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## Effects of fasting intervention regulating anthropometric and metabolic parameters in subjects with overweight or obesity: a systematic review and meta-analysis†

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**Background:** Previous studies have shown that fasting produces a potential effect in the prevention and treatment of many diseases. However, the role of fasting in people with overweight or obesity remains controversial. The aim of this study was to assess the intervention of fasting in the regulation of anthropometric and metabolic parameters of subjects with overweight or obesity. **Methods:** The PubMed, Cochrane library, Web of science and EMBASE databases were searched from the inception dates to October 2019, identifying published literature evaluating the effect of fasting intervention on the people with overweight or obesity. **Results:** Twenty-five studies with 1358 participants with overweight or obesity were included in the meta-analysis. Fasting was associated with the significant reduction of body weight, body mass index (BMI), fat free mass (FEM), fat mass (FM), waist circumference (WC), low density lipoprotein cholesterol (LDL-C), triglycerides (TG), systolic blood pressure (SBP) and diastolic blood pressure (DBP). However, there was no significant difference in the variations in the total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), blood glucose and insulin concentrations. **Conclusion:** Our meta-analysis found that fasting was associated with a significant effect on the regulation of anthropometric (body weight, BMI, FEM, FM and WC) and metabolic parameters (LDL-C, TG, SBP and DBP) in people with overweight or obesity. Considering some limitations found in this study, additional data from large clinical trials are needed.

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### 1. Introduction

Obesity is a pathological state in which excess abdominal weight is accumulated due to the imbalance between energy intake and consumption.<sup>1</sup> The prevalence of obesity has doubled in more than 70 countries in the past 30 years and has constantly increased in most other countries.<sup>2</sup> As excess weight gain increases the risk of cardiovascular disease, diabetes, cancer and other diseases; the increasing prevalence of obesity is a worldwide health problem and causes a large financial burden in all countries.<sup>3,4</sup> By 2030, a 5% decrease in body mass index (BMI) parameter is expected to lead to a

reduction of €495 million in obesity related direct health care expenses over 20 years.<sup>5</sup>

Fasting is regarded as ingesting no or minimal energy for a period of time, which including periodic fasting (PF), intermittent fasting (IF), very low calorie diet (VLCD) and other fasting.<sup>6,7</sup> Among them, PF consists of fasting only 1 or 2 days per week with consuming food *ad libitum* on 5 to 6 days per week and VLCD is regarded as an energy intake of 800 kcal or less per day.<sup>7–9</sup> IF includes limiting or no food consumption on 1–3 day per week and eating freely on the no restriction days, which comprises complete alternate-day fasting (CADF), alternate day modified fasting (ADMF), time-restricted feeding (TRF) and others.<sup>10,11</sup> The main difference between CADF and ADMF is the energy intake on fasting day (CADF: zero calorie intake; ADMF: 20–25% of energy needs).<sup>11,12</sup> Specially, TRF is an eating pattern in which daily food consumption is limited to 8 hours or less.<sup>13</sup> Previous studies have indicated that fasting produces a potential effect in the prevention and treatment of many diseases. Several studies have found that fasting was profitable for symptoms and inflammatory parameters in patients with

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rheumatic diseases.<sup>14,15</sup> Meanwhile, the risk of hypertension, cardiovascular and metabolic disease was reduced through fasting intervention.<sup>7</sup> In addition, fasting may protect from cancer *via* reducing the harm to cells and DNA, and increasing the death of precancerous cells.<sup>16</sup> Simultaneously, fasting could also debase the capacity of cancer cells to adapt and survive, thereby improving the effects of cancer therapies.<sup>17</sup>

Some studies have reported that IF and VLCD may improve the body composition, reduce cardiovascular risk factors, and positively affect glucose control in people with overweight or obesity.<sup>18,19</sup> However, recent research has also shown that the advantages of IF for weight loss, weight management, or cardio-protection in subjects with overweight or obesity were not obvious.<sup>20</sup> The role of fasting in people with overweight or obesity remains controversial. Therefore, a meta-analysis of all related randomized control trials (RCTs) was conducted focusing on the intervention of fasting in the regulation of anthropometric and metabolic parameters of people with overweight or obesity.

## 2. Materials and methods

### 2.1. Sources and methods of data retrieval

We searched the PubMed, Cochrane library, Web of science and EMBASE databases from the inception dates to October 2019, using the keywords fasting, very low calorie diet, intermittent fasting, alternate day fasting, periodic fasting, modified fasting regimen, time-restricted feeding, overweight, obesity and obese to identify published literature evaluating the effect of fasting intervention on regulating anthropometric and metabolic parameters in people with overweight or obesity. The literature search was limited to English language and human subjects. The detailed search strategy is shown in Table S1.†

### 2.2. Inclusion criteria

The inclusion criteria were (1) RCTs comparing fasting intervention and a normal diet or energy restriction group; (2) overweight or obesity was defined based on a local criterion; (3) the outcomes were quantitative data that could be extracted or

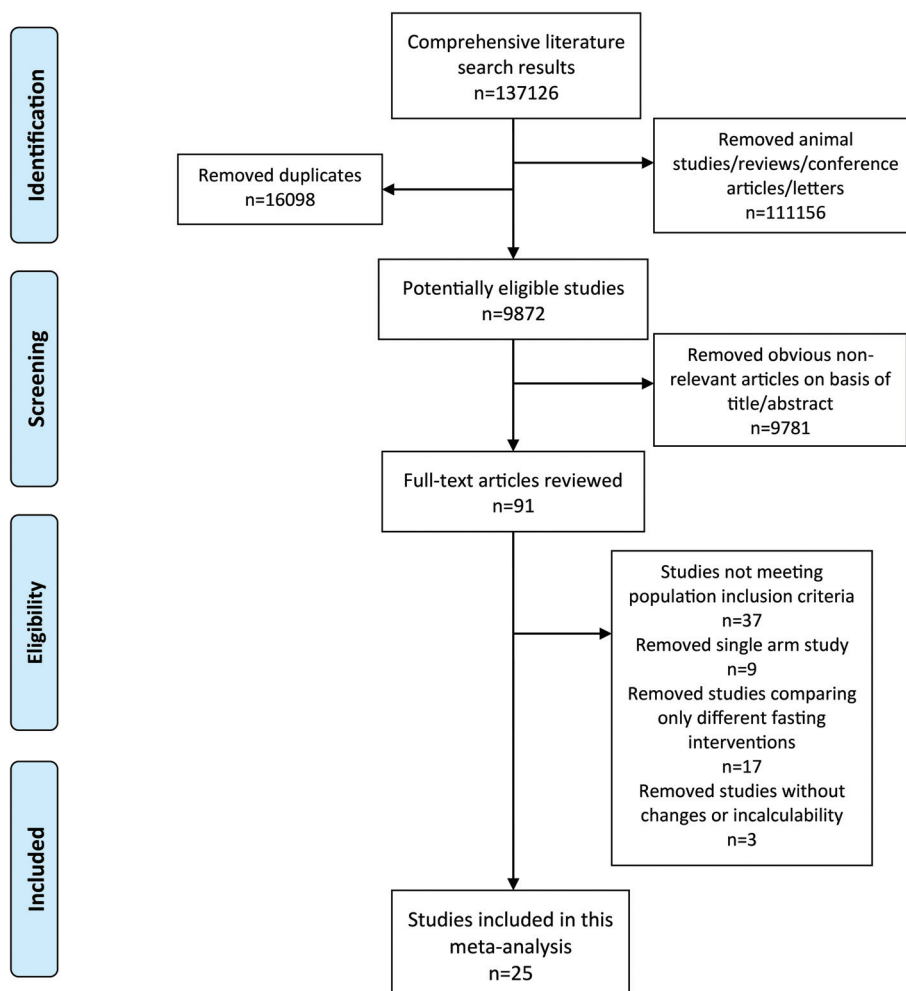


Fig. 1 Flow diagram of the literature search and selection.



Table 1 Characteristics of studies examining the effects of fasting intervention on regulating anthropometric and metabolic parameters

Author	Region	Year	Fasting type	Subjects	Outcome type	Fasting time	Fasting dose	Diabetes	n		Gender(M/F)		Age	
									IG	CG	IG	CG	IG	CG
Bowen J. <i>et al.</i> <sup>a</sup>	Australia	2018	ADMF	A(W + M)	Non follow-up	16 weeks	573.6 kcal	ND	67	68	15/67	16/65	40.0 ± 8.3	40.6 ± 8.8
Varady K. A. <i>et al.</i>	US	2013	ADMF	A(W + M)	Non follow-up	12 weeks	400–600 kcal	ND	15	15	5/10	3/12	47 ± 3	48 ± 2
Bhutani S. <i>et al.</i> <sup>a</sup>	US	2013	ADMF	A(W + M)	Non follow-up	12 weeks	450 kcal	ND	16	16	1/24	1/15	42 ± 2	49 ± 2
Catenacci V. A. <i>et al.</i>	US	2016	CADF	A(W + M)	Non follow-up	8 weeks	0 kcal	ND	13	12	3/10	3/9	39.6 ± 9.5	42.7 ± 7.9
Hutchison A. T. <i>et al.</i> (1)	Australia	2019	CADF	A(W)	Non follow-up	8 weeks	0 kcal	ND	22	11	0/22	0/11	51 ± 2	49 ± 3
Hutchison A. T. <i>et al.</i> (2)	Australia	2019	CADF	A(W)	Non follow-up	8 weeks	0 kcal	ND	22	11	0/22	0/11	49 ± 2	49 ± 3
Moro T. <i>et al.</i>	Italy	2016	TRF	A(M)	Non follow-up	8 weeks	2735 kcal	ND	17	17	17/0	17/0	29.9 ± 4.1	28.5 ± 3.5
Tinsley G. M. <i>et al.</i>	US	2017	TRF	A(M)	Non follow-up	8 weeks	1674 kcal	ND	10	8	10/0	8/0	22.9 ± 4.1	22.0 ± 2.4
Li C. <i>et al.</i> <sup>a</sup>	Germany	2017	VLCD	A(W + M)	Follow-up	1 week	300 kcal	D	16	16	—	—	64.7 ± 7.0	65.4 ± 5.7
Haywood C. J. <i>et al.</i> (1)	Australia	2017	VLCD	A(W + M)	Non follow-up	12 weeks	400–600 kcal	ND	41	36	16/25	13/23	—	—
Haywood C. J. <i>et al.</i> (2)	Australia	2017	VLCD	A(W + M)	Non follow-up	12 weeks	400–600 kcal	ND	41	40	16/25	16/24	—	—
Hussin N. M. <i>et al.</i>	Malaysia	2013	VLCD	A(M)	Non follow-up	12 weeks	300–500 kcal	ND	16	15	16/0	15/0	59.7 ± 6.6	59.7 ± 6.2
Burnand K M. <i>et al.</i>	UK	2016	VLCD	A(W + M)	Follow-up	2 weeks	800 kcal	ND	21	25	0/21	4/21	43.5 ± 31.1	48 ± 35.5
Teng N. I. <i>et al.</i>	Malaysia	2011	VLCD	A(M)	Non follow-up	12 weeks	300–500 kcal	ND	12	13	12/0	13/0	59.3 ± 3.4	58.3 ± 6.3
Arai K. <i>et al.</i>	Japan	1992	VLCD	A(W + M)	Non follow-up	8 weeks	400 kcal	ND	20	25	—	—	31.6 ± 13.1	35.3 ± 11.7
Teng N. I. <i>et al.</i>	Malaysia	2013	VLCD	A(W + M)	Non follow-up	12 weeks	300–500 kcal	ND	28	28	28/0	28/0	59.6 ± 5.4	59.1 ± 6.2
Paisey R. B. <i>et al.</i>	UK	1995	VLCD	A(W + M)	Non follow-up	12 weeks	400–670 kcal	D	14	14	7/7	3/11	53.9 ± 5.7	55.4 ± 7.3
Wing R. R. <i>et al.</i>	US	1994	VLCD	A(W + M)	Follow-up	12 weeks	400–500 kcal	D	45	48	15/30	18/30	52.3 ± 10.7	51.3 ± 8.7
Torgerson J. S. <i>et al.</i>	Sweden	1997	VLCD	A(W + M)	Non follow-up	12 weeks	456–608 kcal	ND	58	55	22/36	17/38	47.3 ± 6.7	46.9 ± 5.8
Wadden T. A. <i>et al.</i> <sup>a</sup>	US	1994	VLCD	A(W)	Non follow-up	16 weeks	420 kcal	ND	26	17	0/28	0/21	36.8 ± 8.9	42.9 ± 10.1
Purcell K. <i>et al.</i> <sup>a</sup>	Australia	2014	VLCD	A(W + M)	Non follow-up	12 weeks	450–800 kcal	ND	76	51	26/71	25/78	49.6 ± 10.9	50.1 ± 11.1
Stenius-Aarniala B. <i>et al.</i>	Finland	2000	VLCD	A(W + M)	Follow-up	8 weeks	420 kcal	ND	19	19	—	—	—	—
Wadden T. A. <i>et al.</i>	US	1986	VLCD	A(W + M)	Non follow-up	8 weeks	400–500 kcal	ND	15	16	2/13	3/13	44.3 ± 8.7	44.3 ± 8.6
Tuomilehto H. <i>et al.</i>	Finland	2010	VLCD	A(W + M)	Follow-up	12 weeks	600–800 kcal	ND	35	36	26/9	27/9	51.8 ± 9.0	51.7 ± 8.8
Tuomilehto H. P. <i>et al.</i>	Finland	2009	VLCD	A(W + M)	Follow-up	12 weeks	600–800 kcal	ND	35	37	26/9	27/10	51.8 ± 9.0	50.9 ± 8.6
Wadden T. A. <i>et al.</i>	US	1988	VLCD	A(W + M)	Follow-up	8 weeks	400–500 kcal	ND	15	16	2/13	3/13	44.3 ± 8.7	44.3 ± 8.6
Williams K. V. <i>et al.</i> <sup>a</sup>	US	1998	PF	A(W + M)	Follow-up	20 weeks	400–600 kcal	D	16	14	9/9	7/11	51.4 ± 7.9	54.1 ± 7.0

