant decrease in adiponectin levels ($n = 4$; WMD= -0.47 ng/ml; 95% CI:-0.85, -0.08; $P = 0.02$; $I^2 = 0$; P-heterogeneity = 0.44). Conversely, in studies where the low-fat diet had a higher protein content ($n = 3$), serum adiponectin levels significantly increased ($n = 3$; WMD = 1.78 ng/ml; 95% CI: 0.95, 2.61; $P < 0.001$; $I^2 = 0\%$; P-heterogeneity = 0.09) (Supplementary Table 5).

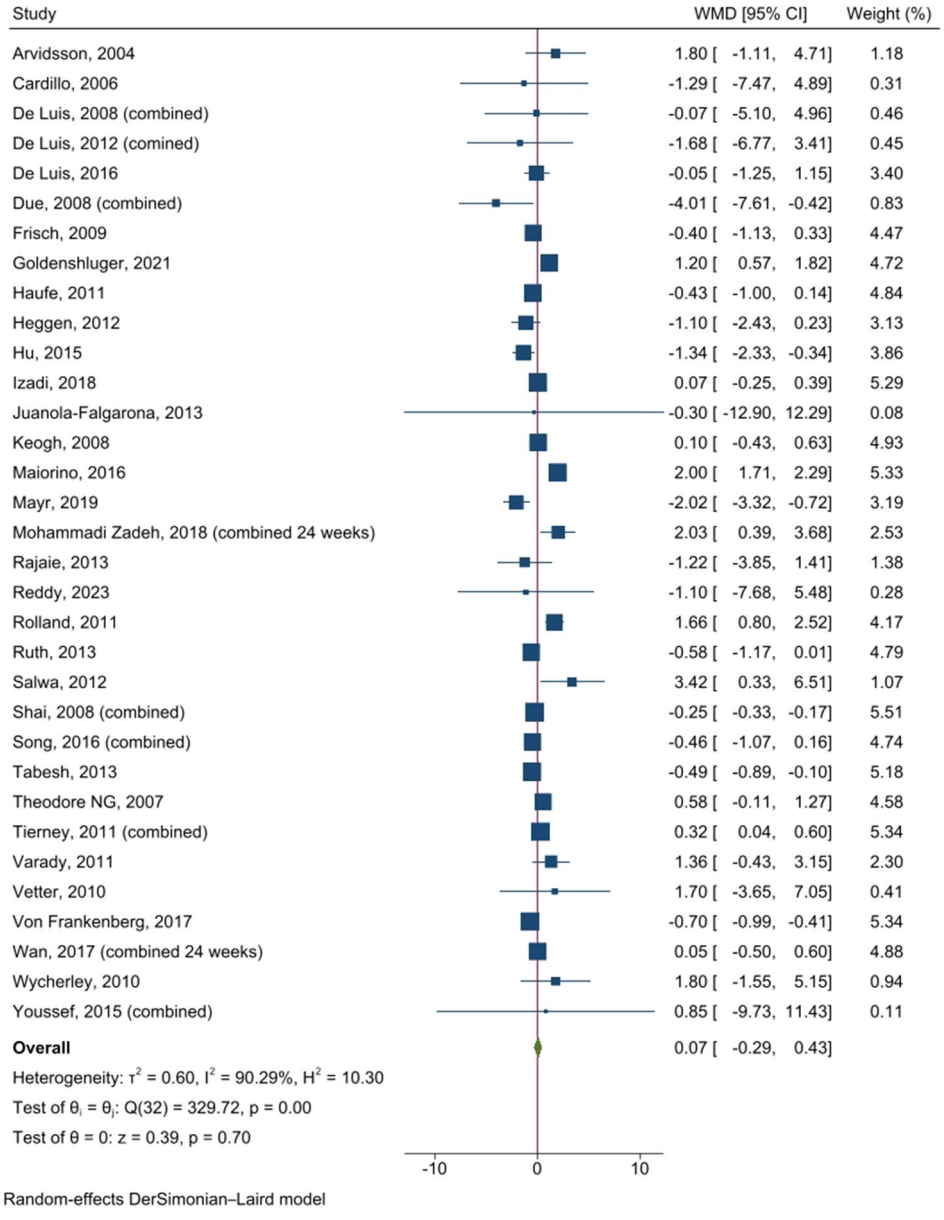

Fig. 2 Effect of Low-Fat Diet vs. High-Fat Diet on Serum Adiponectin Levels Forest plot displaying the Weighted Mean Difference (WMD) and 95% confidence intervals (CIs) for the effect of a low-fat diet compared to a high-fat diet on serum adiponectin levels (measured in ng/mL). Each study is represented by a square, with its size proportional to its weight in the meta-analysis. The diamond represents the pooled effect estimate, with its width indicating the confidence interval. A positive WMD favors the low-fat diet, suggesting an increase in adiponectin levels

Leptin

Thirty-nine trials including a total of 3911 participants, examined the effects of a low-fat diet on serum leptin levels compared with a high-fat diet [10, 11, 17–21, 25–29, 33–37, 39–46, 48–61]. The pooled analysis showed no significant effect of low-fat diets on serum leptin concentrations (WMD = 0. 06 ng/ml; 95% CI: -0.33, 0.45; $P = 0.76$; $I^2 = 64.57\%$; P-heterogeneity < 0.001) (Fig. 3).

