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Dose–response effects of exercise and caloric restriction on visceral adiposity in overweight and obese adults: a systematic review and meta-analysis of randomised controlled trials

Francesco Recchia,¹ Chit K. Leung,¹ Angus P. Yu,¹ Welton Leung ,¹ Danny J. Yu,² Daniel Y. Fong,³ David Montero,¹ Chi-Ho Lee,⁴ Stephen H.S. Wong ,⁵ Parco M. Siu ¹

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¹Division of Kinesiology, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong

²Department of Psychiatry, The Chinese University of Hong Kong, Hong Kong, Hong Kong

³School of Nursing, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong

⁴Department of Medicine, The University of Hong Kong, Hong Kong, Hong Kong

⁵Department of Sports Science and Physical Education, The Chinese University of Hong Kong, Hong Kong, Hong Kong

Correspondence to

Dr Parco M. Siu, The University of Hong Kong, Hong Kong 999077, Hong Kong; pmsiu@hku.hk

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ABSTRACT

Objective To determine and compare the dose–response effects of exercise and caloric restriction on visceral adipose tissue in overweight and obese adults, while controlling for the weekly energy deficit induced by the interventions.

Methods PubMed, Embase, CINAHL and Web of Science were searched for randomised controlled trials comparing exercise or caloric restriction against eucaloric controls in overweight or obese adults. The primary outcome was the change in visceral fat measured by CT or MRI. Meta-analyses and meta-regressions were performed to determine the overall effect size (ES) and the dose–dependent relationship of exercise and caloric restriction on visceral fat. Heterogeneity, risk of bias and the certainty of evidence were also assessed.

Results Forty randomised controlled trials involving 2190 participants were included. Overall, exercise (ES -0.28 (-0.37 to -0.19); $p<0.001$; $I^2=25\%$) and caloric restriction (ES -0.53 (-0.71 to -0.35); $p<0.001$; $I^2=33\%$) reduced visceral fat compared with the controls. Exercise demonstrated a dose–response effect of -0.15 (-0.23 to -0.07); $p<0.001$) per 1000 calories deficit per week, whereas the effect of caloric restriction was not dose-dependent (ES 0.03 (-0.12 to 0.18); $p=0.64$). Most of the studies showed a moderate risk of bias.

Conclusions These findings support the dose–dependent effects of exercise to reduce visceral fat in overweight and obese adults. Caloric restriction did not demonstrate a dose–response relationship, although this may be attributed to the smaller number of studies available for analysis, compared with exercise studies.

PROSPERO registration number CRD42020210096.

BACKGROUND

Obesity as a worldwide pandemic continues to demonstrate a growing prevalence. According to the WHO, 39% of adults worldwide were overweight and 13% were obese in 2016.¹ It is well documented that obesity is a key contributor to cardiovascular disease, type 2 diabetes mellitus, metabolic syndrome, cancer and other chronic diseases.^{2–6} Over the past decades, internationally recognised obesity management guidelines have been developed to promote lifestyle intervention strategies incorporating regular exercise and caloric restriction.^{7–10} These recommendations are

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Obesity management guidelines recommend the use of exercise and caloric restriction for weight loss in obese individuals. However, the comparative effectiveness of exercise and caloric restriction interventions on visceral fat changes has not been established.

WHAT THIS STUDY ADDS

⇒ Both interventions can effectively reduce visceral fat of overweight and obese individuals. However, only exercise showed a dose–dependent relationship between energy expenditure and visceral fat.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Obesity management guidelines should consider the dose-dependent effects of exercise as an effective lifestyle interventional strategy to reduce visceral fat in overweight and obese adults. Further research is needed to elucidate the effects of caloric restriction on visceral fat.

primarily designed to reduce body weight, as an elevated body mass index (BMI) is clinically used to characterise overweight and obesity according to the WHO cut-offs.¹¹

Although BMI satisfactorily correlates with body fat percentage when adjusted for sex, age and ethnicity,¹² it has been shown that visceral fat presents a far greater cardiometabolic risk than subcutaneous fat,¹³ and thus BMI is not entirely indicative of the risk for cardiometabolic diseases, as it cannot reflect individual variability in fat deposition.¹⁴ A recent joint position statement from the International Atherosclerosis Society and the International Chair on Cardiometabolic Risk Working Group on Visceral Obesity supported the notion that visceral fat is an independent risk factor for cardiovascular and metabolic morbidity and mortality, whereas BMI fails to determine cardiometabolic risk.¹⁵ This suggests that visceral fat might be a more important indicator of the efficacy of obesity management strategies.

A previous meta-analysis compared the effects of exercise and caloric restriction on reducing visceral



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fat, but made only head-to-head comparisons based on a small number of studies with both exercise and dietary intervention arms ($n=8$).¹⁶ The meta-analysis indicated a trend towards a greater reduction in visceral fat following exercise, but this conclusion was based on within-group pre-post changes rather than comparing to non-exercising controls.¹⁶ The independent effects of exercise versus caloric restriction on visceral fat, when compared with eucaloric conditions and while controlling for weekly energy deficit, remain unknown. Earlier evidence suggests that both exercise and caloric restriction produce dose-response effects.^{17,18} However, a previous randomised controlled trial indicated a preferential reduction in visceral fat with exercise over caloric restriction.¹⁹ Although both are established lifestyle strategies for the prevention and management of obesity, the physiological and metabolic adaptations to exercise and caloric restriction are fundamentally different.^{20,21} These differences might also reflect distinct responses in reducing visceral fat. Assessing the dose-response effects of exercise and caloric restriction is therefore crucial to provide insights on the potential cumulative effects of these interventions for maximising visceral fat loss in overweight and obese people. This study aimed to determine and compare the dose-response effects of exercise and caloric restriction on visceral fat in overweight and obese adults, while controlling for weekly caloric deficit induced by either an increase in energy expenditure via exercise or a decrease in energy intake via caloric restriction.

METHODS

This review conformed to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and was registered in PROSPERO (CRD42020210096).

Data sources and eligibility criteria

PubMed, Embase, CINAHL and Web of Science were searched for relevant articles written in any language from inception to the search date. Details regarding the search terms used are available in online supplemental appendix S1. The reference lists of relevant meta-analyses and articles of interest were also screened. One independent reviewer performed the search on January 2021 and a second independent reviewer repeated the search on January 2022. Any disagreements between the first and the second reviewers were resolved by consensus.

We included randomised controlled trials comparing exercise or caloric restriction with eucaloric controls in overweight or obese adults (≥ 18 years old). Overweight and obesity were defined using either the WHO cut-off scores for BMI¹¹ or the waist circumference standards set by the International Diabetes Federation.⁶

Outcomes

The primary outcome of this study was the change in visceral fat from baseline, quantified by CT or MRI, which are both considered to be gold-standard methods.²² Studies that assessed visceral fat by other methods were excluded. The secondary outcome was the change in waist circumference. No specific criteria were set for the measurement protocol of waist circumference.