Author	Body weight (kg)		BMI (kg m <sup>-2</sup> )		FEM (kg)		FM (kg)		WC (cm)		TC (mmol L <sup>-1</sup> )		LDL-C (mmol L <sup>-1</sup> )	
	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG
Bowen J. <i>et al.</i> <sup>a</sup>	-10.0 ± 3.9	-12.5 ± 3.4	-3.8 ± 1.2	-4.4 ± 1.1	-1.4 ± 1.8	-1.9 ± 1.6	-8.4 ± 2.6	-10.3 ± 2.4	—	—	-0.5 ± 0.2	-0.6 ± 0.2	-0.4 ± 0.2	-0.4 ± 0.3
Varady K. A. <i>et al.</i>	-5.1 ± 1.0	-0.6 ± 1.0	—	—	-3.6 ± 0.5	-0.3 ± 0.5	-1.6 ± 0.5	-0.2 ± 0.5	—	—	-0.7 ± 0.2	-0.2 ± 0.1	-0.5 ± 0.2	-0.2 ± 0.1
Bhutani S. <i>et al.</i> <sup>a</sup>	-3.0 ± 1.0	0.0 ± 1.0	-1.0 ± 1.0	0.0 ± 1.0	-1.0 ± 1.0	-1.0 ± 1.0	-2.0 ± 1.0	0.0 ± 1.0	-5.0 ± 1.0	-1.0 ± 1.0	0.3 ± 0.1	0.1 ± 0.1	0.0 ± 0.1	0.1 ± 0.1
Catenacci V. A. <i>et al.</i>	-8.2 ± 0.9	-7.1 ± 1.0	-3.2 ± 0.3	-2.4 ± 0.3	—	—	-3.7 ± 0.5	-3.7 ± 0.5	—	—	-0.8 ± 0.2	-0.6 ± 0.2	-0.6 ± 0.1	-0.4 ± 0.1
Hutchison A. T. <i>et al.</i> (1)	-2.7 ± 0.5	0.4 ± 0.4	—	—	-0.5 ± 0.3	-0.4 ± 0.4	-2.3 ± 0.4	-0.2 ± 0.5	-4.3 ± 1.0	-1.4 ± 1.7	-0.4 ± 0.2	-0.3 ± 0.2	-0.2 ± 0.1	-0.2 ± 0.1
Hutchison A. T. <i>et al.</i> (2)	-5.4 ± 0.5	0.4 ± 0.4	—	—	-1.4 ± 0.3	-0.4 ± 0.4	-3.9 ± 0.4	-0.2 ± 0.5	-7.6 ± 1.2	-1.4 ± 1.7	-0.6 ± 0.1	-0.3 ± 0.2	-0.4 ± 0.1	-0.2 ± 0.1
Moro T. <i>et al.</i>	—	—	—	—	0.6 ± 0.9	0.5 ± 0.8	-1.6 ± 1.2	-0.3 ± 0.9	—	—	-0.1 ± 0.1	0.0 ± 0.2	-0.1 ± 0.1	0.0 ± 0.1
Tinsley G. M. <i>et al.</i>	-1.0 ± 4.0	3.0 ± 3.5	—	—	—	—	-0.6 ± 1.7	0.8 ± 1.1	—	—	—	—	—	—
Li C. <i>et al.</i> <sup>a</sup>	-3.5 ± 4.5	-2.0 ± 4.8	-1.2 ± 1.7	-0.6 ± 2.6	—	—	—	—	-4.4 ± 4.3	-0.3 ± 2.0	0.0 ± 0.7	-0.4 ± 0.7	-0.1 ± 0.7	-0.2 ± 0.4
Haywood C. J. <i>et al.</i> (1)	-11.6 ± 1.5	-4.0 ± 1.2	—	—	-7.8 ± 1.5	-2.8 ± 1.2	-10.8 ± 1.8	-3.9 ± 1.1	—	—	—	—	—	—
Haywood C. J. <i>et al.</i> (2)	-11.6 ± 1.5	-5.4 ± 1.2	—	—	-7.8 ± 1.5	-3.1 ± 0.9	-10.8 ± 1.8	-5.6 ± 1.6	—	—	—	—	—	—
Hussin N. M. <i>et al.</i>	-2.8 ± 1.6	-0.6 ± 1.5	-1.0 ± 0.4	-0.3 ± 0.5	—	—	—	—	—	—	—	—	—	—
Burnand K. M. <i>et al.</i>	-3.5 ± 2.0	-1.0 ± 1.7	-1.3 ± 0.7	-0.4 ± 0.6	—	—	—	—	—	—	—	—	—	—
Teng N. I. <i>et al.</i>	-2.3 ± 1.2	0.8 ± 1.7	-0.7 ± 0.6	0.3 ± 0.4	-0.5 ± 0.8	0.2 ± 1.0	—	—	—	—	—	—	—	—
Arai K. <i>et al.</i>	-9.0 ± 5.2	-5.2 ± 3.0	-4.1 ± 1.2	-2.1 ± 1.0	—	—	—	—	—	—	-0.7 ± 0.2	-0.2 ± 0.2	—	—
Teng N. I. <i>et al.</i>	-2.5 ± 1.4	0.0 ± 1.6	-0.9 ± 0.4	0.0 ± 0.4	0.2 ± 1.0	-0.9 ± 3.1	-1.5 ± 0.7	0.3 ± 1.4	—	—	-0.5 ± 0.2	0.1 ± 0.2	-0.3 ± 0.2	0.1 ± 0.2
Paisey R. B. <i>et al.</i>	-14.0 ± 7.0	-2.0 ± 4.6	-5.0 ± 2.4	-1.0 ± 2.4	—	—	—	—	-15.0 ± 7.4	0.0 ± 6.7	-0.6 ± 1.0	-0.1 ± 0.6	—	—





Table 1 (Contd.)

Author	Body weight (kg)		BMI (kg m <sup>-2</sup> )		FEM (kg)		FM (kg)		WC (cm)		TC (mmol L <sup>-1</sup> )		LDL-C (mmol L <sup>-1</sup> )	
	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG
Wing R. <i>et al.</i>	-16.9 ± 0.6	-14.4 ± 0.9	—	—	—	—	—	—	—	—	-0.3 ± 0.3	-0.6 ± 0.2	-0.1 ± 0.3	-0.3 ± 0.2
Torgerson J. S. <i>et al.</i>	-15.8 ± 7.5	-6.4 ± 4.5	—	—	—	—	—	—	—	—	—	—	—	—
Wadden T. A. <i>et al.</i> <sup>a</sup>	-22.6 ± 6.0	-10.1 ± 6.2	—	—	-6.6 ± 3.5	-1.5 ± 2.9	—	—	—	—	—	—	—	—
Purell K. <i>et al.</i> <sup>a</sup>	-14.6 ± 2.7	-14.3 ± 2.9	-5.3 ± 0.4	-5.2 ± 0.7	1.1 ± 4.4	0.5 ± 5.1	-12.7 ± 4.9	-14.1 ± 5.5	-15.5 ± 5.3	-16.2 ± 4.4	—	—	—	—
Stenius-Aarniala B. <i>et al.</i>	-14.2 ± 10.7	-0.3 ± 0.3	—	—	—	—	—	—	—	—	—	—	—	—
Wadden T. A. <i>et al.</i>	-13.2 ± 3.9	-9.6 ± 4.4	—	—	—	—	—	—	—	—	—	—	—	—
Tuomilehto H. <i>et al.</i>	-7.3 ± 6.5	-2.9 ± 7.5	-2.4 ± 2.1	-1.0 ± 2.6	—	—	—	-7.7 ± 6.7	-3.5 ± 7.3	0.1 ± 0.8	-0.1 ± 0.8	—	—	—
Tuomilehto H. P. <i>et al.</i>	-10.7 ± 6.5	-2.4 ± 5.6	-3.5 ± 2.1	-0.8 ± 2.0	—	—	—	-11.6 ± 6.6	-3.0 ± 6.0	—	—	—	—	—
Wadden T. A. <i>et al.</i>	-14.1 ± 5.1	-14.3 ± 6.7	—	—	—	—	—	—	—	—	—	—	—	—
Williams K. V. <i>et al.</i> <sup>a</sup>	-9.6 ± 1.4	-6.2 ± 1.4	—	—	—	—	—	—	—	—	-0.3 ± 0.4	-0.3 ± 0.2	-0.2 ± 0.3	-0.2 ± 0.3

