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Does adaptive thermogenesis occur after weight loss in adults? A systematic review

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Abstract

Adaptive thermogenesis (AT) has been proposed to be a compensatory response that may resist weight loss (WL) and promote weight regain. This systematic review examined the existence of AT in adults after a period of negative energy balance (EB) with or without a weight stabilisation phase. Studies published until 15 May 2020 were identified from PubMed, Cochrane Library, EMBASE, MEDLINE, SCOPUS and Web of Science. Inclusion criteria included statistically significant WL, observational with follow-up or experimental studies, age > 18y, sample size ≥10 participants, intervention period ≥ 1week, published in English, objective measures of total daily energy expenditure (EE) (TDEE), resting EE (REE) and sleeping EE(SEE). The systematic review was registered at PROSPERO (2020 CRD42020165348). A total of thirty-three studies comprising 2528 participants were included. AT was observed in twenty-seven studies. Twenty-three studies showed significant values for AT for REE (82·8 %), four for TDEE (80·0 %) and two for SEE (100 %). A large heterogeneity in the methods used to quantify AT and between subjects and among studies regarding the magnitude of WL and/or of AT was reported. Well-designed studies reported lower or non-significant values for AT. These findings suggest that although WL may lead to AT in some of the EE components, these values may be small or non-statistically significant when higher-quality methodological designs are used. Furthermore, AT seems to be attenuated, or non-existent, after periods of weight stabilisation/neutral EB. More high-quality studies are warranted not only to disclose the existence of AT but also to understand its clinical implications on weight management outcomes.

Key words: **Energy balance: Metabolic adaptation: Metabolic compensations: Behavioural compensations: Weight loss**

Weight loss (WL) occurs when a negative energy balance is sustained over time[1]. However, despite its apparent simplicity, energy balance represents a complex and dynamic system in which its components (i.e. energy intake (EI) and energy expenditure (EE)) fluctuate over time[2] and change in response to perturbations in either side of the equation[3,4].

Although a clinically meaningful WL is usually achieved, levels of recidivism and weight regain are high[5,6]. It has been postulated that difficulties in maintaining a reduced body weight arise not only from a lack of adherence to dietary and physical activity (PA) recommendations[7] but also due to metabolic, psychological and behavioural compensatory responses that occur during periods of negative energy balance. Some of these proposed compensatory responses include reductions in EE[8], PA behaviours[9] and increases in EI[10]. These compensatory responses may act to undermine adherence to the diet and/or PA recommendations, prompting an individual to regain the weight lost.

Adaptive thermogenesis (AT) represents a greater than predicted decrease in EE beyond what would be predicted from the changes in fat mass (FM) and fat-free mass (FFM) occurring during WL[10,11]. It has been postulated to be a compensatory response that resists WL and promotes weight regain[12–15], but its influence on longer-term weight management has been recently questioned[16]. AT in resting EE (REE) has been previously documented in lifestyle[16–33] and surgical[34–39]

Abbreviations: AT, adaptive thermogenesis; EE, energy expenditure; EI, energy intake; FFM, fat-free mass; FM, fat mass; mREE, measured resting energy expenditure; PA, physical activity; pREE, predictive equation to estimate resting energy expenditure; REE, resting energy expenditure; SEE, sleeping energy expenditure; TDEE, total daily energy expenditure; WL, weight loss.

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interventions. However, some studies have reported contrasting findings as they have not observed a significant value for AT[28,32,40].

Several narrative reviews examining the topic of AT in REE have been previously published[3,10,11,14,15,41–44]. However, no systematic reviews have been conducted specifically on this topic, and some of these narrative reviews have also focused exclusively on the occurrence of AT in REE during lifestyle interventions.

Therefore, this is the first systematic review examining the occurrence of AT in REE, total daily EE (TDEE) and sleeping EE (SEE) during or after WL induced by diet and/or exercise, bariatric surgery or pharmacological therapy, followed by weight stabilisation in adults.