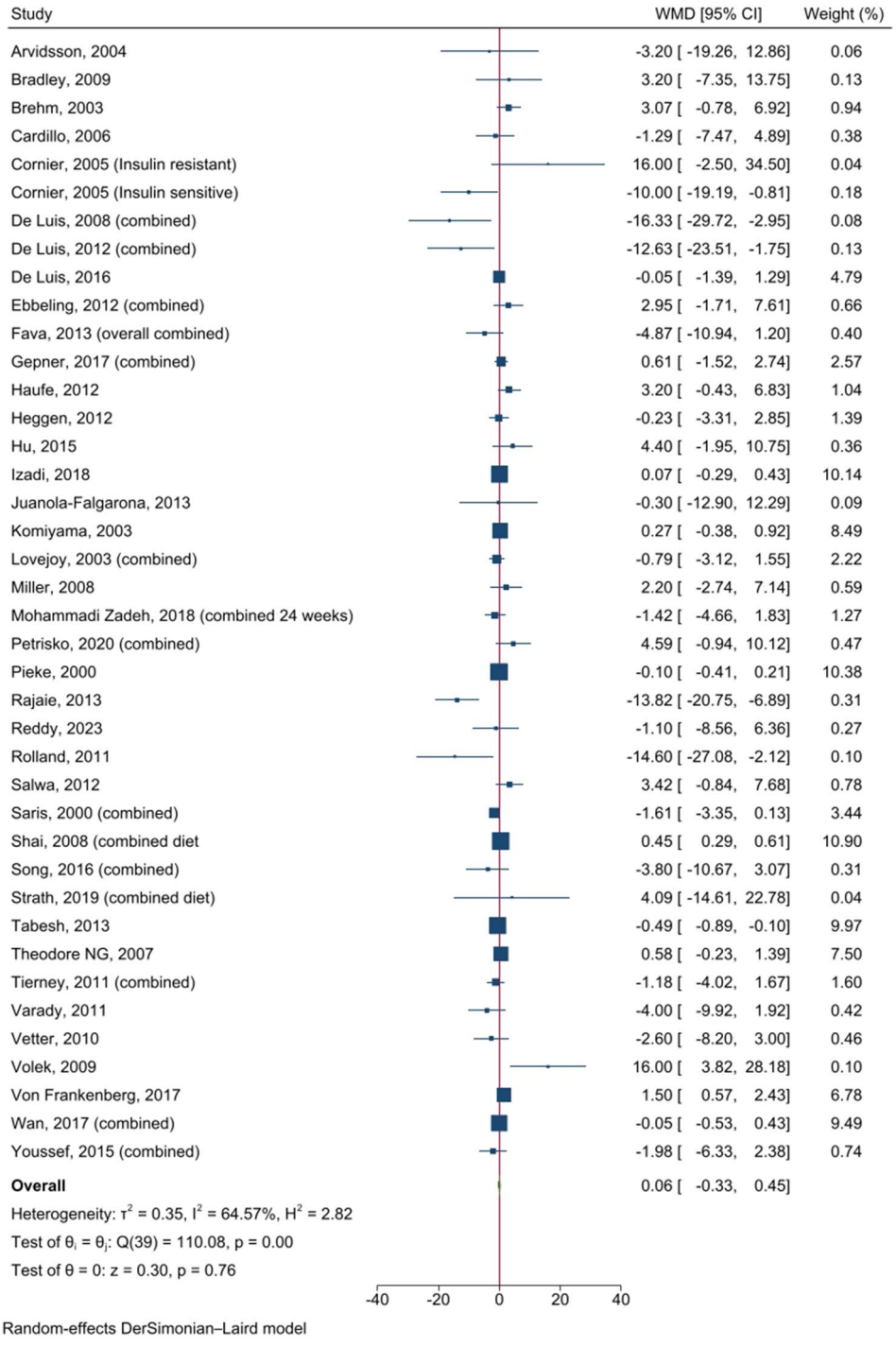

Fig. 3 Effect of Low-Fat Diet vs. High-Fat Diet on Serum Leptin Levels Forest plot illustrating the WMD and 95% CIs for the impact of a low-fat diet versus a high-fat diet on serum leptin levels (measured in ng/mL). Each study is represented by a square, with its size proportional to its weight in the meta-analysis. The diamond represents the pooled effect estimate, with its width indicating the confidence interval. A positive WMD favors the low-fat diet, suggesting an increase in leptin levels

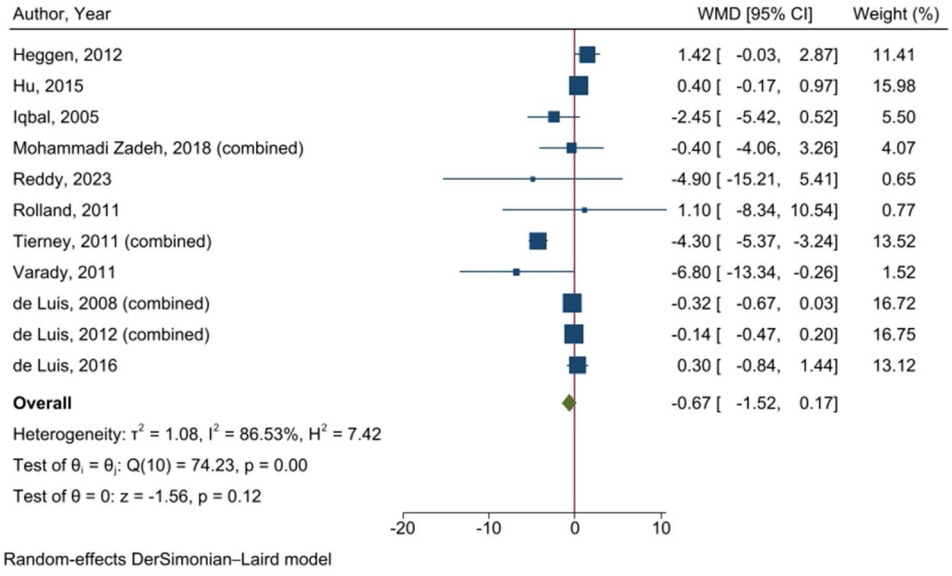

Fig. 4 Effect of Low-Fat Diet vs. High-Fat Diet on Serum Resistin Levels Forest plot summarizing the WMD and 95% CIs for the influence of a low-fat diet relative to a high-fat diet on serum resistin levels (reported in ng/mL). Study-specific estimates are shown as squares, weighted according to their precision, while the overall effect estimate is represented by a diamond. A positive WMD favors the low-fat diet, suggesting an increase in resistin levels

This finding remained consistent across various subgroups (Supplementary Table 6).