Author	HDL-C (mmol L <sup>-1</sup> )		TG (mmol L <sup>-1</sup> )		SBP (mmHg)		DBP (mmHg)		Blood glucose (mmol L <sup>-1</sup> )		Insulin (mIU L <sup>-1</sup> )	
	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG
Bowen J. <i>et al.</i> <sup>a</sup>	-0.1 ± 0.1	0.0 ± 0.1	-0.2 ± 0.1	-0.4 ± 0.5	-7.2 ± 3.8	-8.4 ± 3.8	-4.1 ± 2.3	-3.6 ± 1.8	-0.1 ± 0.1	-0.2 ± 0.2	-4.3 ± 4.1	-4.4 ± 3.3
Varady K. A. <i>et al.</i>	-0.1 ± 0.1	0.0 ± 0.1	-0.2 ± 0.1	0.1 ± 0.1	-7.0 ± 2.0	1.0 ± 3.0	-6.0 ± 2.0	2.0 ± 6.0	—	—	—	—
Bhutani S. <i>et al.</i> <sup>a</sup>	0.0 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	-4.0 ± 0.6	-2.0 ± 1.5	-2.0 ± 0.4	-2.0 ± 2.1	-0.2 ± 0.1	0.1 ± 0.1	-2.0 ± 1.6	-4.0 ± 0.8
Catenacci V. A. <i>et al.</i>	-0.1 ± 0.0	-0.1 ± 0.0	-0.3 ± 0.1	0.0 ± 0.1	—	—	—	—	0.3 ± 0.1	0.2 ± 0.1	3.0 ± 2.3	-0.2 ± 2.4
Hutchison A. T. <i>et al.</i> (1)	-0.1 ± 0.1	0.0 ± 0.1	-0.3 ± 0.1	-0.3 ± 0.1	-5.6 ± 3.4	1.5 ± 1.7	-1.5 ± 2.0	-0.4 ± 1.0	0.1 ± 0.1	0.0 ± 0.1	2.9 ± 1.4	-0.4 ± 1.9
Hutchison A. T. <i>et al.</i> (2)	-0.1 ± 0.0	0.0 ± 0.1	-0.2 ± 0.1	-0.3 ± 0.1	-0.6 ± 3.2	1.5 ± 1.7	-2.5 ± 1.4	-0.4 ± 1.0	-0.2 ± 0.1	0.0 ± 0.1	-3.6 ± 1.0	-0.4 ± 1.9
Moro T. <i>et al.</i>	0.1 ± 0.0	0.0 ± 0.1	-0.1 ± 0.0	0.0 ± 0.0	—	—	—	—	-0.6 ± 0.1	0.0 ± 1.2	-1.0 ± 0.3	-0.3 ± 0.1
Tinsley G. M. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Li C. <i>et al.</i> <sup>a</sup>	0.2 ± 0.6	-0.1 ± 0.2	-0.3 ± 1.0	0.0 ± 0.9	-13.9 ± 15.3	0.4 ± 15.8	-9.0 ± 12.3	3.2 ± 11.9	-0.6 ± 1.7	-2.1 ± 2.6	-3.5 ± 9.3	-0.2 ± 5.4
Haywood C. J. <i>et al.</i> (1)	—	—	—	—	—	—	—	—	—	—	—	—
Haywood C. J. <i>et al.</i> (2)	—	—	—	—	—	—	—	—	—	—	—	—
Hussin N. M. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Burnand K. M. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Teng N. I. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Arai K. <i>et al.</i>	—	—	—	—	-15.6 ± 11.6	3.9 ± 7.5	-9.7 ± 7.1	-5.6 ± 10.9	-0.5 ± 0.9	-0.5 ± 0.4	—	—
Teng N. I. <i>et al.</i>	0.0 ± 0.0	0.0 ± 0.1	-0.2 ± 0.4	-0.1 ± 0.3	-6.5 ± 4.5	3.1 ± 3.4	-2.2 ± 2.1	2.1 ± 1.6	0.2 ± 0.1	0.5 ± 0.7	—	—
Paisey R. B. <i>et al.</i>	—	—	-1.4 ± 1.4	0.3 ± 1.0	0.0 ± 25.9	0.0 ± 22.2	-6.0 ± 18.5	-11.0 ± 16.3	—	—	—	—
Wing R. R. <i>et al.</i>	0.1 ± 0.0	0.1 ± 0.0	-0.8 ± 0.7	-1.0 ± 1.1	-9.0 ± 3.0	-6.0 ± 3.8	-6.0 ± 1.8	-3.0 ± 3.1	-3.6 ± 1.1	-3.2 ± 0.6	-12.3 ± 6.9	-9.3 ± 7.3
Torgerson J. S. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Wadden T. A. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Purell K. <i>et al.</i> <sup>a</sup>	—	—	—	—	—	—	—	—	—	—	—	—
Stenius-Aarniala B. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Wadden T. A. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Tuomilehto H. <i>et al.</i>	0.1 ± 0.2	0.1 ± 0.2	-0.2 ± 0.9	-0.1 ± 0.8	0.6 ± 8.5	-3.0 ± 11.3	0.0 ± 5.4	-1.7 ± 6.9	-0.4 ± 2.1	-0.3 ± 1.3	-2.2 ± 8.4	0.0 ± 4.6
Tuomilehto H. P. <i>et al.</i>	0.1 ± 0.2	0.1 ± 0.2	-0.5 ± 1.1	-0.1 ± 0.7	-1.7 ± 14.7	-1.1 ± 19.6	-1.9 ± 10.6	-0.4 ± 12.6	-0.6 ± 2.3	-0.4 ± 1.4	-5.9 ± 7.0	-1.2 ± 3.4
Wadden T. A. <i>et al.</i>	—	—	—	—	—	—	—	—	—	—	—	—
Williams K. V. <i>et al.</i> <sup>a</sup>	0.0 ± 0.0	-0.2 ± 0.1	-1.2 ± 0.2	-0.7 ± 0.8	—	—	—	—	-1.9 ± 0.6	-1.8 ± 0.6	-5.6 ± 1.0	-4.7 ± 3.1

IG, intervention group; CG, control group; ADMF, alternate day modified fasting; CADF, complete alternate-day fasting; TRF, time-restricted feeding; VLCD, very low calorie diet; PF, periodic fasting; A(W + M), Adult(women + men); A(W), Adult(women); A(M), Adult(men); ND, non-diabetes; D, diabetes; Gender(M/F), Gender(male/female); BMI, body mass index; FEM, fat free mass; FM, fat mass; WC, waist circumference; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure. <sup>a</sup>The variable of gender and age includes dropout.

calculated. Exclusion criteria were as follows: (1) randomized studies were single-arm studies or without a placebo; (2) fasting due to religious habits; and (3) non-human studies, reviews and conference literature. Two researchers independently reviewed the literature and collected all eligible studies. Once disagreements existed, the nutritionist was involved to discuss and solve it (Fig. 1).

### 2.3. Data abstraction

Data collected from all included literature were as follows: (1) first author, nationality, publication year, numbers, mean age and gender of fasting intervention subjects and the control group; (2) the fasting type, subject type, fasting time and dose, diabetes or not, whether measured immediately after fasting or not (outcome type); and (3) the variations in the body weight, BMI, fat free mass (FEM), fat mass (FM), waist circumference (WC), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), systolic blood pressure (SBP), dias-

tolic blood pressure (DBP), blood glucose and insulin parameters in the fasting intervention and control subjects.

### 2.4. Risk of bias within individual studies

The methodological quality for the selected literature was evaluated independently using the Cochrane Collaboration (RevMan Version 5.3) software by two investigators according to Cochrane risk-of-bias criteria,<sup>21</sup> which included seven items (randomization sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias) to estimate bias in each trial. Each quality item was graded as low risk, unclear risk, or high risk. Simultaneously, the GRADE system was used to classify the quality of evidence. The included trials were graded as high quality, moderate quality, low quality, or very low quality according to the risk of bias, inconsistency, indirectness, imprecision and other considerations.<sup>22</sup>

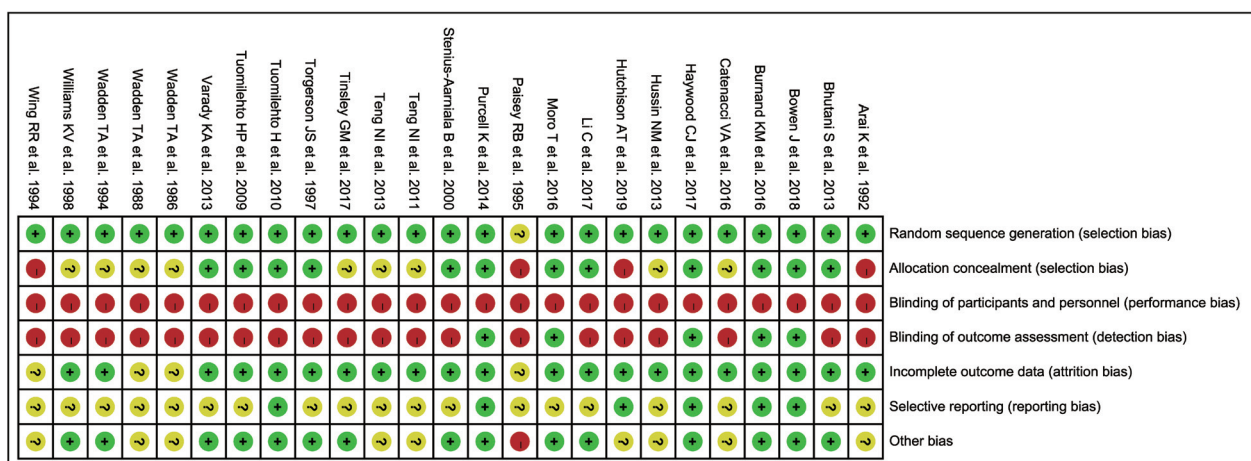
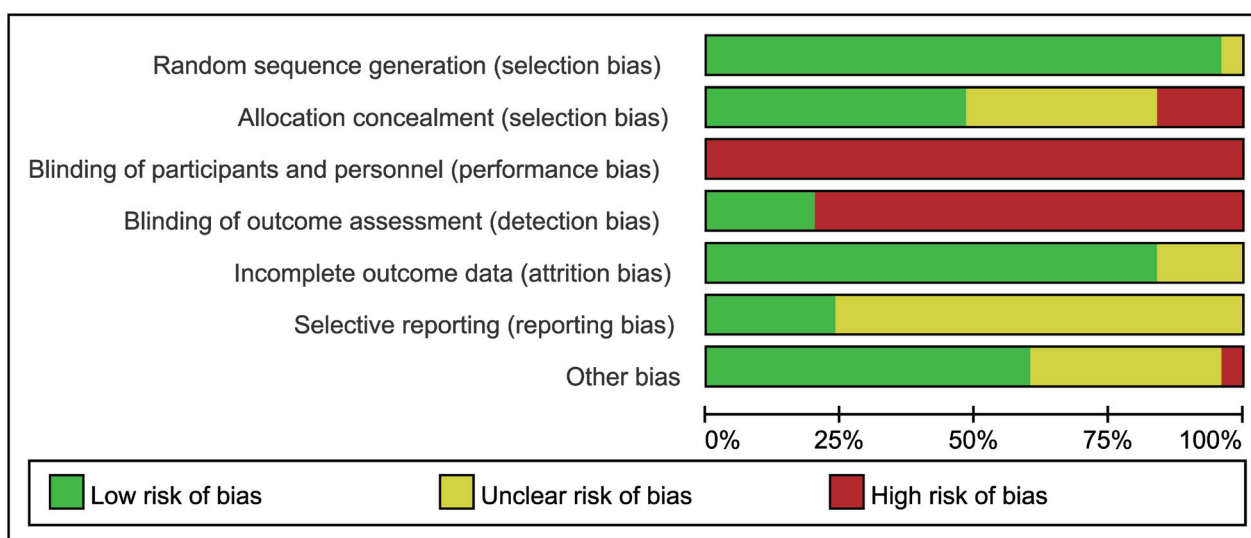


Fig. 2 Risk of within-study bias.



## 2.5. Statistical analysis

Statistical analysis was performed using the statistical software Review Manager 5.3 and Stata 12.0. The mean change (standard deviation) in anthropometric and metabolic parameters from the baseline was used to evaluate the differences between the fasting intervention and control subjects. When it could not be obtained *via* the original literature, we calculated the standard deviation in the mean change in the anthropometric and metabolic parameters using the formula in the Cochrane handbook.<sup>23</sup> The correlation coefficient of the equation was estimated using the data from the included literature providing the baseline and endpoint values and the variations, simultaneously.

$$\sqrt{SD_{\text{Baseline}}^2 + SD_{\text{Final}}^2 - (2 \times 0.98 \times SD_{\text{Baseline}} \times SD_{\text{Final}})}$$

The random effects model was used to compute the summary standard mean difference (SMD) and 95% confidence interval (CI) and to evaluate the differences in the variations in the anthropometric and metabolic parameters between the fasting intervention group and the controls.

We use the  $I^2$  statistic to estimate statistical heterogeneity. The potential publication bias was evaluated *via* the Egger test, where the trim-and-fill method (sensitivity analysis) was used to correct outcomes and evaluate the impact of bias on the

outcomes. Subgroup analyses were conducted based on the fasting type (ADMF, CADF, TRF, VLCD), subject type (Adult (women + men), Adult(women), Adult(men)), Region(Oceania, America, Europe, Asia), fasting time (<12weeks, ≥12 weeks), diabetes or not, and outcome type (follow-up, non follow-up). Because only one literature was for PF, the subgroup analysis was not conducted in view of PF.