Methodology

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[45] and was registered on PROSPERO (PROSPERO 2020 CRD42020165348).

Eligibility criteria

This systematic review included scientific articles published in peer-reviewed journals on or before 15 May 2020 that reported WL induced by diet and/or exercise, bariatric surgery or pharmacological therapy, and reported values for AT. All studies were evaluated according to the following inclusion criteria: (1) the study should include an intervention aimed to reduce weight that resulted in a statistically significant WL, (2) observational with follow-up or experimental study, (3) conducted in adults(>18 years), (4) a total sample size of at least ten participants, (5) intervention period of at least 1 week, (6) published in English, (7) objective measures of TDEE, REE and SEE (indirect calorimetry, metabolic chamber, doubly labelled water) and (8) objective measures of FM and FFM (dual-energy X-ray absorptiometry, air displacement plethysmography, bioelectrical impedance analysis and/or multicompartment molecular models) (e.g. four-compartment models, including combination of several techniques such as dual-energy X-ray absorptiometry, isotope dilution and air displacement plethysmography). Articles were excluded if they did not meet all of the inclusion criteria and/or had an exclusion criterion, such as the inclusion of participants with the following: (1) cancer, (2) thyroid diseases, (3) diabetes; (4) pregnancy or breast-feeding, (5) total parenteral nutrition, (6) organ transplant, (7) acute illnesses, such as infections or traumatic injury and (8) other medical conditions and/or the use of medications known to affect energy balance.

Information sources and search strategy

A comprehensive search of peer-reviewed articles published until 15 May 2020 (including online ahead of print publications) was conducted in the following electronic databases: PubMed, Cochrane Library, EMBASE, MEDLINE, SCOPUS and Web of Science. Searches included all meaningful combinations of the following sets of terms: (i) terms concerning the intervention(s) of interest (e.g. diet or energy restriction, bariatric surgery, PA or exercise, pharmacotherapy), (ii) terms representing the outcomes of interest (e.g. AT, metabolic adaptation, energy metabolism, REE, metabolic compensation), (iii) terms representing the population of interest (e.g. adults) and (iv) terms representing body composition components of interest (e.g. FM, fat-free mass, lean mass). Manual cross-referencing of the literature cited in prior reviews and hand-searches of the content were conducted to strengthen the systematic review. A search strategy example for PubMed is provided as an online Supplementary File 1.

Study selection and data processing

Based on the initial abstracts retrieved, duplicates were removed, and twenty-five were added from manual searching. Abstracts identified from the literature searches were screened for potential inclusion by two authors (C.L.N. and N.C.) and a third author (R.F.) when there was a disagreement between the first two. One-hundred and two articles were assessed for eligibility and thirty-three were included in this review. Data extraction was conducted by C.L.N. according to the PRISMA statement for reporting systematic reviews[45] and included information about each article such as authors, year, study design, participants' information (e.g. demographics and BMI), type of intervention (diet only, exercise only, diet + exercise, bariatric surgery or pharmacological), length of active intervention and/or the duration of follow-up, methodology, outcome measures and main results.

Study quality and risk of bias

To assess the study quality, the Quality Assessment Tool for Quantitative Studies checklist was used[46]. This procedure was performed by two authors (C.L.N. and R.F.). The checklist evaluates six key methodological domains: study design, blinding, representativeness (selection bias), representativeness (withdrawals/dropouts), confounders and data collection. From the interpretation of the scores of each section (classified as strong, moderate or weak methodological quality), an overall score was given to each article. The quality assessment for each study is presented as online Supplementary File 2).

Results

A total of 1332 articles were retrieved by the aforementioned databases. From those, 612 duplicates were removed, and 25 articles identified through other sources were added, leading to a total of 745 articles for title and abstract screening. Six hundred and forty-three articles were excluded during title and abstract screening and 102 full texts were further assessed for eligibility. In this phase, sixty-nine were excluded (online Supplementary File 3) and thirty-three were included in this systematic review. The PRISMA flow chart of the study selection is presented in Fig. 1.