Resistin

Eleven studies (with a total of 1972 participants) evaluated the effects of a low-fat diet on serum levels of resistin compared to a high-fat diet [17, 19–21, 26, 27, 35, 37, 42, 43, 62]. The pooled analysis revealed no significant difference between the two dietary approaches (WMD= -0.67; 95% CI: -1.52, 0.17; $P=0.12$; $I^2=86.53\%$; P-heterogeneity < 0.07) (Fig. 4). This finding remained consistent across different subgroup analyses (Supplementary Table 7). Obesity status and participants' underlying health conditions were identified as significant sources of heterogeneity.

Sensitivity analysis and publication Bias

Sensitivity analysis demonstrated that excluding the study by Heggen et al. (2012) resulted in a statistically significant reduction in serum resistin levels following a low-fat, indicating that this study may have influenced the overall effect estimate (WMD = -0. 93 ng/ml; 95% CI: -1.82, -0.05; $P=0.04$; $I^2=86.9\%$; P-heterogeneity < 0.001). Further sensitivity analyses, excluding studies with either high risk or some concerns of bias, revealed a significant increase in serum adiponectin levels following low-fat diets (WMD = 1.09 ng/ml; 95% CI: 0.33, 2.14; $P=0.04$; $I^2=89.89\%$; P-heterogeneity < 0.001).

In contrast, the results for serum leptin levels remained unchanged across sensitivity analyses, supporting the robustness and consistency of the findings.

Funnel plot assessments also revealed no evidence of publication bias for adiponectin (Begg's test, $P=0.55$; Egger's test, $P=0.48$), leptin (Begg's test, $P=0.49$; Egger's test, $P=0.27$), or resistin (Begg's test, $P=0.75$; Egger's test, $P=0.23$) in the comparison of low-fat versus high-fat diets.

Discussion

Overall, our pooled analysis found no significant effect of low-fat diets on serum levels of adiponectin, leptin, or resistin. However, serum resistin levels showed a significant reduction in sensitivity analysis, suggesting the overall result may have been influenced by specific studies. Subgroup analysis revealed a significant increase in adiponectin levels in studies incorporated higher protein content within the low-fat diet group. Conversely, a significant decrease in adiponectin was observed in studies conducted exclusively in female participants.

To the best of our knowledge, this is the first systematic review and meta-analysis to investigate the effects of low-fat diets on circulating adipokine levels. Previous meta-analyses have examined the association between plant-based diets [68] or vegetarian diets [10] and adipokines, but none reported statistically significant effects. Additionally, two meta-analyses have evaluated the impact of low-carbohydrate diets (LCDs) on adiponectin levels yielding contradictory findings [69, 70], which may be attributed to inconsistent definitions of LCD across studies.

Adiponectin is one of the most important adipokines, known for its cardioprotective, anti-inflammatory, hypoglycemic, and hypolipidemic properties [71–73]. Its

levels are influenced by several factors, including body weight, dietary intake, age, sex, and ethnicity. An inverse relationship between adiponectin concentration and body weight is well established [74–76]. Under eucaloric conditions, the detrimental effects of high-carbohydrate diets on adiponectin may be partly due to their association with greater weight gain [77]. In contrast, protein-rich diets have been shown to benefit adiponectin levels, likely through enhanced satiety and greater weight loss [78], consistent with our subgroup findings.

Although inadequate data prevented us from directly examining the association between weight change and adipokines concentrations, a subgroup analysis based on calorie restriction showed no significant effect. While calorie restriction may not have resulted in substantial weight loss in the included studies, previous research suggests that adiponectin levels can change independently of weight loss, particularly through inflammatory pathways that influence adiponectin expression [79–81]. Moreover, redistribution of adipose tissue depots without changes in total body weight has also been associated with alterations in adiponectin levels [82]. For example, Turer et al. reported that individual with greater fat storage in the lower body exhibited higher adiponectin concentrations compared to those with predominantly central (trunk) fat accumulation [83]. The observed reduction in adiponectin among female participants may be explained by gender-specific differences in fat distribution [84, 85]. Moreover, adiponectin is associated with sex hormones [86, 87], which may partially explain why women generally have higher adiponectin concentrations than men.

Moreover, we observed a significant decrease in resistin levels following low-fat diets after excluding the study by Heggen et al. (2012), suggesting that this study may have influenced the overall effect. is an adipokine involved in insulin resistance, dysglycemia and systemic inflammation [88, 89]. Given that o significant effects were found in calorie-restricted subgroups, he observed reduction in resistin appears to be more closely related to reductions in inflammation rather than weight loss. Furthermore, resistin levels decreased significantly in studies involving participants with metabolic syndrome and diabetes—populations characterized by elevated oxidative stress [90, 91] and higher baseline resistin levels [92, 93]. Previous research has shown that low-fat diets can reduce systemic inflammatory markers [94] and that resistin levels decline in response to reduced inflammation [95–97].