## 3. Results

A total of 25 studies met inclusion criteria, involving 1358 samples, with 690 interventions and 668 controls.<sup>12,24-47</sup> The variations in the body weight, BMI, FEM, FM, WC, TC, LDL-C, HDL-C, TG, SBP, DBP, blood glucose and insulin parameters were evaluated in twenty-four,<sup>12,24-27,29-47</sup> thirteen,<sup>12,25,26,30,32-37,41,44,45</sup> nine,<sup>12,24,25,27,28,34,36,40,41</sup> ten,<sup>12,24-29,31,36,41</sup> eight,<sup>25,27,30,31,37,41,44,45</sup> thirteen,<sup>12,24-28,30,35-38,44,47</sup> ten,<sup>12,24-28,30,34,38,47</sup> twelve,<sup>12,24-28,30,36,38,44,45,47</sup> thirteen,<sup>12,24-28,30,36-38,44,45,47</sup> eleven,<sup>12,24,25,27,30,35-38,44,45</sup> eleven,<sup>12,24,25,27,30,35-38,44,45</sup> twelve<sup>12,25-28,30,35,36,38,44,45,47</sup> and ten<sup>12,25-28,30,38,44,45,47</sup> studies, respectively. The detailed outcomes are performed in Table 1 and Table S2.† Almost all studies<sup>12,24-36,38-47</sup> ( $n = 24$ ) were randomized, and nearly half of the studies<sup>12,24,25,28,30,31,33,39,41,42,44,45</sup> ( $n = 12$ ) described allocation

**Table 2** The summary of findings (SoF) with the GRADE system

### Fasting intervention compared to no fasting intervention for regulating anthropometric and metabolic parameters

**Population:** subjects with overweight or obesity

**Settings:** four studies were conducted in Asia, eight studies were conducted in Europe, nine studies were conducted in America and four studies were conducted in Oceania

**Intervention:** fasting

**Comparison:** no fasting intervention

Outcomes <sup>a</sup>	SMD(95%CI) <sup>b</sup>	No of participants (studies)	Quality of the evidence comments (GRADE)
Body weight	-2.16(-2.76, -1.56) kg	1324 (24RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
BMI	-1.18(-1.72, -0.65) kg m <sup>-2</sup>	725 (13RCTs)	⊕⊕⊕⊕MODERATE <sup>c</sup>
FEM	-0.82(-1.49, -0.15) kg	537 (9RCTs)	⊕⊕⊕⊕ LOW <sup>c,d</sup>
FM	-2.20(-3.29, -1.11) kg	629 (10RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
WC	-2.31(-3.32, -1.30) cm	534 (8RCTs)	⊕⊕⊕⊕MODERATE <sup>c</sup>
TC	-0.62(-1.36, 0.12) mmol L <sup>-1</sup>	666 (13RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
LDL-C	-0.87(-1.57, -0.17) mmol L <sup>-1</sup>	522 (10RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
HDL-C	-0.12(-0.75, 0.52) mmol L <sup>-1</sup>	665 (12RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
TG	-0.61(-1.04, -0.18) mmol L <sup>-1</sup>	693 (13RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
SBP	-1.08(-1.69, -0.47) mmHg	649 (11RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
DBP	-0.70(-1.13, -0.26) mmHg	649 (11RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
Blood glucose	-0.28(-0.75, 0.20) mmol L <sup>-1</sup>	680 (12RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>
Insulin	-0.21(-0.82, 0.40) mIU L <sup>-1</sup>	579 (10RCTs)	⊕⊕⊕⊕ MODERATE <sup>c</sup>

### GRADE working group grades of evidence

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low quality:** Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

**Very low quality:** We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

<sup>a</sup> All subjects were followed up from 1 week to 5 months. <sup>b</sup> Results for variations of treatments compared with controls. SMD: standard mean deviation; CI: confidence interval; RCT: randomized controlled trial; BMI: body mass index; FEM: fat free mass; FM: fat mass; WC: waist circumference; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; TG: triglycerides; SBP: systolic blood pressure; DBP: diastolic blood pressure. <sup>c</sup> Bias risk: Downgraded by one level as most of the included literature did not use the blind method (the main reason is that the intervention method cannot be blind). <sup>d</sup> Inconsistency: Downgraded by one level as a high heterogeneity existed and its source was not completely clear.



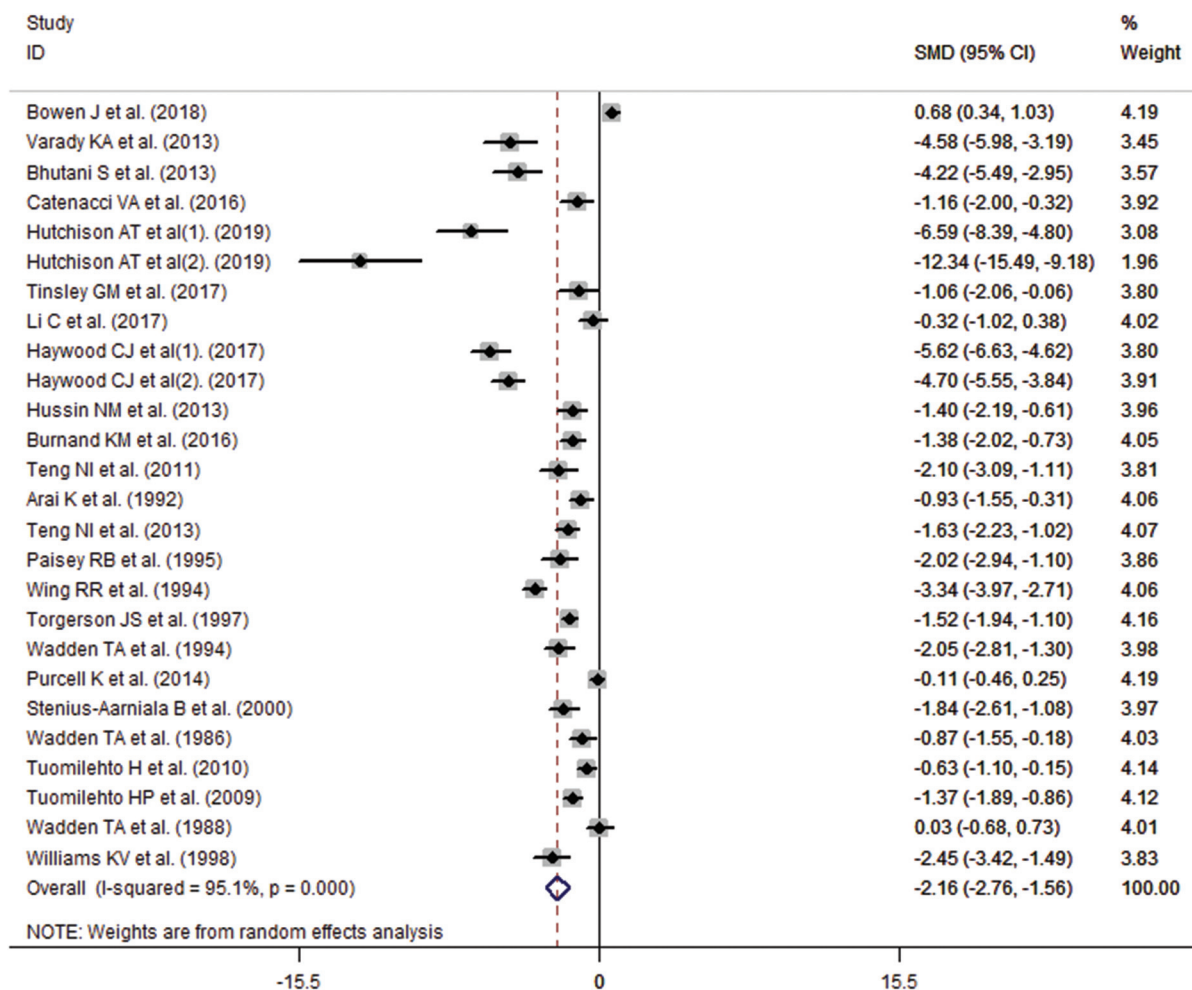


Fig. 3 Meta-analysis results of fasting intervention for the body weight in subjects with overweight or obesity.

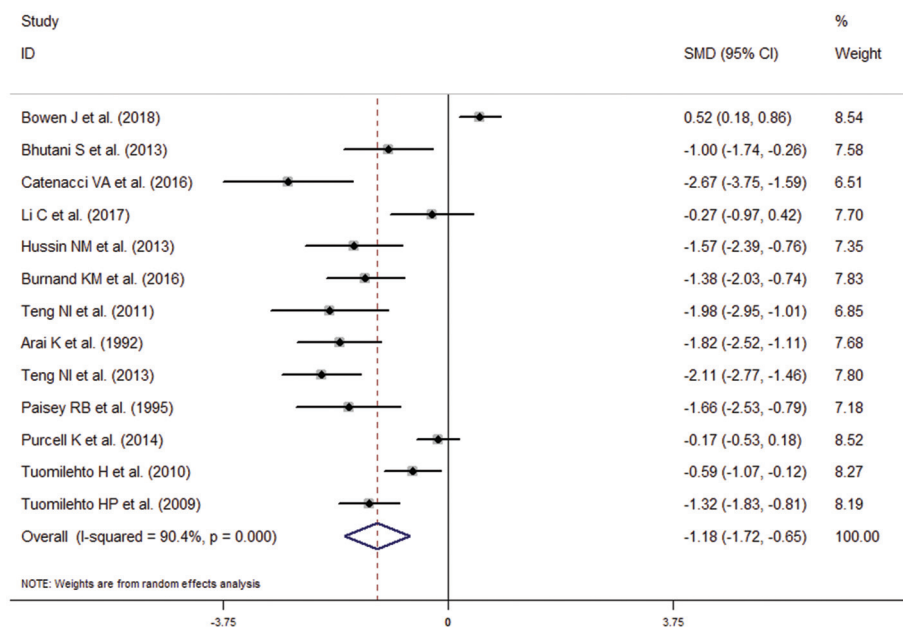


Fig. 4 Meta-analysis results of fasting intervention for the body mass index (BMI) in subjects with overweight or obesity.



concealment methods. Specially, as fasting cannot blind between the intervention group and controls, double-blind setup were lacking in all studies. However, five studies stated that outcome assessments were blinded.<sup>12,28,31,33,41</sup> Four studies were considered to have attrition bias as the reason for the drop out was not explained.<sup>37,38,43,46</sup> Only six trials had clinical trial registration codes, where reporting bias might have existed.<sup>12,27,31,33,41,44</sup> After evaluation comprehensively, other biases existed in ten studies.<sup>26,27,32,34–38,43,46</sup> The risk of bias within individual studies detailed is performed in Fig. 2.

In addition, the GRADE system was performed to determine the quality of evidence for different results. We considered that the grades of evidence were moderate quality in all outcomes except for the FEM parameter (low quality) (Table 2).

The meta-analysis revealed that fasting intervention led to a significantly larger weight loss (SMD =  $-2.16$  kg, 95%CI =  $-2.76, -1.56$  kg; Fig. 3) compared with the control in subjects with overweight or obesity. Fasting intervention was associated with significantly larger reduction in BMI (SMD =  $-1.18$  kg m<sup>-2</sup>, 95% CI =  $-1.72, -0.65$  kg m<sup>-2</sup>; Fig. 4), FEM (SMD =

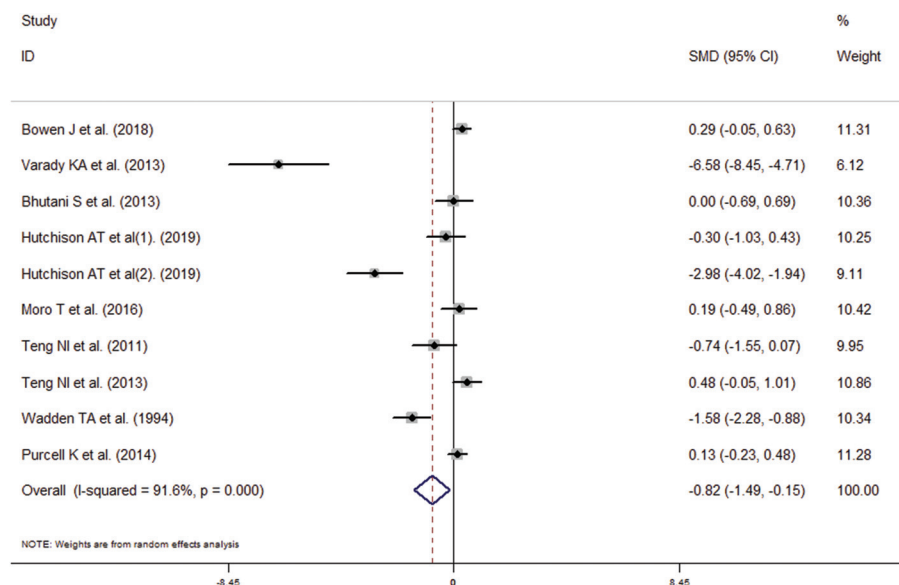


Fig. 5 Meta-analysis results of fasting intervention for the fat free mass (FEM) in subjects with overweight or obesity.