Data extraction and quality assessment

To calculate effect sizes (ESs), two independent reviewers extracted sample sizes, changes in visceral fat and/or waist circumference from baseline and SD, for every study. Any disagreements were resolved by consensus. When SDs were not reported, we used previously validated methods to calculate

them.^{23,24} If other information was missing, an attempt was made to contact the study investigators to obtain the necessary data. If the study authors were unresponsive or unreachable, the study was excluded.

Data related to the study (first author, date, country), the participants (mean age, sex, comorbidities) and the intervention (type of intervention, frequency, intensity, time and volume of the exercise intervention, diet prescription, intervention duration and the method used to quantify visceral fat) were also extracted.

Risk of bias was assessed using the Cochrane's Risk of Bias 2 tool.²⁵ Bias was assessed in the following domains: (1) bias arising from the randomisation process, (2) bias due to deviations from the intended interventions, (3) bias due to missing outcome data, (4) bias in the measurement of the outcomes and (5) bias in the selection of the reported result. Two reviewers independently performed the risk of bias assessment. Disagreements were resolved by discussion. The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach was adopted to assess the certainty in the body of evidence on exercise and caloric restriction interventions for visceral fat reduction.²⁶

Data synthesis and analysis

Statistical analyses were conducted using the metafor package in the statistical software R (V.4.2.0).²⁷ Statistical significance was set at $p < 0.05$.

ESs were synthesised as d_{pcc2} as proposed by Morris;²⁸ namely, the mean change from baseline in the control group was subtracted from the mean change in the intervention group, and the difference was divided by the baseline pooled SD and multiplied by a bias adjustment for small sample size. The formula below was used to calculate the bias adjustment:

$$\sqrt{\frac{2}{df}} \left(\frac{\Gamma[df/2]}{\Gamma[(df-1)/2]} \right)$$

where Γ is the gamma function.²⁹ This method was reported to produce better results in terms of bias, precision and robustness to heterogeneity of variance.²⁸ ESs and CIs were aggregated using the inverse variance model and the Sidik-Jonkman variance estimator with the Hartung-Knapp modification.^{30–32} A negative ES indicated a beneficial effect of the main intervention over the comparison group.

Heterogeneity was assessed using I^2 and interpreted as follows: 0%–40%, might not be important; 30%–60%, may represent moderate heterogeneity; 50%–90%, may represent substantial heterogeneity; and 75%–100%, considerable heterogeneity.³²

Meta-regression was performed to explore the dose-response relationship of exercise and caloric restriction on reducing visceral fat, and to determine the potential superiority of one intervention over the other while controlling for weekly energy deficit. To determine the dose-response relationship of the two interventions, weekly energy deficit was used as an effect modifier. When energy deficits were not provided, they were computed from the available rates of metabolic equivalent or measures of oxygen uptake.^{33,34} If energy deficits could not be computed, the study was included in the meta-analysis but excluded from the meta-regression analyses. The comparison between exercise and caloric restriction was assessed by including an interaction term in the meta-regression model.

Secondary meta-regressions were performed to explore the potential influence of participant, intervention and study characteristics on the overall effects. Exercise frequency, intensity, session duration, intervention duration, supervision, method to

quantify visceral fat, study continent, comorbidities, age, baseline BMI and sex ratio were selected as effect modifiers using univariate meta-regression and subgroup analyses. Exercise frequency was treated as both a continuous and categorical variable (>3.5 or ≤ 3.5 days/week). Exercise intensity was categorised according to the American College of Sports Medicine's guidelines.³³ Details regarding the categorisation of exercise intensity are available in online supplemental table S1A–S1B).

Influential analyses were performed to identify possible outliers.²⁷ Analyses for the primary outcome were repeated after removing influential observations and after removing studies where weekly energy deficits were not provided and had to be calculated and studies with high risk of bias.

Equity, diversity and inclusion statement

The author group consists of junior, mid-career and senior researchers from different countries and disciplines. Our study population included both male and female adults from different socioeconomic and cultural backgrounds; thus, our findings may be generalisable to a wide range of individuals.

RESULTS

Search results

The electronic database search identified 7816 unique records. After assessment for eligibility, 54 records comprising 40 studies were included (online supplemental figure S1). Due to missing outcome data, four studies were excluded from the meta-analysis, but were still included in the systematic review. Of the 36 studies included for meta-analysis, 5 studies were added twice because they had both an exercise and a caloric restriction arm. Overall, 26 studies ($k=46$) were analysed for exercise and 15 studies ($k=16$) were analysed for caloric restriction.

Study characteristics

A summary of the characteristics of the included studies is presented in table 1A,1B. Further information regarding the study and intervention characteristics is provided in online supplemental table S2A–S2B. The majority of studies were conducted in the USA ($n=15$), Asia ($n=11$) and Europe ($n=9$). Overall, 2190 participants were assigned to exercise ($n=983$), caloric restriction ($n=394$) and control ($n=813$). Eight studies included individuals with comorbidities, such as type 2 diabetes, metabolic syndrome, dyslipidaemia and non-alcoholic fatty liver disease. The exercise interventions ranged from 4 weeks to 2 years, whereas caloric restriction interventions ranged from 12 weeks to 1 year. Half of the studies measured visceral fat using MRI and the other half used CT.

Effect of exercise on visceral fat and waist circumference

Exercise significantly reduced visceral fat (ES) -0.28 (-0.37 to -0.19); $p<0.001$; $I^2=25\%$) compared with controls (figure 1). Meta-regression demonstrated a dose-response effect of -0.15 (-0.23 to -0.07); $p<0.001$) per 1000 calories deficit per week (figure 2).

Exercise produced an effect of -0.41 (-0.60 to -0.22); $p<0.001$; $I^2=43\%$) on waist circumference (online supplemental figure S2), equivalent to a mean difference of 3.15 cm. Meta-regression showed a dose-response effect of -0.27 (-0.41 to -0.13); $p<0.001$) per 1000 calories deficit per week (online supplemental figure S3).

Effect of caloric restriction on visceral fat and waist circumference

Caloric restriction significantly reduced visceral fat (ES -0.53 (-0.71 to -0.35); $p<0.001$; $I^2=33\%$) compared with controls (figure 3). Meta-regression showed that the effect of caloric restriction was not dose-dependent (ES 0.03 (-0.12 to 0.18); $p=0.64$) (figure 4).

Caloric restriction produced an effect of -0.59 (-1.03 to -0.16); $p=0.013$; $I^2=76\%$) on waist circumference (online supplemental figure S4), equivalent to a mean difference of 4.67 cm. The effect of caloric restriction on waist circumference was dose-dependent (ES -0.29 (-0.58 to -0.00); $p=0.048$) (online supplemental figure S5).

Effect of exercise versus caloric restriction on visceral fat

Exercise and caloric restriction were compared via meta-regression using weekly energy deficit and the type of treatment as effect modifiers. The results showed that exercise had a superior dose-response effect on reducing visceral fat compared with caloric restriction (ES -0.18 (-0.33 to -0.04); $p=0.012$).