The studies included in this review comprised 2528 participants and were divided by each component of EE as follows:

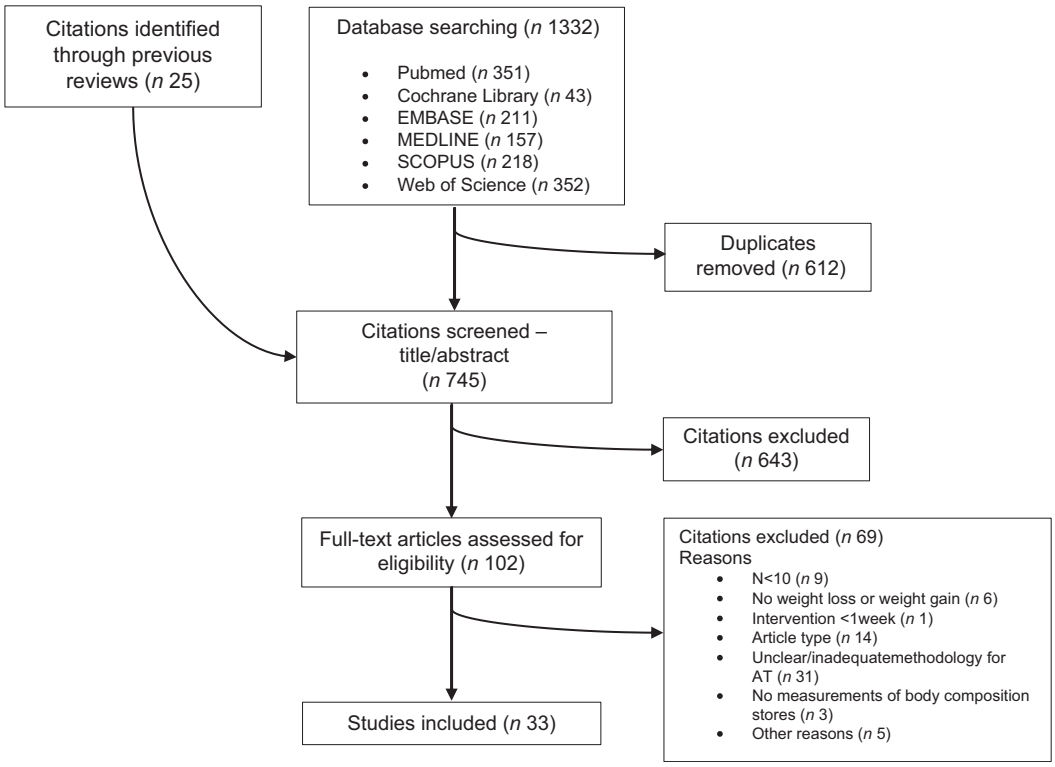

Fig. 1. Flow diagram of studies' selection.

- REE – twenty-nine studies;
- TDEE – seven studies;
- SEE – two studies.

Some articles included more than one intervention type and/or assessed AT in more than one EE component.

From the included studies, six (20·7 %) were randomised controlled trials, two (6·9 %) were randomised trials without a control group (RT), twelve (41·4 %) were non-randomised trials, three (10·3 %) were retrospective observational studies and ten (34·5 %) were considered prospective observational studies. A summary of the results reported in each study, divided by study type and %WL, is presented in Table 1.

Resting energy expenditure

A total of twenty-nine studies reporting changes in REE were included in this review[12,13,16–40,47,48] (Table 2), divided into: randomised controlled trial = four (13·8 %), non-randomised trials = twelve (41·4 %), RT = two (6·9 %), prospective observational = eight (27·6 %), retrospective observational = three (10·3 %).

Diet-only interventions. Eighteen studies using a diet-only intervention were included[16–33]. From those, one used a pharmacological therapy together with caloric restriction[32].