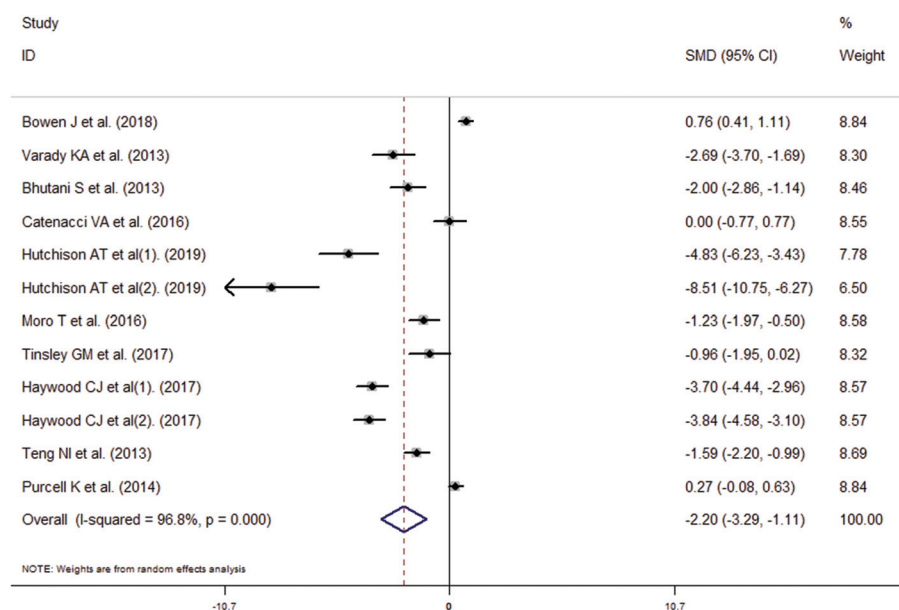


Fig. 6 Meta-analysis results of fasting intervention for the fat mass (FM) in subjects with overweight or obesity.



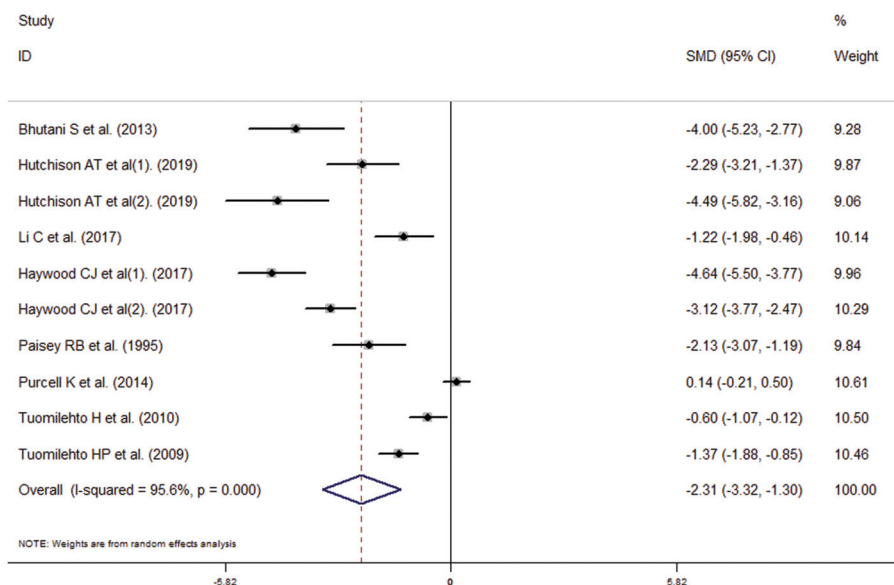


Fig. 7 Meta-analysis results of fasting intervention for the waist circumference (WC) in subjects with overweight or obesity.

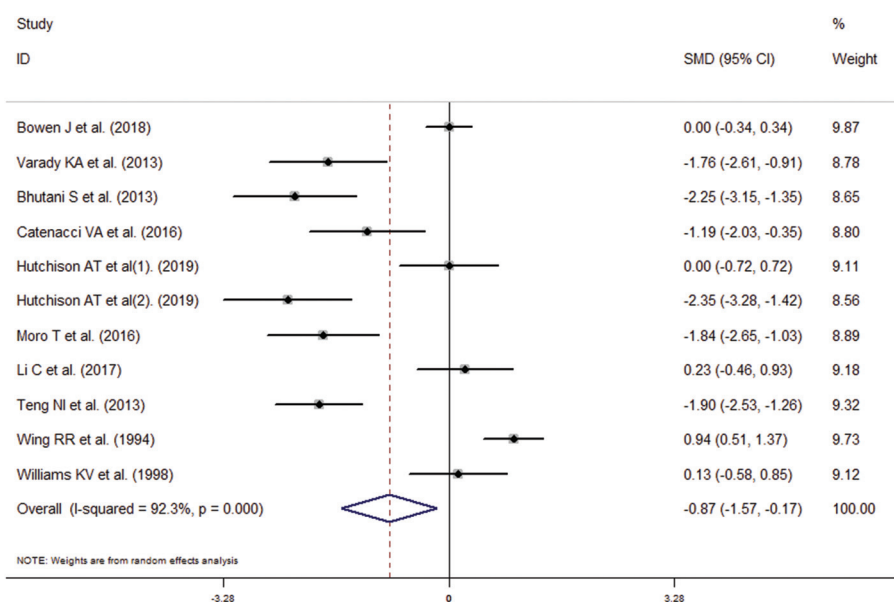


Fig. 8 Meta-analysis results of fasting intervention for the low density lipoprotein cholesterol (LDL-C) in subjects with overweight or obesity.

-0.82 kg, 95% CI = -1.49, -0.15 kg; Fig. 5), FM (SMD = -2.20 kg, 95% CI = -3.29, -1.11 kg; Fig. 6), and WC (SMD = -2.31cm, 95% CI = -3.32, -1.30 cm; Fig. 7). Meanwhile, statistically significant differences in the variations in the LDL-C (SMD = -0.87 mmol L<sup>-1</sup>, 95% CI = -1.57, -0.17 mmol L<sup>-1</sup>; Fig. 8), TG (SMD = -0.61 mmol L<sup>-1</sup>, 95% CI = -1.04, -0.18 mmol L<sup>-1</sup>; Fig. 9), SBP (SMD = -1.08 mmHg, 95% CI = -1.69, -0.47 mmHg; Fig. 10), and DBP (SMD = -0.70 mmHg, 95% CI = -1.13, -0.26 mmHg; Fig. 11) parameters were noticed between the intervention groups and the controls. However, the data obtained from the included literature did

not indicate any significant effect of fasting on the TC (SMD = -0.62 mmol L<sup>-1</sup>, 95% CI = -1.36, 0.12 mmol L<sup>-1</sup>; Fig. 12), HDL-C (SMD = -0.12 mmol L<sup>-1</sup>, 95% CI = -0.75, 0.52 mmol L<sup>-1</sup>; Fig. 13), blood glucose (SMD = -0.28 mmol L<sup>-1</sup>, 95% CI = -0.75, 0.20 mmol L<sup>-1</sup>; Fig. 14) and insulin (SMD = -0.21 mIU L<sup>-1</sup>, 95% CI = -0.82, 0.40 mIU L<sup>-1</sup>; Fig. 15) concentrations.

The outcomes of subgroup analyses for fasting intervention and the change of anthropometric and metabolic parameters in the people with overweight or obesity are summarized in Table 3. Region may be the sources of heterogeneity for body weight, BMI, TC and SBP in the associated studies. Subject



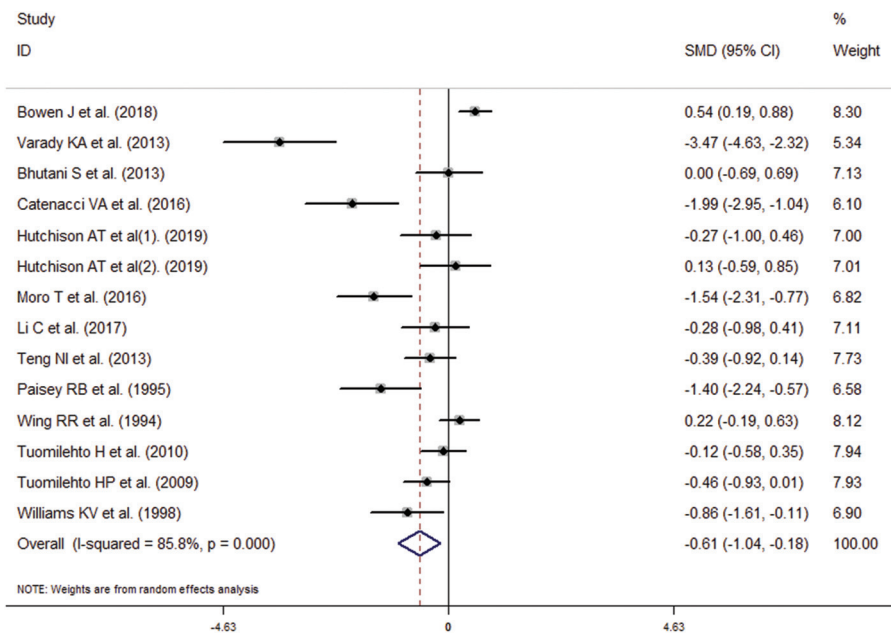


Fig. 9 Meta-analysis results of fasting intervention for the triglycerides (TG) in subjects with overweight or obesity.

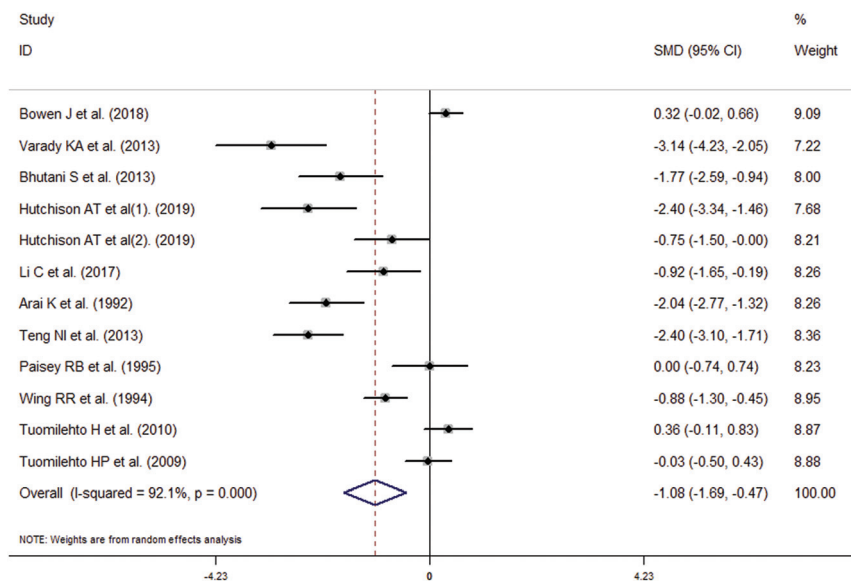


Fig. 10 Meta-analysis results of fasting intervention for the systolic blood pressure (SBP) in subjects with overweight or obesity.

type may be the sources of heterogeneity for FM and LDL-C and outcome type may be the sources of heterogeneity for TG, blood glucose, WC and insulin. In addition, fasting type may be the sources of heterogeneity for HDL-C and fasting time may be the sources of heterogeneity for DBP.

The results of publication bias for included studies are given in Table 4. Publication biases were observed in the body weight, BMI, FEM, FM, WC, TC, LDL-C and SBP ( $P < 0.05$ ). However, there was no significant difference between the SMD and that before the trim and fill. Therefore, the effect of publi-

cation bias was considered slight and the results were stable (Table 4).