The present study has several strengthens. To the best of our knowledge, it is the first systematic review and meta-analysis of RCTs to assess the effect of low-fat diets on adipokine levels. We employed a comprehensive search strategy across multiple databases without restrictions on language or publication date to ensure inclusion of all relevant studies. In addition, subgroup and sensitivity analyses were conducted to explore potential sources of heterogeneity. Moreover, only studies with a follow-up duration of at least one month were included, and comparisons were limited to isocaloric low-fat and high-fat diets to control for total energy intake.

However, several limitations should be noted. First, moderate to high heterogeneity was observed across studies. Although, subgroup analyses identified obesity status, participant health status, and the presence of calorie restriction as major contributors to this variability, residual heterogeneity likely remains. Second, emerging evidence suggests that different types of dietary fat may exert distinct effects on adipokines. For instance, diets high in saturated and trans fatty acids have been associated with adverse effects on adiponectin levels [98]. Unfortunately, we were unable to stratify our analysis by fatty acid composition due to insufficient reporting in the included studies.

Adherence dietary interventions was also not consistently or precisely reported, limiting our ability to assess protocol compliance. Additionally, some studies incorporated co-interventions (e.g., exercise or calorie restriction) alongside dietary fat manipulation. Although subgroup analyses did not indicate significant effects of these co-interventions, their influence cannot be entirely ruled out. Lastly, other potentials confounders, including body composition, physical activity, ethnicity, genetic factors, and sleep duration, are known to influence adipokine levels [98–105] but could not be accounted for in the current analysis due to limited data.

Conclusion

We found that low-fat diets may offer benefits for reducing resistin levels, particularly n individuals with diabetes and metabolic syndrome. Moreover, low-fat diets that are also high in protein may lead to increased adiponectin levels. However, the overall evidence remains unclear, and the true effects of low-fat diets on adipokine levels cannot be conclusively determined. Future high-quality studies are needed to confirm these findings and provide more definitive conclusions.

Abbreviations

LCDs	Low carbohydrate diets
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCTs	Randomized controlled trials
WHO	World Health Organization
WMD	Weighted mean difference

Supplementary Information

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Supplementary Material 1

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Author contributions
S.S contributed to the study conception, literature search, quality assessment, data analysis, and manuscript drafting; O.T data extraction and manuscript drafting; E.R literature screening; F.M & S.ZM literature search and data extraction; A.H literature search and data extraction; ZS.S data extraction; K.T literature search and data extraction; S.A study conception, literature search and manuscript drafting and approving the final manuscript. All authors acknowledge full responsibility for the analyses and interpretation of the report. All authors have read and approved the final manuscript. S.A is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

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Competing interests
The authors declare no competing interests.