Participants' characteristics. These studies involved 1780 participants (559 males). Only three studies had a mean BMI < 30 kg/m^2[16,22,33], while the majority of the studies included participants with obesity[17–21,23–27,29–32]. The amount of weight lost varied between studies, with ten studies reporting a WL > 10 %[16–21,25–27,33] and seven reporting moderate WL (< 10 %)[22–24,29–32].

Diet type. Six studies used a very low-calorie diet(< 3·3 MJ/d) in order to lose weight[18,19,21,26,27,32] and five used a low calorie diet (3·3–5·0 MJ/d)[17,25,28,30,31]. Other studies calculated the prescribed EI as a percentage of participant's energy needs (calculated as measured REE × PAL): ~67 %[10,24] and 50 %[22]. McNeil *et al.* multiplied each participant's REE by 1·4 and then subtracted 3·3MJ from that result[23].

The macronutrient distribution was different among studies. Three reported a high protein intake (> 25 % or > 1·2 g/kg)[17,18,33]. A ketogenic diet was used by Gomez-Arbealez *et al.*[19]. Karl and colleagues used four types of diets differing in carbohydrate (CHO) content: 55 %, 60 %, 70 % or 80 % CHO[24]. Jonge *et al.* also divided the sample into four types of caloric restriction diets differing in fat and/or protein content: (i) 20 % fat/15 % protein (PRO), (ii) 20 % fat/25 % PRO, (iii) 40 % fat/15 % PRO and (iv) 40 % fat/25 % PRO[29]. Dulloo *et al.* prescribed a 6·1 MJ/d diet, consisting of 25 % PRO, 17 % fat and 58 % CHO[33]. Some studies did not report any information about the diet[16] or the macronutrient composition of the diet[16,20,26–28,30,31].

Methodology to assess adaptive thermogenesis. Thirteen studies used a predictive equation to estimate REE (pREE) and then calculated AT by comparing the pREE with a measured REE (mREE) using a statistical approach such as *t* test or ANOVA[16–21,23–25,27,29,32,33]. Byrne *et al.* also used an additional

Table 1. Summary of the results

			REE		TDEE		SEE
	%WL		WL	WM	WL	WM	WL
RCT	< 10 %	Marzullo *et al.*[48]	⊙				
		de Jonge *et al.*[29]	⊙				
		Karl *et al.*[24]	⊙	×			
	10–15 %	Doucet *et al.*[32]	⊙	⊙ Men × Women			
		Byrne *et al.*[20]	⊙	×			
		Redman *et al.*[52]			⊙ CR and LCD × Exercise	× CR	
		Lecoultre *et al.*[51]			⊙ CR and LCD × Diet and Exercise		⊙ CR
NRT	< 5 %	Hopkins *et al.*[40]	×				
		Bosy Westphal *et al.*[31]	⊙				
	5 a 10 %	Müller *et al.*[22]	⊙				
		Camps *et al.*[27]	⊙				
		Goele *et al.*[30]	⊙				
		Camps *et al.*[25]	⊙				
	10–20 %	Bosy-Westphal *et al.*[28]		⊙ Weight regainers			
		Thom *et al.*[17]	⊙				
		Nymo *et al.*[18]	⊙				
	> 20 %	Gomez-Arbelaez *et al.*[19]	×				
		Rosenbaum *et al.*[21]	⊙				
		Dulloo *et al.*[33]	⊙				
RT	< 10 %	McNeil *et al.*[23]	⊙				
Observational	< 10 %	Ten Haaf *et al.*[47]	⊙				
	10–20 %	Pourhassan *et al.*[26]	×				
		Marlatt *et al.*[50]			×		⊙
		Martins *et al.*[16]	⊙				
		Coupaye *et al.*[39]	×				
	20–30 %	Wolfe *et al.*[34]	⊙	×	⊙	×	
		Tam *et al.*[37]	⊙	×			
		Browning *et al.*[36]	×				
		Ravelli *et al.*[53]			⊙	×	
	> 30 %	Bettini *et al.*[35]	⊙				
		Carrasco *et al.*[38]	⊙				
		Johannsen *et al.*[13]	⊙				
		Fothergill *et al.*[12]	⊙	⊙			