## 4. Discussion

According to the existing evidence of relevant animal and human studies, fasting has a beneficial effect on advancing health and reduces the risk of several chronic illnesses in adults, especially for overweight and sedentary people.<sup>6</sup>



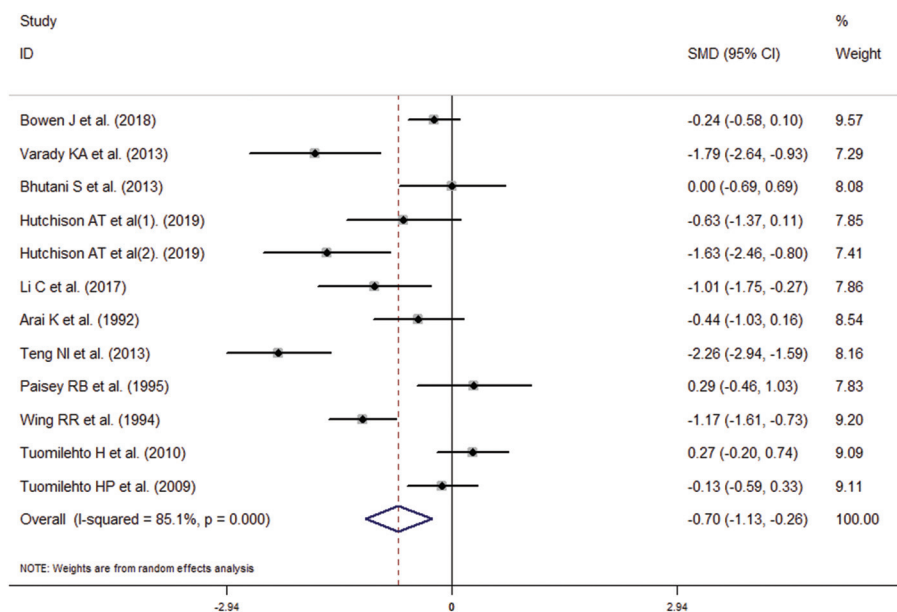


Fig. 11 Meta-analysis results of fasting intervention for the diastolic blood pressure (DBP) in subjects with overweight or obesity.

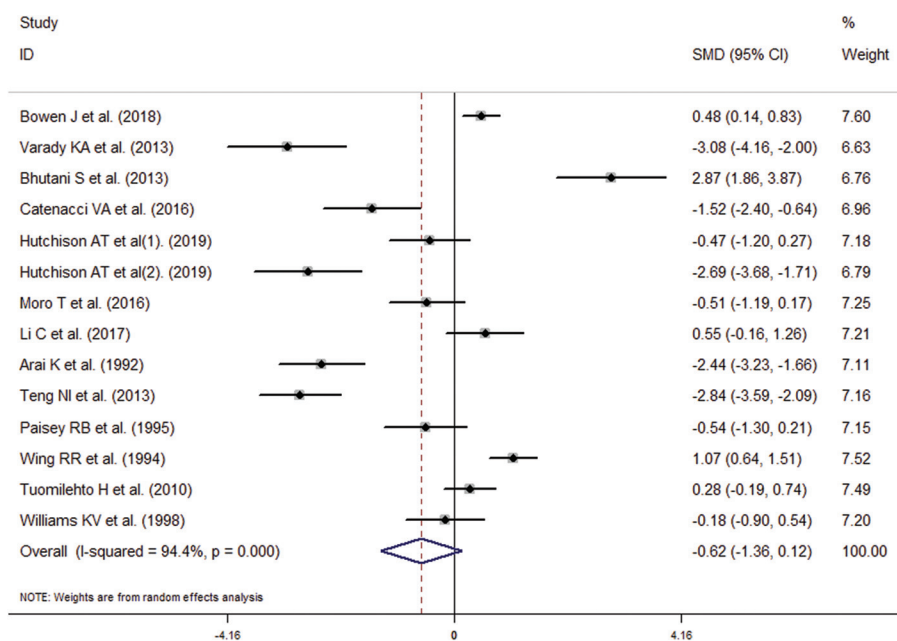


Fig. 12 Meta-analysis results of fasting intervention for the total cholesterol (TC) in subjects with overweight or obesity.

Similarly, our study found that participants with overweight or obesity receiving fasting intervention had significantly larger reductions in body weight, BMI, FEM, FM, WC, LDL-C, TG, SBP and DBP parameters than the control subjects. One crucial mechanism resulting in these profitable influences seems to be “flipping” of the metabolic switch.<sup>8</sup> When the hepatic glycogen is depleted due to fasting, some metabolic adaptations are observed in the liver, thus retaining systemic energy balance and supplying the major organs, tissues and cells with sufficient nutrients.<sup>48</sup> The characteristics are

increased numbers of circulating ketones, whereas circulating fatty acids, amino acids, glucose, and insulin are preserved at low concentrations.<sup>49</sup> And it is owing to the fat mobilization and the oxidative decomposition of fatty acids.<sup>50,51</sup> Ketones are metabolized to acetyl coenzyme A, which then enters the tri-carboxylic acid (TCA) cycle to generate ATP, thus serving as an energy source to sustain the function of muscle and brain cells during fasting.<sup>51</sup> In other words, the primary energy source for the body shifts from glucose to free fatty acids derived from adipose tissue lipolysis and ketones, which means “flipping”



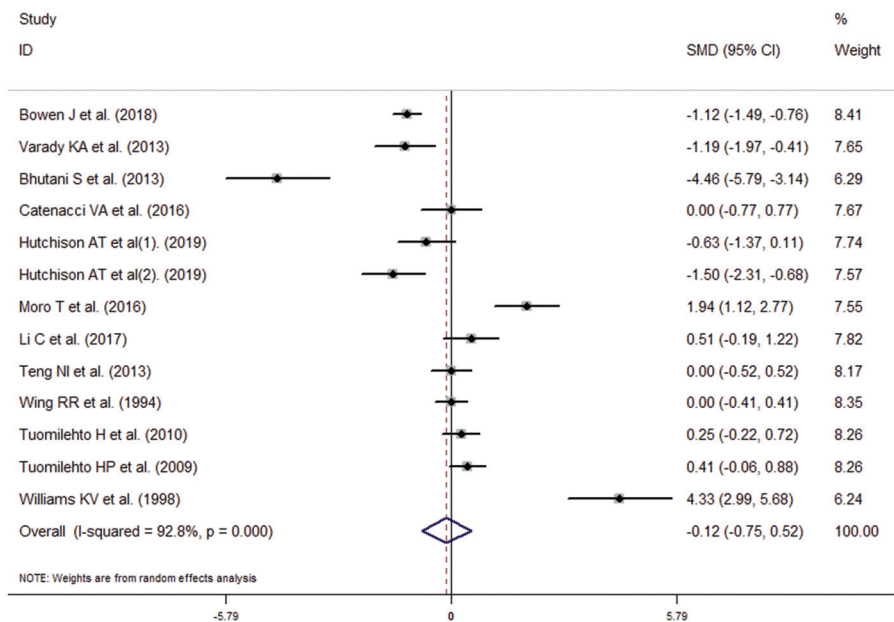


Fig. 13 Meta-analysis results of fasting intervention for the high density lipoprotein cholesterol (HDL-C) in subjects with overweight or obesity.

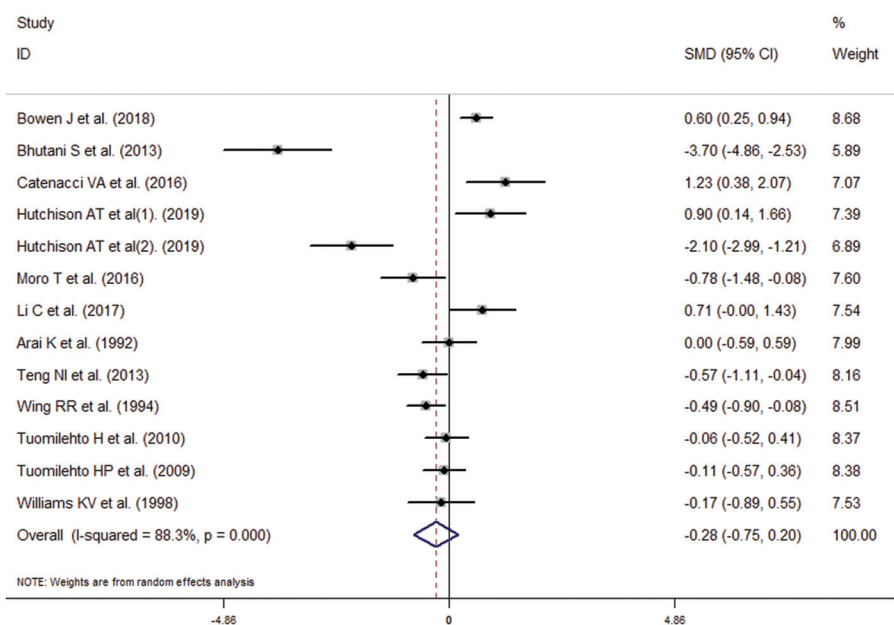


Fig. 14 Meta-analysis results of fasting intervention for the blood glucose in subjects with overweight or obesity.

of the metabolic switch.<sup>8</sup> For this reason, fasting may have a potential effect on the regulation of obesity and related metabolic parameters.

The existence of small LDL particles and higher post-prandial hyperlipemia are markers of myocardial infarction (MI) and ischemic heart disease (IHD) progression.<sup>52,53</sup> Our study found that the fasting intervention group had significant decreases more in LDL-C, and TG parameters than the control group. Recent clinic trials have demonstrated that alternate day fasting could reduce the ratio of small LDL particles,

thereby causing the reduction of LDL-C and TG parameters.<sup>25,54</sup> Meanwhile, weight loss may also be an important factor. Previous literature indicated that only subjects with more weight loss had a significant blood lipid decrease, as with blood pressure.<sup>8</sup> Similarly, in view of our outcomes of the subgroup meta-analysis, after fasting was stopped for a period of time, the amount of weight loss was smaller based on SMD values. Correspondingly, the variations in blood lipids and blood pressure between the fasting intervention subjects and controls change to no statistically significant differences.



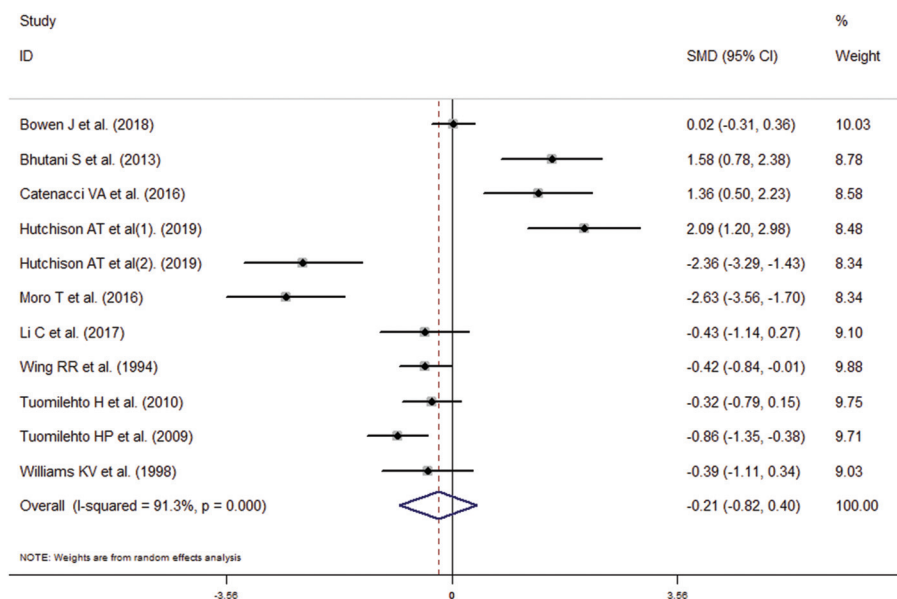


Fig. 15 Meta-analysis results of fasting intervention for the insulin in subjects with overweight or obesity.