Risk of bias and GRADE

For the exercise studies, risk of bias was rated low in 6 studies, moderate in 14 studies and high in 5 studies (online supplemental figure S6A). For the caloric restriction studies, risk of bias was rated low in 3 studies, moderate in 10 studies and high in 2 studies (online supplemental figure S6B). Most of the risk of bias was attributable to issues regarding attrition, randomisation and assessor blinding. The level of certainty of the evidence in the exercise studies of healthy and comorbid individuals was downgraded by one level due to limitations in study bias and heterogeneity, respectively (online supplemental table S3A). The level of certainty of the evidence in the caloric restriction studies was downgraded by one level due to limitations in study bias (online supplemental table S3B). We are moderately confident that the true effects are likely to be close to the estimates of the effects for both interventions.

Meta-regression and subgroup analyses

Meta-regressions were performed to explore the potential influence of baseline characteristics. None of the chosen moderators was associated with the overall effects (online supplemental table S4A–S4B). Similarly, subgroup analyses were performed to explore potential variations in the ESs. A summary of the subgroup analyses performed is provided in online supplemental Table S5A–S5B.

Sensitivity analyses

Leave-one-out diagnostics identified three influential exercise studies and one influential caloric restriction study. After removing the outliers, exercise produced an effect of -0.32 (-0.41 to -0.23); $p<0.001$; $I^2=22\%$) and a dose-response effect of -0.14 (-0.23 to -0.05); $p=0.004$) per 1000 calories deficit per week. The overall effect of caloric restriction became -0.46 (-0.60 to -0.32); $p<0.001$; $I^2=18\%$), with a non-significant dose-response effect of -0.04 (-0.17 to 0.08); $p=0.49$) per 1000 calories deficit per week.

After excluding the studies that did not report the prescribed caloric expenditures, the effects of exercise and caloric restriction interventions became -0.48 (-0.69 to -0.27); $p<0.001$) and -0.59 (-0.79 to -0.39); $p<0.001$), respectively. Consistent with the main results, exercise interventions revealed a dose-response effect of -0.16 (-0.31 to -0.00); $p=0.045$) per

Table 1 (A) characteristics of exercise studies and (B) characteristics of caloric restriction studies

Study	Comorbidity	Age* (years)	BMI* (kg/m ²)	WC* (cm)	Duration (wk)	Groups†	N (M/F)	Measure
A								
Abdelbasset <i>et al</i> ^{63–65} 2019, 2020a, b * †	NAFLD, T2DM	40–60	≥30	NR	8	HIIT (1) MICT (2) CON	16 (10/6) 15 (8/7) 16 (9/7)	MRI‡
Blond <i>et al</i> ⁴¹ 2019	None	20–45	25–35	NR	24	MOD (1) VIG (2) CON	23 (12/11)§ 17 (7/10)§ 12 (6/6)§	MRI
Cho <i>et al</i> ⁴² 2011	None	34–60	≥25	NR	12	HI (1) LI (2) CON	12 (0/12) 13 (0/13) 10 (0/10)	CT
Coker <i>et al</i> ³⁵ 2009*	None	50–80	26 to <40	NR	12	AE CON	9 (3/6) 8 (3/5)	CT
Coker <i>et al</i> ³⁵ 2009† ¶	None	65–90	26 to <37	NR	12	HI (1) MI (2) CON	6 (3/3) 6 (3/3) 6 (3/3)	CT
Cowan <i>et al</i> ⁴⁰ 2018	None	35–65	NR	M>102 F>88	24	LILV (1) LIHV (2) HIHV (3) CON	24 (14/10) 31 (20/11) 40 (19/11) 20 (10/10)	MRI
Davidson <i>et al</i> ⁶⁶ 2009¶	None	60–80	27–34.9‡	M≥102 F≥88	24	AE CON	37 (17/20) 28 (11/17)	MRI
Hallsworth <i>et al</i> ⁶⁷ 2015	NAFLD	30–70‡	25–35‡	NR	12	HIIT CON	12 (NR) 11 (NR)	MRI
Hong <i>et al</i> ⁶⁸ 2014	None	30–40	>25	NR	12	AE CON	10 (0/10) 10 (0/10)	CT
Irving <i>et al</i> ^{69 70} 2008, 2009	MetS	MA	NR	IDF	16	HI (1) LI (2) CON	11 (3/8) 13 (3/10) 10 (4/6)	CT
Johnson <i>et al</i> ²⁹ 2009	None	>18§	≥30	NR	4	AE CON	12 (NR) 7 (NR)	MRI
Jung <i>et al</i> ⁷¹ 2012	T2DM	45–65	>23	NR	12	MOD (1) VIG (2) CON	8 (0/8) 8 (0/8) 12 (0/12)	CT
Keating <i>et al</i> ⁷² 2015	Pre-diabetes‡	29–59	>25	NR	8	HILV (1) LIHV (2) LILV (3) CON	12 (6/6) 12 (5/7) 12 (3/9) 12 (3/9)	MRI
Keating <i>et al</i> ⁷³ 2017	Pre-diabetes‡	29–59	≥25	NR	8	RT CON	15 (2/13) 14 (2/12)	MRI
Koo <i>et al</i> ³⁹ 2010	T2DM	> 18	>23	NR	12	AE CON	13 (0/13) 18 (0/18)	CT
Lee <i>et al</i> ⁷⁴ 2012¶	None	30–50	>25	>80	14	HI (1) LI (2) CON	7 (0/7) 8 (0/8) 7 (0/7)	CT
Lesser <i>et al</i> ⁷⁵ 2016	None	PM	NR	≥80	12	AE CON	23 (0/23) 26 (0/26)	CT
Nordby <i>et al</i> ³⁸ 2012	None	20–40	25–30	NR	12	AE CON	12 (12/0) 12 (12/0)	MRI
Bladbjerg <i>et al</i> ⁷⁶ 2017	None	20–65‡	27–35‡	NR	16	AE CON	30 (23/7) 20 (16/4)	MRI
Pugh <i>et al</i> ⁷⁷ 2014¶	NAFLD	20–65‡	27–35‡	NR	16	AE CON	30 (23/7) 20 (16/4)	MRI
Cuthbertson <i>et al</i> ⁷⁸ 2016¶	None	20–40	25–30	NR	11	HV (1) MV (2) CON	14 (14/0) 13 (13/0) 9 (9/0)	MRI
Ross <i>et al</i> ³⁶ 2000	None	>18§	>27	>100	12	AE CON	16 (16/0) 8 (8/0)	MRI
Thong <i>et al</i> ⁸⁰ 2000	None	>18	>27	>88	14	AE CON	17 (0/17) 10 (0/10)	MRI
Ross <i>et al</i> ³⁷ 2004	None	>18	>27	>88	14	AE CON	17 (0/17) 10 (0/10)	MRI
Saremi <i>et al</i> ⁸¹ 2010	None	MA	≥25	NR	12	AE CON	11 (11/0) 10 (10/0)	CT
Schmitz <i>et al</i> ⁸² 2007	None	25–44	25–35	NR	96	RT CON	82 (0/82) 82 (0/82)	CT
Shojaee-Moradie <i>et al</i> ⁸³ 2007	None	>18§	25–30	NR	6	AE CON	10 (10/0) 7 (7/0)	CT
Slentz <i>et al</i> ⁸⁴ 2005	Dyslipidaemia	40–65	25–35	NR	24	HIHV (1) HILV (2) MILV (3) CON	42 (23/19) 46 (23/23) 40 (22/18) 47 (23/24)	CT
Wu <i>et al</i> ⁸⁵ 2017	None	30–50	≥30	NR	12	HI (1) LI (2) CON	14 (0/14) 11 (0/11) 12 (0/12)	CT
Zhang <i>et al</i> ⁸⁶ 2015	None	NR	≥25	NR	12	HIIT (1) MICT (2) CON	12 (0/12) 12 (0/12) 11 (0/11)	CT