WL, weight loss; WM, weight maintenance; CR, caloric restriction; LCD, low-calorie diet; ⊙ reported a higher-than-expected decrease for REE/TDEE/SEE (AT), × did not report AT.

two approaches: (i) an equation developed by Muller *et al.*[49] to predict REE and (ii) adjusted REE to FM and/or FFM followed by a comparison between baseline and post-intervention adjusted baseline values[20]. Bosy-Westphal *et al.* used the sum of seven tissue-level components obtained by MRI multiplied by their tissue-specific metabolic rates to predict REE and then subtracted the baseline REE with the post-intervention REE[22,26,28,31].

Adaptive thermogenesis. A significant value for AT was observed in fifteen studies[16–18,20–25,27–31,33]. Only three studies did not report a significant AT after WL[19,26,32]. Byrne *et al.*[20], which compared a continuous energy restriction *v.* an intermittent energy restriction, only reported AT for the continuous energy restriction group (~209 kJ/d), which lost ~8·4 % of their initial weight. For the intermittent energy restriction group, AT was not significant despite a greater WL (~−12·9 %). Jonge *et al.* compared four types of caloric restriction diets varying in fat and/or protein (PRO) content[29]. AT was only presented for the 20 % fat/15 %PRO and 20 %fat/25 %PRO groups, while the other two groups (40 % fat/15 %PRO and 40 % fat/25 % PRO) did not report AT despite significant WL. Despite the evidence for AT when measured immediately after the WL intervention, some intervention studies reported that this