Based on the outcomes of the subgroup meta-analysis, apart from HDL-C, blood glucose and insulin, the anthropometric and metabolic parameters had a larger reduction in the CADF group than the VLCD group in view of SMD values (especially at body weight, WC, TC and DBP parameters). Although the previous literature showed that the differences between intermittent and continuous energy restriction were not observed in boosting weight reduction and metabolic improvements, our study especially indicated that CADF is more effective in regulating anthropometric and metabolic parameters than VLCD for people with overweight or obesity.<sup>55</sup> The possible mechanisms include improving autophagy *via* sirtuin-1 activity stimulation, changing cell apoptosis, increasing the expression of vascular endothelial growth factor (VEGF), and reducing glycosylation end products.<sup>56–59</sup> Meanwhile, some studies indicated that subjects of IF usually did not take enough energy in the normal diet period to compensate for the fasting period, thus indicating that IF could decrease the total energy intake.<sup>8,60</sup> In addition, the incidence of adverse events of short-term intermittent fasting was lower than that of long-term fasting.<sup>8</sup> Similarly, the results of subgroup analysis indicated no differences in the influence of fasting time on regulating anthropometric and metabolic parameters. Therefore, short-term CADF may be a better choice for people with overweight or obesity. However, as previous studies have shown, due to differences in trial design, participant characteristics, and subject compliance, as well as limited sample size and studies, more clinic trials are needed to estimate the role of CADF in people with overweight or obesity.<sup>61</sup>

Although the differences between the fasting intervention and control subjects were not found in the variations in the insulin parameter, significant differences were noticed for the VLCD intervention in view of subgroup analysis. It is univer-

sally known that weight gain and obesity are critical risk factors in terms of insulin resistance.<sup>62</sup> Simultaneously, insulin-resistant patients with obesity need more insulin to regulate blood glucose, leading to weight gain progressively, thus a vicious circle formation.<sup>63</sup> Previous studies found that the VLCD could normalize insulin sensitivity and total insulin secretion *via* reducing the hepatic and pancreatic fat.<sup>64</sup> Meanwhile, as an anabolic hormone, insulin could induce cell growth and advance the storage of fatty acids in adipose and muscle tissue, irritating muscle hypertrophy and restraining proteolysis.<sup>65,66</sup> Therefore, the insulin secretion returns to normal and can reduce body weight and a virtuous circle is established. Correspondingly, fasting intervention can effectively improve patients with obesity and diabetes through the dual regulation of body weight and insulin levels in terms of the outcomes of subgroup analysis. Moreover, statistically significant differences in the variations in insulin parameter were noticed between the fasting intervention and control subjects after fasting was stopped for a period of time. This beneficial effect may result from a cellular stress response induced by the fasting state. However, the theory has been proved only in animal experiments, human trials are needed.<sup>67</sup>

This study has some limitations. The blind method is not applicable to all included studies due to the intervention contents and methods for participants and nutritionists could not be masked. Although the research staff of some studies evaluating the outcome were unaware of the apportion of the participants, true intervention effects could be biased by the restricted quality of the methodology.<sup>68</sup> Meanwhile, the heterogeneity of most results is high. The reasons may be the differences of subjects and region, as well as the outcome type and other factors. In addition, due to the lack of control or changes before and after the intervention in many studies, there are few studies of IF meeting the inclusion criteria.



Table 3 Subgroup analyses were performed for anthropometric and metabolic parameters

Factors	Number of studies												
	BW	BMI	FEM	FM	WC	TC	LDL-C	HDL-C	TG	SBP	DBP	BG	Insulin
<b>Fasting type</b>													
ADMF	3	2	3	3	—	3	3	3	3	3	3	2	2
CADF	2	—	1	2	1	2	2	2	2	1	1	2	2
TRF	—	—	—	2	—	—	—	—	—	—	—	—	—
VLCD	17	10	4	3	6	6	3	5	6	7	7	6	4
<b>Subjects</b>													
Adult(W + M)	18	10	4	6	7	10	7	9	10	9	9	9	8
Adult(W)	2	—	2	1	1	1	1	1	1	1	1	1	1
Adult(M)	4	3	3	3	—	2	2	2	2	—	—	2	—
<b>Outcome type</b>													
NF	16	9	—	—	5	9	7	7	8	7	7	7	5
F	8	4	—	—	3	4	3	5	5	4	4	5	5
<b>Fasting time</b>													
<12 weeks	9	4	2	4	2	5	4	4	4	3	3	5	4
≥12 weeks	15	9	7	6	6	8	6	8	9	8	8	7	6
<b>Region</b>													
Oceania	4	2	3	4	3	2	2	2	2	2	2	2	2
America	10	2	3	4	—	5	5	5	5	3	3	4	4
Europe	7	5	—	—	4	4	2	4	5	4	4	4	4
Asia	4	4	2	—	—	2	—	—	—	2	2	2	—
<b>Diabetes</b>													
No	20	11	—	—	6	9	7	9	9	8	8	9	7
Yes	4	2	—	—	2	4	3	3	4	3	3	3	3

Standard mean difference (95% CI), *P*

Factors	BW	BMI	FEM	FM
<b>Fasting type</b>				
ADMF	−2.67(−6.67,1.34), 0.192	−0.20(−1.69,1.29), 0.790	−1.78(−3.93,0.37), 0.105	−1.28(−3.67,1.11), 0.295
CADF	−6.53(−12.33,−0.73), 0.027	—	−1.61(−4.24,1.02), 0.229	−4.36(−9.13,0.42), 0.074
TRF	—	—	—	−1.14(−1.73,−0.55), <0.001
VLCD	−1.73(−2.31,−1.15), <0.001	−1.25(−1.73,−0.76), <0.001	−0.39(−1.21,0.44), 0.360	−2.20(−4.31,−0.08), 0.042
<b>Subjects</b>				
Adult(W + M)	−1.85(−2.53,−1.17), <0.001	−0.97(−1.54,−0.40), 0.001	−0.94(−2.04,0.17), 0.097	−1.58(−3.00,−0.15), 0.030
Adult(W)	−6.80(−11.97,−1.62), 0.010	—	−1.58(−2.97,−0.18), 0.027	−6.56(−10.16,−2.96), <0.001
Adult(M)	−1.56(−1.95,−1.16), <0.001	−1.92(−2.37,−1.46), <0.001	0.03(−0.64,0.70), 0.926	−1.36(−1.78,−0.94), <0.001
<b>Outcome type</b>				
NF	−2.58(−3.42,−1.75), <0.001	−1.34(−2.11,−0.56), 0.001	—	—
F	−1.40(−2.15,−0.65), <0.001	−0.90(−1.41,−0.39), 0.001	—	—
<b>Fasting time</b>				
<12 weeks	−1.94(−2.85,−1.04), <0.001	−1.48(−2.37,−0.59), 0.001	−0.99(−2.65,0.68), 0.245	−2.88(−4.90,−0.86), 0.005
≥12 weeks	−2.26(−3.06,−1.45), <0.001	−1.05(−1.68,−0.42), 0.001	−0.75(−1.52,0.02), 0.057	−1.80(−3.21,−0.39), 0.012
<b>Region</b>				
Oceania	−4.39(−6.64,−2.15), <0.001	0.18(−0.51,0.86), 0.614	−0.57(−1.46,0.31), 0.205	−3.12(−5.07,−1.16), 0.002
America	−2.13(−3.09,−1.17), <0.001	−1.78(−3.42,−0.15), 0.032	−2.52(−5.02,−0.03), 0.047	−1.39(−2.59,−0.20), 0.022
Europe	−1.26(−1.68,−0.84), <0.001	−1.02(−1.50,−0.54), <0.001	—	—
Asia	−1.44(−1.89,−0.99), <0.001	−1.89(−2.27,−1.51), <0.001	−0.09(−1.28,1.11), 0.880	—
<b>Diabetes</b>				
No	−2.19(−2.84,−1.53), <0.001	−1.23(−1.82,−0.63), <0.001	—	—
Yes	−2.03(−3.47,−0.60), 0.006	−0.94(−2.30,0.42), 0.174	—	—

Standard mean difference (95% CI), *P*

Factors	WC	TC	LDL-C	HDL-C
<b>Fasting type</b>				
ADMF	—	0.10(−2.47,2.68), 0.937	−1.30(−2.86,0.27), 0.104	−2.11(−3.59,−0.64), 0.005
CADF	−3.33(−5.49,−1.18), 0.002	−1.53(−2.79,−0.26), 0.018	−1.16(−2.49,0.18), 0.091	−0.70(−1.53,0.13), 0.098
TRF	—	—	—	—
VLCD	−1.82(−2.95,−0.69), 0.002	−0.63(−1.86,0.60), 0.313	−0.23(−1.95,1.49), 0.790	0.19(−0.02,0.41), 0.082
<b>Subjects</b>				
Adult(W + M)	−2.07(−3.17,−0.96), <0.001	−0.22(−1.01,0.56), 0.579	−0.50(−1.27,0.27), 0.200	−0.15(−0.94,0.64), 0.717
Adult(W)	−3.33(−5.49,−1.18), 0.002	−1.55(−3.74,0.63), 0.163	−1.16(−3.46,1.15), 0.325	−1.05(−1.89,−0.20), 0.015
Adult(M)	—	−1.67(−3.95,0.61), 0.152	−1.87(−2.37,−1.37), <0.001	0.94(−0.96,2.85), 0.331
<b>Outcome type</b>				



Table 3 (Contd.)

Factors	Standard mean difference (95% CI), <i>P</i>			
	WC	TC	LDL-C	HDL-C
NF	-2.90(-4.56,-1.24), 0.001	-1.06(-2.09,-0.04), 0.042	-1.38(-2.15,-0.61), <0.001	-0.80(-1.66,0.07), 0.071
F	-1.04(-1.56,-0.52), <0.001	0.47(-0.07,1.00), 0.087	0.50(-0.06,1.06), 0.081	0.85(0.07,1.62), 0.032
<b>Fasting time</b>				
<12 weeks	-2.59(-4.26,-0.91), 0.002	-1.15(-2.15,-0.16), 0.023	-1.00(-1.99,-0.02), 0.046	0.06(-1.01,1.14), 0.907
≥12 weeks	-2.20(-3.44,-0.95), 0.001	-0.22(-1.18,0.74), 0.654	-0.77(-1.76,0.22), 0.129	-0.23(-1.06,0.60), 0.590
<b>Region</b>				
Oceania	-2.85(-4.97,-0.73), 0.008	-0.84(-2.49,0.82), 0.321	-0.72(-1.96,0.51), 0.251	-1.09(-1.45,-0.72), <0.001
America	—	-0.15(-1.79,1.49), 0.858	-0.79(-2.09,0.50), 0.228	-0.27(-1.97,1.43), 0.756
Europe	-1.25(-1.83,-0.67), <0.001	-0.03(-0.55,0.49), 0.914	-0.79(-2.82,1.23), 0.443	0.71(0.10,1.32), 0.024
Asia	—	-2.65(-3.19,-2.11), <0.001	—	—
<b>Diabetes</b>				
No	-2.48(-3.71,-1.26), <0.001	-0.98(-1.96,0.01), 0.052	-1.38(-2.15,-0.61), <0.001	-0.55(-1.24,0.15), 0.125
Yes	-1.63(-2.51,-0.75), <0.001	0.26(-0.51,1.03), 0.506	0.50(-0.06,1.06), 0.081	1.48(-0.32,3.29), 0.108