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References

1. Mehta NK. Obesity as a main threat to future improvements in population health: policy opportunities and challenges. Milbank Q. 2023;101(S1):460–77.
2. WHO. World Health Organization. Obesity 2022 [Available from: https://www.who.int/health-topics/obesity#tab=tab_1
3. Kirichenko TV, Markina YV, Bogatyreva AI, Tolstik TV, Varaeva YR, Starodubova AV. The role of adipokines in inflammatory mechanisms of obesity. Int J Mol Sci. 2022;23(23).
4. Kim JE, Kim JS, Jo MJ, Cho E, Ahn SY, Kwon YJ, Ko GJ. The roles and associated mechanisms of adipokines in development of metabolic syndrome. Molecules. 2022;27(2).
5. Lee AM, Cardel MI, Donahoo WT, editors. Social and Environmental Factors Influencing Obesity2019.
6. Gherasim A, Arhire LI, Niță O, Popa AD, Graur M, Mihalache L. The relationship between lifestyle components and dietary patterns. Proc Nutr Soc. 2020;79(3):311–23.
7. Liu AG, Ford NA, Hu FB, Zelman KM, Mozaffarian D, Kris-Etherton PM. A healthy approach to dietary fats: Understanding the science and taking action to reduce consumer confusion. Nutr J. 2017;16(1):53.
8. Bhandari P, Sapra A. Low fat diet. StatPearls. Treasure Island (FL): StatPearls publishing copyright © 2023. StatPearls Publishing LLC.; 2023.
9. Schwingshackl L, Hoffmann G. Long-term effects of low-fat diets either low or high in protein on cardiovascular and metabolic risk factors: a systematic review and meta-analysis. Nutr J. 2013;12:48.
10. Arvidsson E, Viguerie N, Andersson I, Verdich C, Langin D, Arner P. Effects of different hypocaloric diets on protein secretion from adipose tissue of obese women. Diabetes. 2004;53(8):1966–71.
11. Cornier MA, Donahoo WT, Pereira R, Gurevich I, Westergren R, Enerback S, et al. Insulin sensitivity determines the effectiveness of dietary macronutrient composition on weight loss in obese women. Obes Res. 2005;13(4):703–9.
12. Higgins J. January. Cochrane handbook for systematic reviews of interventions. Version 5.1. 0 [updated March 2011]. The Cochrane Collaboration. London: The Cochrane Collaboration Available from: https://doi.org/handbookcochraneorg/ (accessed 12 2016). 2011.
13. Moher D, Liberati A, Tetzlaff J, Altman DG, medicine PGJAoi. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. 2009;151(4):264–9.
14. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD et al. Cochrane Collaboration's Tool Assess Risk bias Randomised Trials. 2011;343.
15. Schünemann H, Bro ek J, Guyatt G, Oxman A, editors. GWG. GRADE handbook for grading quality of evidence and strength of recommendations. 2013.
16. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. Introduction to meta-analysis: Wiley; 2021.
17. Asle Mohammadi Zadeh M, Kargarfard M, Marandi SM, Habibi A. Diets along with interval training regimes improves inflammatory & anti-inflammatory condition in obesity with type 2 diabetes subjects. J Diabetes Metabolic Disorders. 2018;17:253–67.
18. Cardillo S, Seshadri P, Iqbal N. The effects of a low-carbohydrate versus low-fat diet on adipocytokines in severely obese adults: three-year follow-up of a randomized trial. Eur Rev Med Pharmacol Sci. 2006;10(3):99–106.
19. De Luis D, Aller R, Izaola O, Sagrado MG, Conde R. Influence of Ala54Thr polymorphism of fatty acid-binding protein 2 on weight loss and insulin levels secondary to two hypocaloric diets: a randomized clinical trial. Diabetes Res Clin Pract. 2008;82(1):113–8.
20. de Luis DA, Aller R, Izaola O, de la Fuente B, Conde R, Sagrado MG, Primo D. Evaluation of weight loss and adipocytokines levels after two hypocaloric diets with different macronutrient distribution in obese subjects with rs9939609 gene variant. Diab/Metab Res Rev. 2012;28(8):663–8.
21. de Luis DA, Aller R, Izaola O, Romero E. Effect of -55CT polymorphism of UCP3 on insulin resistance and cardiovascular risk factors after a high protein/low carbohydrate versus a standard hypocaloric diet. Ann Nutr Metab. 2016;68(3):157–63.
22. Due A, Larsen TM, Hermansen K, Stender S, Holst JJ, Toubro S, et al. Comparison of the effects on insulin resistance and glucose tolerance of 6-mo high-monounsaturated-fat, low-fat, and control diets. Am J Clin Nutr. 2008;87(4):855–62.
23. Frisch S, Zittermann A, Berthold HK, Götting C, Kuhn J, Kleesiek K, et al. A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program. Cardiovasc Diabetol. 2009;8(1):1–10.
24. Goldenshluger A, Constantini K, Goldstein N, Shelef I, Schwarzfuchs D, Zelicha H et al. Effect of dietary strategies on respiratory quotient and its association with clinical parameters and organ fat loss: A randomized controlled trial. Nutrients. 2021;13(7).
25. Haufe S, Engeli S, Kast P, Böhnke J, Utz W, Haas V, et al. Randomized comparison of reduced fat and reduced carbohydrate hypocaloric diets on intrahepatic fat in overweight and obese human subjects. Hepatology (Baltimore MD). 2011;53(5):1504–14.
26. Heggen E, Klemsdal TO, Haugen F, Holme I, Tonstad S. Effect of a low-fat versus a low-gycemic-load diet on inflammatory biomarker and adipokine concentrations. Metab Syndr Relat Disord. 2012;10(6):437–42.
27. Hu T, Yao L, Reynolds K, Whelton PK, Niu T, Li S, et al. The effects of a low-carbohydrate diet vs. a low-fat diet on novel cardiovascular risk factors: a randomized controlled trial. Nutrients. 2015;7(9):7978–94.
28. Izadi V, Haghighatdoost F, Moosavian P, Azadbakht L. Effect of Low-Energy-Dense diet rich in multiple functional foods on Weight-Loss maintenance, inflammation, and cardiovascular risk factors: A randomized controlled trial. J Am Coll Nutr. 2018;37(5):399–405.
29. Juanola-Falgarona M, Salas-Salvadó J, Ibarrola-Jurado N, Rabassa-Soler A, Díaz-López A, Guasch-Ferré M, et al. Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: a randomized controlled trial. Am J Clin Nutr. 2014;100(1):27–35.
30. Keogh JB, Brinkworth GD, Noakes M, Belobrajdic DP, Buckley JD, Clifton PM. Effects of weight loss from a very-low-carbohydrate diet on endothelial function and markers of cardiovascular disease risk in subjects with abdominal obesity. Am J Clin Nutr. 2008;87(3):567–76.
31. Maiorino MI, Bellastella G, Petrizzo M, Scappaticcio L, Giugliano D, Esposito K. Mediterranean diet cools down the inflammatory milieu in type 2 diabetes: the MÉDITA randomized controlled trial. Endocrine. 2016;54:634–41.
32. Mayr HL, Itsiopoulos C, Tierney AC, Kucianski T, Radcliffe J, Garg M, et al. Ad libitum mediterranean diet reduces subcutaneous but not visceral fat in patients with coronary heart disease: a randomised controlled pilot study. Clin Nutr ESPEN. 2019;32:61–9.