Continued

Table 1 Continued

Study	Comorbidity	Age* (years)	BMI* (kg/m ²)	WC* (cm)	Duration (wk)	Groupst	N (M/F)	Measure
Zhang <i>et al</i> ⁸⁷ 2016	NAFLD	40–65	NR	M≥90 F≥85	24	MOD (1) VIG (2) CON	73 (22/51) 73 (21/52) 74 (28/46)	CT
Zhang <i>et al</i> ⁸⁸ 2017	None	18–22	≥25	NR	12	HIIT (1) MICT (2) CON	15 (0/15) 15 (0/15) 13 (0/13)	CT
B								
Bouchonville <i>et al</i> ⁸⁹ 2014	Mild-to-moderate frailty	≥65	≥30	NR	48	CR CON	26 (9/17) 27 (9/18)	MRI
Napoli <i>et al</i> ⁹⁰ 2014								
Brennan <i>et al</i> ⁹¹ 2021	None	60–80	≥30	NR	24	CR CON	21 (7/14) 20 (7/13)	MRI
Coker <i>et al</i> ⁹⁵ 2009*	None	50–80	26 to <40	NR	12	CR CON	9 (3/6) 8 (3/5)	CT
Ibáñez <i>et al</i> ⁹² 2010	None	40–60	30–40	NR	16	WL CON	12 (0/12) 9 (0/9)	MRI
Ildate <i>et al</i> ⁹³ 2011								
García-Unciti <i>et al</i> ⁹⁴ 2012								
Kang <i>et al</i> ⁹⁵ 2018	None	20–65‡	25 to <30	NR	12	LCD CON	47 (13/34) 50 (14/36)	CT
Koo <i>et al</i> ⁹⁹ 2010	T2DM	> 18	> 23	NR	12	CR CON	19 (0/19) 18 (0/18)	CT
Larson-Meyer <i>et al</i> ^{96 97} 2006, 2010	None	25–50 M 25–45 F	25–30	NR	24	CR CON	12 (6/6) 11 (5/6)	CT
Redman <i>et al</i> ^{98 99} 2007, 2010								
Lee <i>et al</i> ¹⁰⁰ 2018	None	20–60	25 to <30	NR	12	WL WM	37 (15/22) 38 (11/27)	CT
Ng <i>et al</i> ^{101 102} 2007, 2009	MetS	> 18§	NR	IDF	14	WL WM	20 (20/0) 15 (15/0)	MRI
Chan <i>et al</i> ¹⁰³ 2008								
Nordby <i>et al</i> ³⁸ 2012	None	20–40	25–30	NR	12	CR CON	12 (12/0) 12 (12/0)	MRI
Bladbjerg <i>et al</i> ¹⁶ 2017								
Ross <i>et al</i> ³⁶ 2000	None	>18§	>27	>100	12	CR CON	14 (14/0) 8 (8/0)	MRI
Thong <i>et al</i> ⁸⁰ 2000								
Ross <i>et al</i> ⁹⁷ 2004	None	>18	>27	>88	14	WL CON	15 (0/15) 10 (0/10)	MRI
Schübel <i>et al</i> ¹⁰⁴ 2018	None	35–65	25 to <40	NR	12	CR CON	48 (NR) 49 (NR)	MRI
Schutte <i>et al</i> ¹⁰⁵ 2022	None	40–70	>27	M>102 F>88	12	LNCr (1) HNCR (2) CON	39 (16/23) 34 (15/19) 27 (12/15)	MRI
Trepanowski <i>et al</i> ¹⁰⁶ 2018	None	18–65	25 to <40	NR	24	CR CON	29 (6/23) 25 (4/21)	MRI

*Inclusion criteria unless otherwise specified.

†Study arms being synthesised.

‡Retrieved from clinical trial registration.

§Ascertained from study investigators.

¶Not included in the meta-analysis due to insufficient data.

AE, aerobic exercise; BMI, body mass index; CON, control group; CR, caloric restriction; EX, exercise; HI, high intensity; HIIT, high-intensity interval training; HN, High nutrient; HV, high volume; IDF, International Diabetes Federation; LCD, low-calorie diet; LI, low intensity; LN, Low nutrient; LV, low volume; MA, middle aged; MetS, metabolic syndrome; MICT, moderate-intensity continuous training; MI/MOD, moderate intensity; MV, moderate volume; NAFLD, non-alcoholic fatty liver disease; NR, not reported; PM, postmenopausal; RT, resistance training; T2DM, type II diabetes mellitus; VIG, vigorous intensity; WC, waist circumference; WL, weight loss; WM, weight maintenance.

1000 calories deficit per week, while the effect of caloric restriction interventions was not dose-dependent (ES, 0.10 (−0.07 to 0.27); $p=0.23$).

We repeated the analyses after excluding studies with high risk of bias and the overall effect did not change for exercise (ES −0.27 (−0.38 to −0.17); $p<0.001$) and caloric restriction (ES −0.53 (−0.72 to −0.33); $p<0.001$). Similarly, there were

no substantial differences changes in the dose–response effects of exercise (ES −0.13 (−0.22 to −0.03); $p=0.009$) and caloric restriction (ES 0.03 (−0.14 to 0.19); $p=0.728$).

DISCUSSION

This study aimed to determine the dose–response effectiveness of two lifestyle interventional strategies, physical exercise and

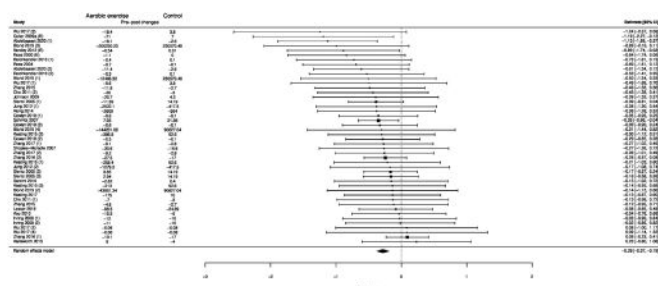


Figure 1 Forest plot of the effect of exercise on visceral fat.

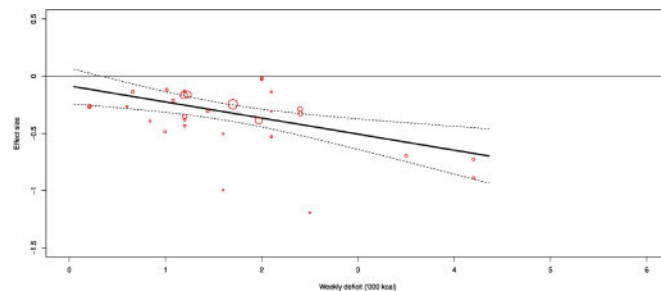


Figure 2 Dose–response effect of exercise on visceral fat.