Factors	Standard mean difference (95% CI), <i>P</i>			
	TG	SBP	DBP	BG
<b>Fasting type</b>				
ADMF	-0.89(-2.68,0.90), 0.331	-1.48(-3.58,0.62), 0.166	-0.62(-1.49,0.26), 0.168	-1.51(-5.72,2.69), 0.481
CADF	-0.67(-1.83,0.49), 0.255	-1.55(-3.16,0.07), 0.060	-1.11(-2.10,-0.13), 0.026	0.02(-1.97,2.01), 0.986
TRF	—	—	—	—
VLCD	-0.33(-0.69,0.04), 0.079	-0.83(-1.55,-0.10), 0.027	-0.63(-1.26,0.01), 0.054	-0.14(-0.45,0.17), 0.384
<b>Subjects</b>				
Adult(W + M)	-0.66(-1.21,-0.12), 0.017	-0.82(-1.46,-0.19), 0.011	-0.44(-0.84,-0.04), 0.033	-0.13(-0.66,0.41), 0.644
Adult(W)	-0.07(-0.58,0.44), 0.791	-1.55(-3.16,0.07), 0.060	-1.11(-2.10,-0.13), 0.026	-0.59(-3.53,2.35), 0.694
Adult(M)	-0.93(-2.05,0.20), 0.107	—	—	-0.65(-1.07,-0.22), 0.003
<b>Outcome type</b>				
NF	-0.86(-1.57,-0.14), 0.019	-1.49(-2.47,-0.51), 0.003	-0.81(-1.42,-0.21), 0.008	-0.49(-1.32,0.35), 0.252
F	-0.24(-0.58,0.11), 0.178	-0.35(-0.98,0.28), 0.280	-0.49(-1.20,0.22), 0.174	-0.08(-0.43,0.26), 0.641
<b>Fasting time</b>				
<12 weeks	-0.76(-1.51,-0.00), 0.049	-1.50(-2.28,-0.72), 0.001	-0.88(-1.38,-0.38), 0.001	0.00(-0.88,0.89), 0.995
≥12 weeks	-0.53(-1.05,-0.01), 0.046	-0.87(-1.61,-0.13), 0.021	-0.61(-1.18,-0.03), 0.039	-0.49(-1.10,0.11), 0.108
<b>Region</b>				
Oceania	0.22(-0.27,0.71), 0.384	-0.89(-2.40,0.61), 0.245	-0.77(-1.56,0.02), 0.056	-0.16(-1.68,1.35), 0.832
America	-1.14(-2.28,-0.00), 0.049	-1.85(-3.08,-0.61), 0.003	-0.97(-1.88,-0.06), 0.037	-0.72(-2.13,0.69), 0.317
Europe	-0.69(-1.22,-0.17), 0.010	-0.10(-0.58,0.39), 0.692	-0.11(-0.62,0.40), 0.664	-0.06(-0.55,0.42), 0.793
Asia	—	-2.23(-2.74,-1.73), <0.001	-1.34(-3.13,0.45), 0.141	-0.30(-0.86,0.26), 0.294
<b>Diabetes</b>				
No	-0.65(-1.21,-0.10), 0.021	-1.26(-2.09,-0.43), 0.003	-0.71(-1.24,-0.19), 0.007	-0.38(-0.99,0.23), 0.221
Yes	-0.53(-1.25,0.20), 0.156	-0.64(-1.18,-0.11), 0.018	-0.66(-1.52,0.20), 0.134	-0.02(-0.73,0.68), 0.947

Factors	Standard mean difference (95% CI), <i>P</i>		Heterogeneity <i>I</i> <sup>2</sup> (%), <i>P</i>			
	Insulin	BW	BMI	FEM	FM	WC
<b>Fasting type</b>						
ADMF	0.76(-0.76,2.28), 0.329	98.0, <0.001	92.6, <0.001	96.0, <0.001	97.0, <0.001	—
CADF	0.37(-2.27,3.01), 0.784	97.0, <0.001	—	94.2, <0.001	97.3, <0.001	85.9, 0.008
TRF	—	—	—	—	0.0,0.667	—
VLCD	-0.51(-0.75,-0.26), <0.001	93.5, <0.001	83.6, <0.001	88.3, <0.001	98.1, <0.001	96.2, <0.001
<b>Subjects</b>						
Adult(W + M)	0.00(-0.47,0.47), 0.997	95.6, <0.001	90.3, <0.001	94.1, <0.001	97.6, <0.001	96.1, <0.001
Adult(W)	-0.13(-4.49,4.23), 0.953	96.4, <0.001	—	88.8, <0.001	86.6, 0.006	85.9, <0.001
Adult(M)	—	0.0, 0.509	0.0, 0.595	67.2, 0.047	0.0, 0.522	—
<b>Outcome type</b>						
NF	0.02(-1.31,1.35), 0.974	96.1, <0.001	92.9, <0.001	—	—	96.9, <0.001
F	-0.50(-0.73,-0.26), <0.001	90.8, <0.001	68.2, 0.024	—	—	60.0, 0.082
<b>Fasting time</b>						
<12 weeks	-0.39(-2.15,1.37), 0.665	91.4, <0.001	81.9, 0.001	92.4, <0.001	94.7, <0.001	88.7, <0.001
≥12 weeks	-0.12(-0.61,0.37), 0.628	96.3, <0.001	91.5, <0.001	92.2, <0.001	97.7, <0.001	96.6, <0.001
<b>Region</b>						
Oceania	-0.07(-2.02,1.88), 0.941	98.5, <0.001	86.9, 0.006	91.6, <0.001	98.4, <0.001	97.7, <0.001
America	0.50(-0.56,1.55), 0.355	91.2, <0.001	84.0, 0.012	95.5, <0.001	85.9, <0.001	—
Europe	-0.99(-1.77,-0.20), 0.014	70.4, 0.002	66.8, 0.017	—	—	69.9, 0.019
Asia	—	35.5, 0.199	0.0, 0.778	83.5, 0.014	—	—
<b>Diabetes</b>						



Table 3 (Contd.)

Factors	Standard mean difference (95% CI), <i>P</i>		Heterogeneity <i>I</i> <sup>2</sup> (%), <i>P</i>			
	Insulin	BW	BMI	FEM	FM	WC
No	-0.13(-1.01,0.74), 0.764	95.3, <0.001	91.6, <0.001	—	—	96.6, <0.001
Yes	-0.42(-0.74,-0.10), 0.010	92.5, <0.001	83.3, 0.014	—	—	53.7, 0.142

Factors	Heterogeneity <i>I</i> <sup>2</sup> (%), <i>P</i>							
	TC	LDL-C	HDL-C	TG	SBP	DBP	BG	Insulin
<b>Fasting type</b>								
ADMF	96.8, <0.001	93.6, <0.001	91.2, <0.001	95.3, <0.001	96.1, <0.001	83.6, 0.002	97.9, <0.001	91.9, 0.001
CADF	84.4, 0.002	87.2, <0.001	70.9, 0.032	84.2, 0.002	86.2, 0.007	68.0, 0.077	94.2, <0.001	96.2, <0.001
TRF	—	—	—	—	—	—	—	—
VLCD	95.9, <0.001	96.2, <0.001	0.0, 0.550	63.7, 0.017	91.1, <0.001	88.8, <0.001	54.2, 0.053	0.0, 0.411
<b>Subjects</b>								
Adult(W + M)	93.8, <0.001	91.1, <0.001	93.8, <0.001	88.5, <0.001	91.3, <0.001	79.5, <0.001	88.2, <0.001	83.5, <0.001
Adult(W)	92.1, <0.001	93.5, <0.001	57.8, 0.124	0.0, 0.445	86.2, 0.007	68.0, 0.077	96.0, <0.001	97.8, <0.001
Adult(M)	95.1, <0.001	0.0, 0.911	93.4, <0.001	82.9, 0.016	—	—	0.0, 0.645	—
<b>Outcome type</b>								
NF	95.0, <0.001	90.0, <0.001	92.3, <0.001	90.3, <0.001	93.7, <0.001	85.9, <0.001	92.6, <0.001	95.0, <0.001
F	72.3, 0.013	60.9, 0.078	89.2, <0.001	51.9, 0.081	83.9, <0.001	87.2, <0.001	52.1, 0.079	0.0, 0.563
<b>Fasting time</b>								
<12 weeks	89.6, <0.001	87.1, <0.001	89.8, <0.001	79.3, 0.001	74.8, 0.008	48.1, 0.123	88.4, <0.001	95.3, <0.001
≥12 weeks	95.3, <0.001	94.4, <0.001	94.4, <0.001	87.6, <0.001	93.2, <0.001	89.2, <0.001	89.8, <0.001	83.1, <0.001
<b>Region</b>								
Oceania	94.7, <0.001	91.0, <0.001	18.8, 0.292	53.1, 0.119	93.7, <0.001	79.0, 0.009	93.9, <0.001	95.6, <0.001
America	95.7, <0.001	93.9, <0.001	95.6, <0.001	91.9, <0.001	87.4, <0.001	83.1, 0.003	93.4, <0.001	89.8, <0.001
Europe	61.3, 0.051	93.1, <0.001	76.8, 0.005	72.2, 0.006	64.0, 0.040	67.2, 0.027	65.0, 0.036	84.9, <0.001
Asia	0.0, 0.474	—	—	—	0.0, 0.485	93.7, <0.001	49.7, 0.159	—
<b>Diabetes</b>								
No	95.3, <0.001	90.0, <0.001	92.2, <0.001	88.2, <0.001	94.0, <0.001	86.5, <0.001	90.4, <0.001	93.8, <0.001
Yes	82.8, 0.001	60.9, 0.078	94.6, <0.001	79.9, 0.002	54.9, 0.109	82.0, 0.004	75.4, 0.017	0.0, 0.995

ADMF, alternate day modified fasting; CADF, complete alternate-day fasting; TRF, time-restricted feeding; VLCD, very low calorie diet; Adult(W + M), Adult(women + men); Adult(W), Adult(women); Adult(M), Adult(men); NF, non follow-up; F, follow-up; BW, body weight; BMI, body mass index; FEM, fat free mass; FM, fat mass; WC, waist circumference; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; BG, blood glucose.

Table 4 Publication bias (Egger test) and sensitivity analysis (trim and fill method) performed for included studies

	Egger test ( <i>t</i> , <i>P</i> )	Number of trim and fill	SMD(95%CI), <i>P</i> <sup>a</sup>	SMD(95%CI), <i>P</i> <sup>b</sup>
Body weight (kg)	-5.72, <0.001	3	-2.16(-2.76,-1.56), <0.001	-2.58(-3.39,-1.77), <0.001
BMI (kg m <sup>-2</sup> )	-5.03, <0.001	0	-1.18(-1.72,-0.65), <0.001	-1.18(-1.72,-0.65), <0.001
FEM (kg)	-3.96, 0.004	1	-0.82(-1.49,-0.15), 0.016	-1.04(-1.79,-0.28), 0.007
FM (kg)	-4.60, 0.001	0	-2.20(-3.29,-1.11), <0.001	-2.20(-3.29,-1.11), <0.001
WC (cm)	-4.55, 0.002	0	-2.31(-3.32,-1.30), <0.001	-2.31(-3.32,-1.30), <0.001
TC (mmol L <sup>-1</sup> )	-2.42, 0.032	0	-0.62(-1.36,0.12), 0.099	-0.62(-1.36,0.12), 0.099
LDL-C (mmol L <sup>-1</sup> )	-2.88, 0.018	0	-0.87(-1.57,-0.17), 0.014	-0.87(-1.57,-0.17), 0.014
HDL-C (mmol L <sup>-1</sup> )	0.37, 0.717	—	-0.12(-0.75,0.52), 0.720	—
TG (mmol L <sup>-1</sup> )	-5.29, <0.001	—	-0.61(-1.04,-0.18), 0.005	-0.61(-1.04,-0.18), 0.005
SBP (mmHg)	-3.93, 0.003	0	-1.08(-1.69,-0.47), 0.001	-1.08(-1.69,-0.47), 0.001
DBP (mmHg)	-1.44, 0.181	—	-0.70(-1.13,-0.26), 0.002	—
Blood glucose (mmol L <sup>-1</sup> )	-1.47, 0.169	—	-0.28(-0.75,0.20), 0.253	—
Insulin (mIU L <sup>-1</sup> )	0.08, 0.941	—	-0.21(-0.82,0.40), 0.496	—

BMI: body mass index; FEM: fat free mass; FM: fat mass; WC: waist circumference; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; TG: triglycerides; SBP: systolic blood pressure; DBP: diastolic blood pressure. <sup>a</sup> Original variation. <sup>b</sup> Variation after trim and fill.

## 5. Conclusion

Our study found that fasting intervention had a significant effect on the regulation of anthropometric and metabolic parameters by significantly reducing the body weight, BMI, FEM,

FM, WC, LDL-C, TG, SBP and DBP in people with overweight or obesity. Considering some limitations found in this study, more data from large clinical trials are needed to affirm the efficacy of fasting for the regulation of anthropometric and metabolic parameters in people with overweight or obesity.



## Author contributions

BL, WC, and SY made the study design; SY, CW, and HZ conducted the study; SY, CW, and YP analyzed the data and wrote the manuscript; SY, HW, YG and NY attended the manuscript revision. All authors agreed with the final manuscript.

## Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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