Table 2. Resting energy expenditure

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
Diet-only intervention								
Martins *et al.*[16]	O (retrospective)	*n* 171 females BMI = 28·3 (SD 1·3) kg/m^2 Age = 35·2(SD 6·3) years Three groups: diet only diet + aerobic training diet + resistance training	Diet: ~3·3 MJ/d, 20–22 % fat, 20–22 % protein, 56–58 % CHO	2 years follow-up	Body composition: 4C model (BODPOD, DXA (DPX-L Lunar) and isotope dilution) REE: indirect calorimetry (Delta Trac II)	AT was tested with *t* tests by comparing mREE with pREE. pREE was achieved by a predictive equation (predictors: age, sex, race, FM and FFM) AT was measured after a 4-week period of weight stabilisation	WL = –12·2(SD 2·6) kg (–15·7 % (SD 2·9) %) No metabolic adaptation was seen at 1- and 2-year follow-up in all participants	AT = –226(SD 439) kJ/d AT is minimal when measurements are taken under conditions of weight stability
Thom *et al.*[17]	NRT	*n* 15 females BMI = 39·4 (SD 4·3) kg/m^2 Age = 46·3(SD 9·5) years	Diet only: 3·5–3·7 MJ/d, 59 % CHO, 13 % fat, 26 % protein, 2 % fibre	6 months + 18 months follow-up	Body composition: MRI; REE: computerised open-circuit ventilated hood system (Oxycon Pro). Leptin, PYY, ghrelin, GLP-1 – ELISA kits	Sample-specific linear regression equation to predict REE (predictors: total adipose tissue – TAT (kg), skeletal muscle mass residuals (SMM) (kg) and age) AT is considered the difference between measured and predicted REE + *t* test AT was measured immediately after WL	WL = –13·8(SD 6·3) kg (~13·5 %); Significant reductions in TAT (–11·5(SD 4·9) kg) with preservation of SMM Reductions in Leptin and GLP-1 Increases in Ghrelin	AT = –628(SD 678) kJ/d Large inter-individual variability in adaptive thermogenesis
Nymo *et al.*[18]	NRT	*n* 31 (18 males) BMI = 36·7(SD 4·5) kg/m^2 Age = 43(SD 10) years	Diet only: VLCD 2·3–2·8 MJ/d, 42 % CHO, 36% PRO, 18% fat and 4% fibre	8 weeks + 4 weeks follow-up	Body composition: BodPod; REE: indirect calorimetry (Vmax Encore 29N); PA – Armbands (BodyMedia); exercise-induced	REE was predicted by an equation using FM, FFM, sex, age and height AT was present when mEE (REE or EIEE) was lower than pEE, given the body composition (FM and FFM) measured at each time point AT was measured immediately after WL and after a 4-week period of weight stabilisation	WL: (week 9) –18·7(SD 4·1) kg FM and FFM were reduced by 5 and 9 % WL in all participants, respectively.	Evidence of AT-REE only after 10 %WL AT = –465 (SEM 691) kJ/d
Gomez-Arbelaez *et al.*[19]	NRT	*n* 20 (8 males) BMI = 35·5(SD 4·4) kg/m^2 Age = 47·2(SD 10·2) years	Diet only: ketogenic diet; VLCD (2·5–3·3 MJ/d), < 50 g/d HC and only 10 g olive oil per day. Protein 0·8–1·2 g/kg per d	4 months	Body composition: DXA (GE healthcare lunar) and MF-BIA (InBody 720) REE: indirect calorimetry (FitMate PRO)	pREE predicted through an equation using baseline values of FM and FFM AT = mREE-pREE AT was measured immediately after WL	WL: –20·7 (SD 6·9); (~–21 %) Significant reductions for FM and FFM Severe reductions for leptin	Non-significant AT
Byrne *et al.*[20]	RCT	*n* 36 males Age: 25–54 years Two groups: –continuous energy restriction (CER) *n* 19 BMI = 34·3 (SD 3·0) kg/m^2 Age = 41·2 (SD 5·5) years – intermittent energy restriction (IER) *n* 17 BMI 34·1(SD 4·0) kg/m^2 Age = 39·5(SD 8·4) years	Diet only: ~67 % of individual weight maintenance energy requirements IER: 2 weeks of ER + 2 weeks EB CER: continuous ER	CER: 28 weeks IER: 42 weeks + 8 weeks weight maintenance	Body composition: air displacement plethysmography (BodPod). REE – ventilated hood system (TrueOne 2400 Metabolic System)	pREE calculated using 3 approaches: adjustment for changes in FM and FFM; group-specific equations using baseline data in function of age, FM and FFM; equation published by Muller et al.[49]. AT was achieved by comparing mREE and pREE AT was measured after WL	CER: WL: –9·2 (SD 3·7) kg (~–8·4 %); IER: WL: –14·1 (SD 5·6) kg (~–12·9 %) Significant reductions for FM in both groups	Significant AT only for CER group (~–209 kJ/d) No information about AT after weight maintenance phase
Rosenbaum *et al.* [21]	NRT	*n* 17 (3 males) BMI = 44·6(SD 11·2) kg/m^2 Age = 28·4 (SD 8·8) years	Diet only 3·3 MJ/d liquid formula diet, 40 % fat, 45 % CHO, 15 % protein + mineral supplementation	7–13 weeks to achieve 10 % WL + 8–14 weeks to achieve 20 %	Body composition: DXA; TEE – doubly labelled water REE – indirect calorimetry (Beckman MMC Horizon Metabolic Cart)	Regression equation to predict REE using weight, FFM and FM. The observed-minus-predicted values were test if they differed from zero to calculate AT AT was measured after 10 and 20 % WL	Significant WL (~80 % were fat) Reductions in FM but not in FFM	10 %WL = –795(SD 870) kJ/d 20 %WL = –778(SD 983) kJ/d

Table 2. (*Continued*)