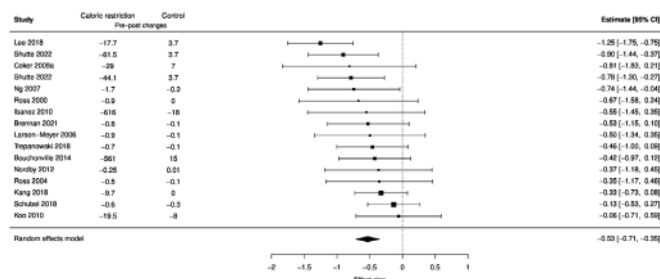


Figure 3 Forest plot of the effect of caloric restriction on visceral fat.

caloric restriction, on reducing visceral fat in overweight and obese adults. Our findings support the notion that both interventions can effectively decrease the volume of visceral fat in this population; however, only exercise demonstrated a dose-dependent relationship with visceral fat. In contrast, both exercise and caloric restriction showed dose-response effects on reducing waist circumference.

To our knowledge, this is the first meta-analysis comparing the dose-response effects of exercise and caloric restriction by controlling for the weekly caloric deficit induced by the interventions. Our findings align with a previous meta-analysis comparing exercise and hypocaloric diets for visceral fat loss, which showed that exercise interventions induced greater reductions in visceral fat compared with caloric restriction.¹⁶ In the absence of weight loss, exercise produced a 6.1% reduction in visceral fat, whereas hypocaloric diets showed essentially no change.¹⁶ A study that randomised obese individuals to exercise or caloric restriction interventions with matching energy deficits found that participants in the exercise group had a two-fold greater reduction in visceral fat compared with the caloric restriction group.³⁵ Similarly, Murphy *et al* reported a twofold greater loss of visceral adipose tissue in the exercise group compared with the caloric restriction group after adjusting for total fat changes in sedentary adults.¹⁹ However, several studies comparing exercise and caloric restriction within the same trial observed no differences in visceral fat changes between the two interventions,^{36–39} and several multiarm exercise studies involving interventions with different volumes or intensities failed to detect a dose-response relationship among the intervention groups.^{40–42} Under-reporting of caloric intake or over-compensating for the energy expended with excess food intake are common challenges in nutrition and metabolic research,^{43 44} which might explain the lack of differences in the treatment effects between groups. Overall, our results showed a dose-dependent effect of exercise on visceral fat, which was superior to the effect of caloric restriction. More evidence is warranted to elucidate the comparative effectiveness and the dose-dependent responses of these two lifestyle interventions.

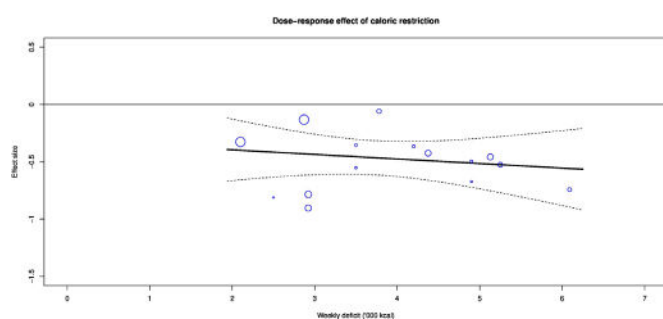


Figure 4 Dose-response effect of caloric restriction on visceral fat.

Clinical implications

Exercise and caloric restriction can both stimulate weight loss via a negative energy balance, which is achieved through an increased energy expenditure or a decreased caloric intake, respectively. Evidence shows that hypocaloric diets may be superior to exercise in achieving weight loss.^{16 45} This is likely because during caloric restriction both fat and muscle mass are reduced.^{46 47} On the other hand, exercise might stimulate fat loss while maintaining muscle mass.^{48 49} In fact, exercise-induced fat loss is achievable independently of weight loss.^{35–37} Research shows that metabolic adaptations to a low-calorie diet can differ among individuals, despite similar increases in fat oxidation rates, and that strong metabolic adaptations might mitigate the effect of caloric restriction on visceral fat.^{50–54} Conversely, previous literature emphasised the role of muscle mass in the regulation of resting energy expenditure.^{55–57} Our results suggest that exercise might be more suitable than caloric restriction for visceral fat loss in overweight and obese individuals. Differential metabolic adaptations and individual variations are potential causes for the difference in treatment responses to the two interventions.

Our results showed a dose-dependent effect for waist circumference in both exercise and caloric restriction interventions. These findings are promising, although they contrast with the primary outcome analyses, as visceral fat is strongly correlated with waist circumference,^{58 59} but our primary outcome analyses did not reveal a dose-response effect of caloric restriction on visceral fat. These findings align with a recent Consensus Statement by the International Atherosclerosis Society and the International Chair on Cardiometabolic Risk Working Group on Visceral Obesity, which described a plausible relationship between reductions in visceral fat and waist circumference, but concluded that a precise estimation of visceral fat from waist circumference is not possible.⁶⁰ The relationship between visceral fat and anthropometric measurements such as waist circumference and BMI varies greatly among individuals in different age and sex groups.^{61 62} Therefore, it is not surprising that the large cohort analysed in this study showed differential responses to visceral fat and waist circumference outcomes. Taken together, our results support the dose-response effects of both exercise and caloric restriction strategies in reducing waist circumference in overweight and obese adults.

Limitations

A limitation of this study was the disproportion between the number of exercise and caloric restriction studies. In fact, 46 and 16 effects were extrapolated from exercise and caloric restriction studies, respectively. This imbalance might have caused the lack of a significant dose-response effect for caloric restriction studies on visceral fat. Furthermore, four studies could not be included in the analyses due to missing data, which could not be obtained after contacting the respective authors. Similarly, information regarding caloric deficits or exercise intensities was at times lacking, and had to be calculated from the available data or requested from authors. Future research should adhere to validated reporting guidelines (eg, Consolidated Standards of Reporting Trials [CONSORT]) to facilitate the reporting and analysis of data. Lastly, the overall effect of exercise as well as its dose-response effect on visceral fat were small, which limits the interpretation of our results. Although the overall effect was increased after removing potential outliers and studies that did not report the prescribed caloric expenditure, the dose-response effect was essentially unchanged. Future studies should further explore the dose-response relationships of exercise and caloric

restriction interventions on visceral fat to corroborate our findings.

CONCLUSION

The findings of this study support the dose-dependent effects of exercise as an effective lifestyle interventional strategy to reduce visceral fat in overweight and obese adults. Caloric restriction did not demonstrate a dose-response relationship, although this may be attributed to the smaller number of studies available for analysis when compared with exercise studies. Secondary outcome analyses showed that both interventions produced dose-dependent responses on waist circumference. Further research is needed to elucidate the effects of caloric restriction on visceral fat.