33. Ng TW, Watts GF, Barrett PH, Rye KA, Chan DC. Effect of weight loss on LDL and HDL kinetics in the metabolic syndrome: associations with changes in plasma retinol-binding protein-4 and adiponectin levels. Diabetes Care. 2007;30(11):2945–50.
34. Rajaie S, Azadbakht L, Saneei P, Khazaei M, Esmaillzadeh A. Comparative effects of carbohydrate versus fat restriction on serum levels of adipocytokines, markers of inflammation, and endothelial function among women with the metabolic syndrome: a randomized cross-over clinical trial. Annals Nutr Metabolism. 2013;63(1–2):159–67.
35. Reddy A, Gatta PD, Mason S, Nicoll AJ, Ryan M, Itsiopoulos C, et al. Adherence to a mediterranean diet May improve serum adiponectin in adults with non-alcoholic fatty liver disease: the MEDINA randomized controlled trial. Volume 119. New York, NY: Nutrition research; 2023. pp. 98–108.
36. Rizkalla SW, Prifti E, Cotillard A, Pelloux V, Rouault C, Allouche R, et al. Differential effects of macronutrient content in 2 energy-restricted diets on cardiovascular risk factors and adipose tissue cell size in moderately obese individuals: a randomized controlled trial. Am J Clin Nutr. 2012;95(1):49–63.
37. Rolland C, Hession M, Broom I. Effect of weight loss on adipokine levels in obese patients. Diabetes, metabolic syndrome and obesity: targets and therapy. 2011:315– 23.
38. Ruth MR, Port AM, Shah M, Bourland AC, Istfan NW, Nelson KP, et al. Consuming a hypocaloric high fat low carbohydrate diet for 12 weeks lowers C-reactive protein, and raises serum adiponectin and high density lipoprotein-cholesterol in obese subjects. Metabolism. 2013;62(12):1779–87.
39. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, et al. Weight loss with a Low-Carbohydrate, mediterranean, or Low-Fat diet. N Engl J Med. 2008;359(3):229–41.
40. Song X, Kestin M, Schwarz Y, Yang P, Hu X, Lampe JW, Kratz M. A low-fat high-carbohydrate diet reduces plasma total adiponectin concentrations compared to a moderate-fat diet with no impact on biomarkers of systemic inflammation in a randomized controlled feeding study. Eur J Nutr. 2016;55:237–46.
41. Tabesh M, Hosseinzadeh MJ, Tabesh M, Esmaillzadeh A. Effects of dietary energy density on serum adipocytokine levels in diabetic women. Hormone and metabolic research = Hormon- und stoffwechselforschung = hormones et metabolisme. 2013;45(11):834–9.
42. Tierney AC, McMonagle J, Shaw D, Gulseth H, Helal O, Saris W, et al. Effects of dietary fat modification on insulin sensitivity and on other risk factors of the metabolic syndrome—LIPGENE: a European randomized dietary intervention study. Int J Obes. 2011;35(6):800–9.
43. Varady KA, Bhutani S, Klempel MC, Phillips SA. Improvements in vascular health by a low-fat diet, but not a high-fat diet, are mediated by changes in adipocyte biology. Nutr J. 2011;10:1–9.
44. Vetter ML, Wade A, Womble LG, Dalton-Bakes C, Wadden TA, Iqbal N. Effect of a low-carbohydrate diet versus a low-fat, calorie-restricted diet on adipokine levels in obese, diabetic participants. Diabetes, metabolic syndrome and obesity: targets and therapy. 2010:357– 61.
45. von Frankenberg AD, Marina A, Song X, Callahan HS, Kratz M, Utzschneider KM. A high-fat, high-saturated fat diet decreases insulin sensitivity without changing intra-abdominal fat in weight-stable overweight and obese adults. Eur J Nutr. 2017;56(1):431–43.
46. Wan Y, Wang F, Yuan J, Li J, Jiang D, Zhang J, et al. Effects of macronutrient distribution on weight and related cardiometabolic profile in healthy non-obese Chinese: a 6-month, randomized controlled-feeding trial. EBioMedicine. 2017;22:200–7.
47. Wycherley TP, Brinkworth G, Keogh J, Noakes M, Buckley J, Clifton P. Long-term effects of weight loss with a very low carbohydrate and low fat diet on vascular function in overweight and obese patients. J Intern Med. 2010;267(5):452–61.
48. Youssef M. The effect of dietary intervention by low carbohydrate diet, and low fat diet, on weight loss, leptin and adiponectin. Life Sci J. 2015;12:33–42.
49. Bradley U, Spence M, Courtney CH, McKinley MC, Ennis CN, McCance DR, et al. Low-fat versus low-carbohydrate weight reduction diets: effects on weight loss, insulin resistance, and cardiovascular risk: a randomized control trial. Diabetes. 2009;58(12):2741–8.
50. Brehm BJ, Seeley RJ, Daniels SR, Alessio D. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. J Clin Endocrinol Metab. 2003;88(4):1617–23.
51. Ebbeling CB, Swain JF, Feldman HA, Wong WW, Hachey DL, Garcia-Lago E, Ludwig DS. Effects of dietary composition on energy expenditure during weight-loss maintenance. JAMA. 2012;307(24):2627–34.