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
Müller *et al.*[22]	NRT	*n* 32 men BMI: 20·7–29·3 kg/m^2 Age: 20–37 years	Diet only: CR: 50 % of energy needs. Protein intake: 49 (SD 6) g/d. food and drinks provided	6 weeks (1 week overfeeding, 3 weeks CR, 2 weeks overfeeding)	Body composition: MRI (ECHOMRI-AH) REE: indirect calorimetry (Vmax Spectra, SensorMedics); PA: 24 h heart rate and accelerometry	pREE was based on the sum of seven body compartments multiplied by their corresponding specific tissue respiration rates. AT = REEadj at caloric restriction – REEadj after CR AT was measured after WL and after refeeding	WL = –4·22 (SD 0·873) kg (~–8 %); Decreases in FM (~–18 %) Leptin decreased No associations between hormones and AT	AT = –301 (SD 481) kJ/d Considerable between-subject variance in AT and weight loss Non-significant after refeeding
McNeil *et al.*[23]	RT w/ no CG	*n* 93 women BMI = 32·1(SD 4·3) kg/m^2 Age = 58·1 (SD 4·8) years Two groups: Diet only (*n* 65) diet + exercise (*n* 28)	Diet: REE × 1·4 and then ~3·3 MJ was subtracted from this result 30 % lipids and 15 % proteins Resistance training 3 × week	6 months	Body composition: DXA (General Electric Lunar Prodigy) REE: indirect calorimetry TEE: doubly labelled water	pREE by a multiple regression analysis using age, FFM, leptin and PYY AT was achieved by comparing pREE with mREE via a repeated-measures ANOVA AT was measured after WL	Both interventions decreased weight and FFM Diet only: WL = –4·8 (SD 4·6) kg Diet + exercise: WL = –6·7 (SD 4·5) kg Leptin and PYY were not significant predictors of the differences between pREE and mREE	Greater predicted *v.* measured REE was noted post-intervention (data not shown, ~126 kJ/d) This significant effect disappeared after correcting for the degree of energy restriction
Karl *et al.*[24]	RCT	*n* 91 (39 males) BMI = 28–38 kg/m^2 Age = 45–65 years	Diet only: Phase 1–5 weeks of weight maintenance 12·2 MJ/d with 48 % CHO, 16 % PRO and 36 % fat Phase 2–4 different diets differed by its carbohydrate content: 55 %, 60 %, 70 % or 80 % CHO, 67 % of phase 1 EI Phase 3 – weight maintenance	22 weeks (5 weeks phase 1 + 12 weeks phase 2 + 5 weeks phase 3) + 12 month *ad libitum*-diet follow-up period	Body composition: BODPOD; REE: portable metabolic cart (Deltatrac metabolic monitor, SensorMedica)	pREE for each phase was calculated by a regression model developed from baseline vales of age, sex, FM, FFM and REE. AT was calculated as the difference between mREE and pREE for that phase AT was calculated after WL and after weight maintenance phase	The four groups lost weight (~–7·5 %) ~80 % WL was FM No difference in CHO content	Existence of AT after WL (–226 kJ/d (95 % CI –314 kJ/d, –138 kJ/d() but not after 5 weeks of weight stabilisation
Camps *et al.*[25]	NRT	*n* 82 (23 males) BMI = 31·9 (SD 3·0) kg/m^2 Age = 41 (SD 8) years	Diet only: VLCD 2·1 MJ/d, 51·9 g of protein, 50·2 g of carbohydrates and 6·9 g of lipids	8 weeks	Body composition: Siri's 3C Model; BodPod System REE: open-circuit ventilated hood-system + Brouwer's formula TEE – doubly labelled water	REE was predicted (REEp) by an equation using FM and FFM AT was calculated as REEm divided by REEp AT was calculated after WL	WL = –10·7(SD 4·1) % Reductions in FM and FFM Reductions in leptin	mREE/pREE = 0·96 (SD 0·07). Six percentage of the variation in REEm/REEp after the diet was explained by the decrease in leptin
Pourhassan *et al.*[26] *(information only about WL group)*	O (prospective)	*n* 30 BMI = 33·6 (SD 5·4) kg/m^2 Age = 36·9 (SD 8·4) years	Diet only: very low-calorie diet	6 months	Body composition: Fuller 4C model. (BodPod + ^{2}H dilution + DXA (QDR4500A Hologic Inc)); MRI REE – indirect calorimetry (Vmax Spectra 29n)	pREE from individual organ and tissue masses by using constant specific metabolic rate AT was calculated as REEm minus REEp AT was calculated after WL	36 % of the sample had significant WL (–11·2 (SD 4·9) kg), which ~–72 % was FM Reductions in T3 and T4	Non-significant AT (0·01 (SD 0·93) MJ/d)
Camps *et al.*[27]	NRT	*n* 91 (22 males) BMI = 31·9 (SD 3·0) kg/m^2 Age = 40 (SD 9) years	Diet only: VLCD (2·1 MJ/d) 51·9 g PRO, 50·2 g CHO, 6·9 g lipids	8 weeks + 44 weeks follow-up	Body composition – Siri's 3C model. BODPOD and ^{2}H dilution. REE –open circuit ventilated hood system	pREE was calculated through an equation using FM and FFM AT = mREE/ pREE AT was calculated after WL and after a weight maintenance period	8 weeks: WL = –9·6 (SD 4·1) kg (~–10 %) 52 weeks: WL = –6·0 (SD 5·7) kg (~–7 %)	8 weeks: AT = 0·967 (SD 0·007) 52 weeks: AT = 0·979 (SD 0·007)