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ORCID iDs

Welton Leung <http://orcid.org/0000-0002-0679-6703>

Stephen H.S. Wong <http://orcid.org/0000-0002-6821-4545>

Parco M. Siu <http://orcid.org/0000-0002-3548-5058>

REFERENCES

- World Health Organization. Obesity and overweight [Fact sheet]; 2021.
- Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and Cancer-viewpoint of the IARC working group. *N Engl J Med Overseas Ed* 2016;375:794–8.
- Singh GM, Danaei G, Farzadfar F, et al. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One* 2013;8:e65174.
- Tchernof A, Després J-P. Pathophysiology of human visceral obesity: an update. *Physiol Rev* 2013;93:359–404.
- Emerging Risk Factors Collaboration, Wormser D, Kaptoge S, et al. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet* 2011;377:1085–95.
- Alberti KGMM, Zimmet P, Shaw J, et al. The metabolic syndrome—a new worldwide definition. *Lancet* 2005;366:1059–62.
- Durrer Schutz D, Busetto L, Dicker D, et al. European practical and patient-centred guidelines for adult obesity management in primary care. *Obes Facts* 2019;12:40–66.
- Garvey WT, Mechanick JL, Brett EM, et al. American association of clinical endocrinologists and American college of endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract* 2016;22 Suppl 3:1–203.
- Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American college of cardiology/American heart association task force on practice guidelines and the obesity society. *Circulation* 2014;129:S102–38.
- Yumuk V, Tsigos C, Fried M, et al. European guidelines for obesity management in adults. *Obes Facts* 2015;8:402–24.
- Clinical guidelines on the Identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. National institutes of health. *Obes Res* 1998;6 Suppl 2:51–209.
- Jackson AS, Stanforth PR, Gagnon J, et al. The effect of sex, age and race on estimating percentage body fat from body mass index: the heritage family study. *Int J Obes* 2002;26:789–96.
- Després J-P, Cartier A, Côté M, et al. The concept of cardiometabolic risk: bridging the fields of diabetology and cardiology. *Ann Med* 2008;40:514–23.
- Hall ME, Clark D, Jones DW. Fat and cardiometabolic risk: location, location, location. *J Clin Hypertens* 2019;21:963–5.
- Neeland IJ, Ross R, Després J-P, et al. Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. *Lancet Diabetes Endocrinol* 2019;7:715–25.
- Verheggen RJHM, Maessen MFH, Green DJ, et al. A systematic review and meta-analysis on the effects of exercise training versus hypocaloric diet: distinct effects on body weight and visceral adipose tissue. *Obesity Reviews* 2016;17:664–90.
- Finkler E, Heymsfield SB, St-Onge M-P. Rate of weight loss can be predicted by patient characteristics and intervention strategies. *J Acad Nutr Diet* 2012;112:75–80.
- Ohkawara K, Tanaka S, Miyachi M, et al. A dose-response relation between aerobic exercise and visceral fat reduction: systematic review of clinical trials. *Int J Obes* 2007;31:1786–97.
- Murphy JC, McDaniel JL, Mora K, et al. Preferential reductions in intermuscular and visceral adipose tissue with exercise-induced weight loss compared with calorie restriction. *J Appl Physiol* 2012;112:79–85.
- De Feo P, Di Loreto C, Lucidi P, et al. Metabolic response to exercise. *J Endocrinol Invest* 2003;26:851–4.
- Greenway FL. Physiological adaptations to weight loss and factors favouring weight regain. *Int J Obes* 2015;39:1188–96.
- Shuster A, Patlas M, Pinthus JH, et al. The clinical importance of visceral adiposity: a critical review of methods for visceral adipose tissue analysis. *Br J Radiol* 2012;85:1–10.
- Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for systematic reviews of interventions version 6.2*, 2021.
- Furukawa TA, Barbui C, Cipriani A, et al. Imputing missing standard deviations in meta-analyses can provide accurate results. *J Clin Epidemiol* 2006;59:7–10.
- Sterne JAC, Savović J, Page MJ, et al. Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;2:14898.
- The GRADE working group. *Handbook for grading the quality of evidence and the strength of recommendations using the grade approach updated October 2013*, 2013. <https://guidelinedevelopment.org/handbook>
- Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2010;36:1–48.
- Morris SB. Estimating effect sizes from pretest-posttest-control group designs. *Organ Res Methods* 2008;11:364–86.
- Johnson NL, Kotz S. *Continuous univariate distributions*. New York: John Wiley, 1970.
- Doi SAR, Barendregt JJ, Khan S, et al. Advances in the meta-analysis of heterogeneous clinical trials I: the inverse variance heterogeneity model. *Contemp Clin Trials* 2015;45:130–8.
- Sidik K, Jonkman JN. A simple confidence interval for meta-analysis. *Stat Med* 2002;21:3153–9.
- Borenstein M, Hedges LV, Higgins JPT. *Introduction to meta-analysis*, 2009.
- American College of Sports Medicine. *ACSM's guidelines for exercise testing and prescription*. Philadelphia: Lippincott Williams & Wilkins, 2000.
- Heyward VH, Gibson AL. Advanced fitness assessment and exercise prescription. In: Kinetics H, ed. 7th. Champaign, IL, 2010.
- Coker RH, Williams RH, Kortebein PM, et al. Influence of exercise intensity on abdominal fat and adiponectin in elderly adults. *Metab Syndr Relat Disord* 2009;7:363–8.
- Ross R, Dagnone D, Jones PJ, et al. Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. A randomized, controlled trial. *Ann Intern Med* 2000;133:92–103.
- Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obes Res* 2004;12:789–98.