52. Fava F, Gitau R, Griffin BA, Gibson G, Tuohy K, Lovegrove J. The type and quantity of dietary fat and carbohydrate alter faecal Microbiome and short-chain fatty acid excretion in a metabolic syndrome 'at-risk'population. Int J Obes. 2013;37(2):216–23.
53. Gepner Y, Shelef I, Schwarzfuchs D, Zelicha H, Tene L, Yaskolka Meir A, et al. Effect of distinct lifestyle interventions on mobilization of fat storage pools: CENTRAL magnetic resonance imaging randomized controlled trial. Circulation. 2018;137(11):1143–57.
54. Komiyama N, Saito T, Hosaka Y, Aida K, Kaneko T, Sato A, et al. Effects of a 4-week 70% high carbohydrate/15% low fat diet on glucose tolerance and on lipid profiles. Diabetes Res Clin Pract. 2004;64(1):11–8.
55. Lovejoy J, Bray G, Lefevre M, Smith S, Most M, Denkins Y, et al. Consumption of a controlled low-fat diet containing Olestra for 9 months improves health risk factors in conjunction with weight loss in obese men: the ole'study. Int J Obes. 2003;27(10):1242–9.
56. Miller LE, Volpe JJ, Coleman-Kelly MD, Gwazdauskas FC, Nickols-Richardson SM. Anthropometric and leptin changes in women following different dietary approaches to weight loss. Obesity. 2009;17(1):199–201.
57. Petrisko M, Kloss R, Bradley P, Birrenkott E, Spindler A, Clayton ZS, Kern M. Biochemical, anthropometric, and physiological responses to carbohydrate-restricted diets versus a low-fat diet in obese adults: A randomized crossover trial. J Med Food. 2020;23(3):206–14.
58. Pieke B, Von Eckardstein A, Gülbahçe E, Chirazi A, Schulte H, Assmann G, Wahrburg U. Treatment of hypertriglyceridemia by two diets rich either in unsaturated fatty acids or in carbohydrates: effects on lipoprotein subclasses, lipolytic enzymes, lipid transfer proteins, insulin and leptin. Int J Obes. 2000;24(10):1286–96.
59. Saris WH, Astrup A, Prentice AM, Zunft HJ, Formiguera X, Verboeket-van de Venne WP, et al. Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple vs complex carbohydrates on body weight and blood lipids: the CARMEN study. The carbohydrate ratio management in European National diets. Int J Obes Relat Metabolic Disorders: J Int Association Study Obes. 2000;24(10):1310–8.
60. Strath LJ, Jones CD, Philip George A, Lukens SL, Morrison SA, Soleymani T, et al. The effect of low-carbohydrate and low-fat diets on pain in individuals with knee osteoarthritis. Pain Med. 2020;21(1):150–60.
61. Volek JS, Phinney SD, Forsythe CE, Quann EE, Wood RJ, Puglisi MJ, et al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. Lipids. 2009;44:297–309.
62. Iqbal N, Seshadri P, Stern L, Loh J, Kundu S, Jafar T, Samaha FF. Serum resistin is not associated with obesity or insulin resistance in humans. Eur Rev Med Pharmacol Sci. 2005;9(3):161–5.
63. Esposito K, Maiorino MI, Ciotola M, Di Palo C, Scognamiglio P, Gicchino M, et al. Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. Ann Intern Med. 2009;151(5):306–14.
64. Haufe S, Utz W, Engeli S, Kast P, Böhnke J, Pofahl M, et al. Left ventricular mass and function with reduced-fat or reduced-carbohydrate hypocaloric diets in overweight and obese subjects. Hypertension. 2012;59(1):70–5.
65. Saris W, Astrup A, Prentice A, Zunft H, Formiguera X, Verboeket-Van De Venne W, et al. Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple vs complex carbohydrates on body weight and blood lipids: the CARMEN study. Int J Obes. 2000;24(10):1310–8.
66. Lovejoy JC, Windhauser MM, Rood JC, de la Bretonne JA. Effect of a controlled high-fat versus low-fat diet on insulin sensitivity and leptin levels in African-American and Caucasian women. Metabolism. 1998;47(12):1520–4.
67. Klempel MC, Varady KAJN. Reliability of leptin, but not adiponectin, as a biomarker for diet-induced weight loss in humans. 2011;69(3):145–54.
68. Eichelmann F, Schwingshackl L, Fedirko V, Aleksandrova KJOR. Effect of plant-based diets on obesity-related inflammatory profiles: a systematic review and meta-analysis of intervention trials. 2016;17(11):1067–79.
69. Morshedzadeh N, Ahmadi AR, Tahmasebi R, Tavasolian R, Heshmati J, Rahimlou MJJoD, Disorders M. Impact of low-carbohydrate diet on serum levels of leptin and adiponectin levels: a systematic review and meta-analysis in adult. 2022:1–12.
70. Shemirani F, Golzarand M, Salari-Moghaddam A, Mahmoudi M. Effect of low-carbohydrate diet on adiponectin level in adults: a systematic review and dose-response meta-analysis of randomized controlled trials. 2022;62(14):3969–78.
71. Izadi V, Azadbakht L. Specific dietary patterns and concentrations of adiponectin. J Res Med Sci. 2015;20(2):178–84.