- 38 Nordby P, Auerbach PL, Rosenkilde M, *et al.* Endurance training *per se* increases metabolic health in young, moderately overweight men. *Obesity* 2012;20:2202–12.
- 39 Koo BK, Han KA, Ahn HJ, *et al.* The effects of total energy expenditure from all levels of physical activity vs. physical activity energy expenditure from moderate-to-vigorous activity on visceral fat and insulin sensitivity in obese type 2 diabetic women. *Diabet Med* 2010;27:1088–92.
- 40 Cowan TE, Brennan AM, Stotz PJ, *et al.* Separate effects of exercise amount and intensity on adipose tissue and skeletal muscle mass in adults with abdominal obesity. *Obesity* 2018;26:1696–703.
- 41 Blond MB, Rosenkilde M, Gram AS, *et al.* How does 6 months of active bike commuting or leisure-time exercise affect insulin sensitivity, cardiorespiratory fitness and intra-abdominal fat? a randomised controlled trial in individuals with overweight and obesity. *Br J Sports Med* 2019;53:1183–92.
- 42 Cho J-K, Lee S-H, Lee J-Y, *et al.* Randomized controlled trial of training intensity in adiposity. *Int J Sports Med* 2011;32:468–75.
- 43 Hill RJ, Davies PSW. The validity of self-reported energy intake as determined using the doubly labelled water technique. *Br J Nutr* 2001;85:415–30.
- 44 Thomas DM, Bouchard C, Church T, *et al.* Why do individuals not lose more weight from an exercise intervention at a defined dose? An energy balance analysis. *Obes Rev* 2012;13:835–47.
- 45 Franz MJ, VanWormer JJ, Crain AL, *et al.* Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc* 2007;107:1755–67.
- 46 Weiss EP, Racette SB, Villareal DT, *et al.* Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss. *J Appl Physiol* 2007;102:634–40.
- 47 Janssen I, Fortier A, Hudson R, Martin CK, *et al.* Effects of an energy-restrictive diet with or without exercise on abdominal fat, intermuscular fat, and metabolic risk factors in obese women. *Diabetes Care* 2002;25:431–8.
- 48 Martin-Rincon M, Pérez-López A, Morales-Alamo D, *et al.* Exercise mitigates the loss of muscle mass by attenuating the activation of autophagy during severe energy deficit. *Nutrients* 2019;11:2824.
- 49 Boulé NG, Haddad E, Kenny GP, *et al.* Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. *JAMA* 2001;286:1218–27.
- 50 Whytock KL, Corbin KD, Parsons SA, *et al.* Metabolic adaptation characterizes short-term resistance to weight loss induced by a low-calorie diet in overweight/obese individuals. *Am J Clin Nutr* 2021;114:267–80.
- 51 Redman LM, Heilbronn LK, Martin CK, *et al.* Metabolic and behavioral compensations in response to caloric restriction: implications for the maintenance of weight loss. *PLoS One* 2009;4:e4377.
- 52 Redman LM, Ravussin E. Caloric restriction in humans: impact on physiological, psychological, and behavioral outcomes. *Antioxid Redox Signal* 2011;14:275–87.
- 53 Ravussin E, Lillioja S, Knowler WC, *et al.* Reduced rate of energy expenditure as a risk factor for body-weight gain. *N Engl J Med* 1988;318:467–72.
- 54 Dulloo AG, Jacquet J. Adaptive reduction in basal metabolic rate in response to food deprivation in humans: a role for feedback signals from fat stores. *Am J Clin Nutr* 1998;68:599–606.
- 55 Zurlo F, Larson K, Bogardus C, *et al.* Skeletal muscle metabolism is a major determinant of resting energy expenditure. *J. Clin. Invest.* 1990;86:1423–7.
- 56 Müller MJ, Bosy-Westphal A, Kutzner D, *et al.* Metabolically active components of fat-free mass and resting energy expenditure in humans: recent lessons from imaging technologies. *Obesity Reviews* 2002;3:113–22.
- 57 McNab BK. What determines the basal rate of metabolism? *J Exp Biol* 2019;166.
- 58 Snijder MB, van Dam RM, Visser M, *et al.* What aspects of body fat are particularly hazardous and how do we measure them? *Int J Epidemiol* 2006;35:83–92.
- 59 Pouliot M-C, Després J-P, Lemieux S, *et al.* Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. *Am J Cardiol* 1994;73:460–8.
- 60 Ross R, Neeland IJ, Yamashita S, *et al.* Waist circumference as a vital sign in clinical practice: a consensus statement from the IAS and ICCR working group on visceral obesity. *Nat Rev Endocrinol* 2020;16:177–89.
- 61 Camhi SM, Bray GA, Bouchard C, *et al.* The relationship of waist circumference and BMI to visceral, subcutaneous, and total body fat: sex and race differences. *Obesity* 2011;19:402–8.
- 62 Kuk JL, Lee S, Heymsfield SB, *et al.* Waist circumference and abdominal adipose tissue distribution: influence of age and sex. *Am J Clin Nutr* 2005;81:1330–4.
- 63 Abdelbasset WK, Tantawy SA, Kamel DM, *et al.* A randomized controlled trial on the effectiveness of 8-week high-intensity interval exercise on intrahepatic triglycerides, visceral lipids, and health-related quality of life in diabetic obese patients with nonalcoholic fatty liver disease. *Medicine (Baltimore)* 2019;98:e14918.
- 64 Abdelbasset WK, Elsayed SH, Nambi G, *et al.* Effect of moderate-intensity aerobic exercise on hepatic fat content and visceral lipids in hepatic patients with diabetes: a single-blinded randomised controlled trial. *Evid Based Complement Alternat Med* 2020;2020:1923575:1923575..
- 65 Abdelbasset WK, Tantawy SA, Kamel DM, *et al.* Effects of high-intensity interval and moderate-intensity continuous aerobic exercise on diabetic obese patients with nonalcoholic fatty liver disease: a comparative randomized controlled trial. *Medicine (Baltimore)* 2020;99:e19471.
- 66 Davidson LE, Hudson R, Kilpatrick K, *et al.* Effects of exercise modality on insulin resistance and functional limitation in older adults: a randomized controlled trial. *Arch Intern Med* 2009;169:122–31.
- 67 Hallsworth K, Thoma C, Hollingsworth KG, *et al.* Modified high-intensity interval training reduces liver fat and improves cardiac function in non-alcoholic fatty liver disease: a randomized controlled trial. *Clin Sci (Lond)* 2015;129:1097–105.
- 68 Hong H-R, Jeong J-O, Kong J-Y, *et al.* Effect of walking exercise on abdominal fat, insulin resistance and serum cytokines in obese women. *J Exerc Nutrition Biochem* 2014;18:277–85.
- 69 Irving BA, Davis CK, Brock DW, *et al.* Effect of exercise training intensity on abdominal visceral fat and body composition. *Med Sci Sports Exerc* 2008;40:1863–72.
- 70 Irving BA, Weltman JY, Patrie JT, *et al.* Effects of exercise training intensity on nocturnal growth hormone secretion in obese adults with the metabolic syndrome. *J Clin Endocrinol Metab* 2009;94:1979–86.
- 71 Jung JY, Han KA, Ahn HJ, *et al.* Effects of aerobic exercise intensity on abdominal and thigh adipose tissue and skeletal muscle attenuation in overweight women with type 2 diabetes mellitus. *Diabetes Metab J* 2012;36:211–21.
- 72 Keating SE, Hackett DA, Parker HM, *et al.* Effect of aerobic exercise training dose on liver fat and visceral adiposity. *J Hepatol* 2015;63:174–82.
- 73 Keating SE, Hackett DA, Parker HM, *et al.* Effect of resistance training on liver fat and visceral adiposity in adults with obesity: a randomized controlled trial. *Hepatol Res* 2017;47:622–31.
- 74 Lee MG, Park KS, Kim DU, *et al.* Effects of high-intensity exercise training on body composition, abdominal fat loss, and cardiorespiratory fitness in middle-aged Korean females. *Appl Physiol Nutr Metab* 2012;37:1019–27.
- 75 Lesser IA, Singer J, Hoogbruin A, *et al.* Effectiveness of exercise on visceral adipose tissue in older south Asian women. *Med Sci Sports Exerc* 2016;48:1371–8.
- 76 Bladbjerg EM, Skov J, Nordby P, *et al.* Endurance exercise per se reduces the cardiovascular risk marker t-PA antigen in healthy, younger, overweight men. *Thromb Res* 2017;152:69–73.
- 77 Pugh CJA, Spring VS, Kemp GJ, *et al.* Exercise training reverses endothelial dysfunction in nonalcoholic fatty liver disease. *Am J Physiol Heart Circ Physiol* 2014;307:H1298–306.
- 78 Cuthbertson DJ, Shojaaee-Moradie F, Sprung VS, *et al.* Dissociation between exercise-induced reduction in liver fat and changes in hepatic and peripheral glucose homeostasis in obese patients with non-alcoholic fatty liver disease. *Clin Sci (Lond)* 2016;130:93–104.
- 79 Reichkender MH, Auerbach P, Rosenkilde M, *et al.* Exercise training favors increased insulin-stimulated glucose uptake in skeletal muscle in contrast to adipose tissue: a randomized study using FDG PET imaging. *Am J Physiol Endocrinol Metab* 2013;305:E496–506.
- 80 Thong FS, Hudson R, Ross R, *et al.* Plasma leptin in moderately obese men: independent effects of weight loss and aerobic exercise. *Am J Physiol Endocrinol Metab* 2000;279:E307–13.
- 81 Saremi A, Shavandi N, Parasteh M, *et al.* Twelve-week aerobic training decreases chemerin level and improves cardiometabolic risk factors in overweight and obese men. *Asian J Sports Med* 2010;1:151–8.
- 82 Schmitz KH, Hannan PJ, Stovitz SD, *et al.* Strength training and adiposity in premenopausal women: strong, healthy, and empowered study. *Am J Clin Nutr* 2007;86:566–72.
- 83 Shojaaee-Moradie F, Baynes KCR, Pentecost C, *et al.* Exercise training reduces fatty acid availability and improves the insulin sensitivity of glucose metabolism. *Diabetologia* 2007;50:404–13.
- 84 Slentz CA, Aiken LB, Houmard JA, *et al.* Inactivity, exercise, and visceral fat. STRRIDE: a randomized, controlled study of exercise intensity and amount. *J Appl Physiol* (1985) 2005;99:1613–8.
- 85 Wu S, Park KS, McCormick JB. Effects of exercise training on fat loss and lean mass gain in Mexican-American and Korean premenopausal women. *Int J Endocrinol* 2017;2017:5465869.
- 86 Zhang H, Tong T, Qiu W, *et al.* Effect of high-intensity interval training protocol on abdominal fat reduction in overweight Chinese women: A randomized controlled trial. *Kinesiology* 2015;47:57–66.
- 87 Zhang H-J, He J, Pan L-L, *et al.* Effects of moderate and vigorous exercise on nonalcoholic fatty liver disease: a randomized clinical trial. *JAMA Intern Med* 2016;176:1074–82.
- 88 Zhang H, Tong TK, Qiu W, *et al.* Comparable effects of high-intensity interval training and prolonged continuous exercise training on abdominal visceral fat reduction in obese young women. *J Diabetes Res* 2017;2017:5071740.
- 89 Bouchonville M, Armamento-Villareal R, Shah K, *et al.* Weight loss, exercise or both and cardiometabolic risk factors in obese older adults: results of a randomized controlled trial. *Int J Obes (Lond)* 2014;38:423–31.
- 90 Napoli N, Shah K, Waters DL, *et al.* Effect of weight loss, exercise, or both on cognition and quality of life in obese older adults. *Am J Clin Nutr* 2014;100:189–98.
- 91 Brennan AM, Standley RA, Anthony SJ, *et al.* Weight loss and exercise differentially affect insulin sensitivity, body composition, cardiorespiratory fitness, and muscle