72. Sasso FC, Pafundi PC, Marfella R, Calabrò P, Piscione F, Furbatto F, et al. Adiponectin and insulin resistance are related to restenosis and overall new PCI in subjects with normal glucose tolerance: the prospective AIRE study. Cardiovasc Diabetol. 2019;18:1–13.
73. Yanai H, Yoshida H. Beneficial effects of adiponectin on glucose and lipid metabolism and atherosclerotic progression: mechanisms and perspectives. Int J Mol Sci. 2019;20(5):1190.
74. Ahl S, Guenther M, Zhao S, James R, Marks J, Szabo A, Kidambi S. Adiponectin levels differentiate metabolically healthy vs unhealthy among obese and Nonobese white individuals. J Clin Endocrinol Metabolism. 2015;100(11):4172–80.
75. Gariballa S, Alkaabi J, Yasin J, Al Essa A. Total adiponectin in overweight and obese subjects and its response to visceral fat loss. BMC Endocr Disorders. 2019;19:1–6.
76. Hivert MF, Sun Q, Shrader P, Mantzoros CS, Meigs JB, Hu FB. Higher adiponectin levels predict greater weight gain in healthy women in the nurses' health study. Obesity. 2011;19(2):409–15.
77. Wan Y, Tobias DK, Dennis KK, Guasch-Ferré M, Sun Q, Rimm EB et al. Association between changes in carbohydrate intake and long term weight changes: prospective cohort study. BMJ. 2023;382.
78. Moon J, Koh G. Clinical evidence and mechanisms of high-protein diet-induced weight loss. J Obes Metabolic Syndrome. 2020;29(3):166.
79. Fantuzzi G. Adiponectin and inflammation: consensus and controversy. J Allergy Clin Immunol. 2008;121(2):326–30.
80. Ouchi N, Walsh K. Adiponectin as an anti-inflammatory factor. Clin Chim Acta. 2007;380(1–2):24–30.
81. Yeung EH, Appel LJ, Miller ER III, Kao WL. The effects of macronutrient intake on total and High-molecular weight adiponectin: results from the OMNI-Heart trial. Obesity. 2010;18(8):1632–7.
82. Paniagua JA, De La Sacristana AG, Romero I, Vidal-Puig A, Latre J, Sanchez E, et al. Monounsaturated fat–rich diet prevents central body fat distribution and decreases postprandial adiponectin expression induced by a carbohydrate-rich diet in insulin-resistant subjects. Diabetes Care. 2007;30(7):1717–23.
83. Turer AT, Khera A, Ayers C, Turer CB, Grundy SM, Vega GL, Scherer PE. Adipose tissue mass and location affect Circulating adiponectin levels. Diabetologia. 2011;54:2515–24.
84. Doumatey AP, Bentley AR, Zhou J, Huang H, Adeyemo A, Rotimi CN. Paradoxical hyperadiponectinemia is associated with the metabolically healthy obese (MHO) phenotype in African Americans. J Endocrinol Metabolism. 2012;2(2):51.
85. Ziemke F, Mantzoros CS. Adiponectin in insulin resistance: lessons from translational research. Am J Clin Nutr. 2010;91(1):S258–61.
86. Riestra P, Garcia-Anguita A, Ortega L, Garcés C. Relationship of adiponectin with sex hormone levels in adolescents. Hormone Res Paediatrics. 2013;79(2):83–7.
87. Yasui T, Tomita J, Miyatani Y, Yamada M, Uemura H, Irahara M, et al. Associations of adiponectin with sex hormone-binding Globulin levels in aging male and female populations. Clin Chim Acta. 2007;386(1–2):69–75.
88. Wijetunge S, Ratnayake R, Kotakadeniya H, Rosairo S, Albracht-Schulte K, Ramalingam L, et al. Association between serum and adipose tissue resistin with dysglycemia in South Asian women. Nutr Diabetes. 2019;9(1):5.
89. Luo R, Li X, Jiang R, Gao X, Lü Z, Hua W. Serum concentrations of resistin and adiponectin and their relationship to insulin resistance in subjects with impaired glucose tolerance. J Int Med Res. 2012;40(2):621–30.
90. Bhatti JS, Sehrawat A, Mishra J, Sidhu IS, Navik U, Khullar N, et al. Oxidative stress in the pathophysiology of type 2 diabetes and related complications: current therapeutics strategies and future perspectives. Free Radic Biol Med. 2022;184:114–34.
91. Caturano A, D'Angelo M, Mormone A, Russo V, Mollica MP, Salvatore T, et al. Oxidative stress in type 2 diabetes: impacts from pathogenesis to lifestyle modifications. Curr Issues Mol Biol. 2023;45(8):6651–66.
92. McTernan CL, McTernan PG, Harte AL, Levick P, Barnett A, Kumar S. Resistin, central obesity, and type 2 diabetes. Lancet. 2002;359(9300):46–7.
93. Park HK, Ahima RS. Resistin in rodents and humans. Diabetes Metabolism J. 2013;37(6):404–14.
94. Fritsch J, Garces L, Quintero MA, Pignac-Kobinger J, Santander AM, Fernández I, et al. Low-fat, high-fiber diet reduces markers of inflammation and dysbiosis and improves quality of life in patients with ulcerative colitis. Clin Gastroenterol Hepatol. 2021;19(6):1189–99. e30.
95. Dzięgielewska-Gęsiak S, Wyszomirska K, Fatyga E, Wysocka E, Muc-Wierzgoń M. The role of oxidant-antioxidant markers and resistin in metabolic syndrome elderly individuals. Sci Prog. 2021;104(2):00368504211006510.
96. Kadoglou NP, Perrea D, Iliadis F, Angelopoulou N, Liapis C, Alevizos M. Exercise reduces resistin and inflammatory cytokines in patients with type 2 diabetes. Diabetes Care. 2007;30(3).
97. Park H-K, Qatanani M, Briggs ER, Ahima RS, Lazar MA. Inflammatory induction of human resistin causes insulin resistance in endotoxemic mice. Diabetes. 2011;60(3):775–83.
98. Janiszewska J, Ostrowska J, Szostak-Węgierek DJN. The influence of nutrition on adiponectin—A narrative review. 2021;13(5):1394.
99. Senesi P, Luzi L, Terruzzi IJIJMS. Adipokines, myokines, and cardiokines: the role of nutritional interventions. 2020;21(21):8372.
100. Mendoza-Herrera K, Florio AA, Moore M, Marrero A, Tamez M, Bhupathiraju SN, Mattei J. The leptin system and diet: a mini review of the current evidence. 2021;12:749050.
101. Klimcakova E, Kovacikova M, Stich V, Langin DJO. Adipokines and dietary interventions in human obesity. 2010;11(6):446–56.
102. Khalafi M, Sakhaei MH, Kheradmand S, Symonds ME, Rosenkranz SKJAN. The impact of exercise and dietary interventions on Circulating leptin and adiponectin in individuals who are overweight and those with obesity: A systematic review and meta-analysis. 2023;14(1):128.
103. Becic T, Studenik C, Hoffmann G. Exercise increases adiponectin and reduces leptin levels in prediabetic and diabetic individuals: systematic review and meta-analysis of randomized controlled trials. 2018;6(4):97.
104. Lin J, Jiang Y, Wang G, Meng M, Zhu Q, Mei H et al. Associations of short sleep duration with appetite-regulating hormones and adipokines: A systematic review and meta-analysis. 2020;21(11):e13051.
105. Fedewa MV, Hathaway ED, Ward-Ritacco CL, Williams TD, Dobbs, WCJSm. The effect of chronic exercise training on leptin: a systematic review and meta-analysis of randomized controlled trials. 2018;48:1437–50.

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