- strength in older adults with obesity: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci* 2022;77:1088–97.
- 92 Ibáñez J, Izquierdo M, Martínez-Labari C, *et al.* Resistance training improves cardiovascular risk factors in obese women despite a significant decrease in serum adiponectin levels. *Obesity (Silver Spring)* 2010;18:535–41.
 - 93 Idoate F, Ibáñez J, Gorostiaga EM, *et al.* Weight-loss diet alone or combined with resistance training induces different regional visceral fat changes in obese women. *Int J Obes (Lond)* 2011;35:700–13.
 - 94 García-Unciti M, Izquierdo M, Idoate F, *et al.* Weight-loss diet alone or combined with progressive resistance training induces changes in association between the cardiometabolic risk profile and abdominal fat depots. *Ann Nutr Metab* 2012;61:296–304.
 - 95 Kang M, Yoo HJ, Kim M, *et al.* Metabolomics identifies increases in the acylcarnitine profiles in the plasma of overweight subjects in response to mild weight loss: a randomized, controlled design study. *Lipids Health Dis* 2018;17:237.
 - 96 Larson-Meyer DE, Heilbronn LK, Redman LM, *et al.* Effect of calorie restriction with or without exercise on insulin sensitivity, beta-cell function, fat cell size, and ectopic lipid in overweight subjects. *Diabetes Care* 2006;29:1337–44.
 - 97 Larson-Meyer DE, Redman L, Heilbronn LK, *et al.* Caloric restriction with or without exercise: the fitness versus fatness debate. *Med Sci Sports Exerc* 2010;42:152–9.
 - 98 Redman LM, Heilbronn LK, Martin CK, *et al.* Effect of calorie restriction with or without exercise on body composition and fat distribution. *J Clin Endocrinol Metab* 2007;92:865–72.
 - 99 Redman LM, Veldhuis JD, Rood J, *et al.* The effect of caloric restriction interventions on growth hormone secretion in nonobese men and women. *Aging Cell* 2010;9:32–9.
 - 100 Lee YJ, Lee A, Yoo HJ, *et al.* Effect of weight loss on circulating fatty acid profiles in overweight subjects with high visceral fat area: a 12-week randomized controlled trial. *Nutr J* 2018;17:28.
 - 101 Ng TWK, Watts GF, Barrett PHR, *et al.* 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;30:2945–50.
 - 102 Ng TWK, Chan DC, Barrett PHR, *et al.* Effect of weight loss on HDL-apoA-II kinetics in the metabolic syndrome. *Clin Sci (Lond)* 2009;118:79–85.
 - 103 Chan DC, Watts GF, Ng TWK, *et al.* Effect of weight loss on markers of triglyceride-rich lipoprotein metabolism in the metabolic syndrome. *Eur J Clin Invest* 2008;38:743–51.
 - 104 Schübel R, Nattenmüller J, Sookthai D, *et al.* Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: a randomized controlled trial. *Am J Clin Nutr* 2018;108:933–45.
 - 105 Schutte S, Esser D, Siebelink E, *et al.* Diverging metabolic effects of 2 energy-restricted diets differing in nutrient quality: a 12-week randomized controlled trial in subjects with abdominal obesity. *Am J Clin Nutr* 2022;116:nqac025:132–50.
 - 106 Trepanowski JF, Kroeger CM, Barnosky A, *et al.* Effects of alternate-day fasting or daily calorie restriction on body composition, fat distribution, and circulating adipokines: secondary analysis of a randomized controlled trial. *Clin Nutr* 2018;37(6 Pt A):S0261-5614(17)31416-4:1871–8.