Table 2. (*Continued*)

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
Bosy-Westphal *et al.*[28]	NRT	*n* 47 (11 males) Two groups: weight stable (*n* 20) weight regainers (regain > 30 % of their weight) (*n* 27)	Diet only: low calorie diet (3·3–4·2 MJ/d)	13 (SD 3) weeks	Body composition: BODPOD, MRI, DXA (Hologic); REE: Indirect calorimetry (Vmax Spectra 29n).	pREE was based on the sum of eight body compartments (brain, heart, liver, kidneys, skeletal muscle mass, bone mass, adipose tissue and residual mass) × the specific tissue metabolic rate AT calculated as mREE minus pREE AT was calculated after WL and after a follow-up period	Weight stable: WL = –12·3 (SD 3·3) kg Weight regainers: WL = –9·0 (SD 4·3) kg Decreases in T3 only for weight regainers after WL and follow-up	Significant AT only at weight regainers after WL (–0·39 (SD 0·57) MJ/d)
de Jonge *et al.*[29]	RCT	*n* 811 (296 males) BMI from 25 – ≤ 40 kg/m^2 Age from 30 to 70 years	Diet only: four types of caloric restriction: (i) 20 % fat/15 % PRO (ii) 20 % fat/25 % PRO (iii) 40 % fat/15 % PRO (iv) 40 % fat/25 % PRO	6 months + 18 months follow-up	Body composition: methodology not shown REE: metabolic cart (Deltatrac II Metabolic Monitor)	Predicted REE was achieved by an equation using weight, age and sex AT calculated as mREE minus pREE AT was calculated after WL and after a follow-up period	6 months: significant WL for all groups. From –6·37 (SD 0·42) (iii) to –6·80 (SD 0·42) (ii) 24 months: From –3·26 (SD 0·56) (i) to –5·03 (SD 0·58) (ii)	6 months: only groups (i) and (ii) reported significant values for AT AT = –76 (SD 28) kJ/d 24 months: +91 (SD 42) kJ/d
Goele *et al.* 2009[30]	NRT	*n* 48 women BMI = 35·4 (SD 4·4) kg/m^2 Age = 31·5 (SD 6·1) years	Diet only: 4·2 MJ/d (2 meals of a formula diet and a low-fat meal per d)	13·9 (SD 2·4) weeks	Body composition: BODPOD REE: Indirect calorimetry (Vmax Spectra 29n) PA: Pedometers (walking Style pro, OMRON) TEE: PAL × REE	AT was calculated by a comparison between mREE and mREE adjusted for FFM. AT was assessed after WL.	WL = –8·4 (SD 3·9) kg (~–8·4 %)	Significant AT in 26 of 48 women (–13·4 (SD 5·0) kJ/kg FFM)
Bosy Westphal *et al.*[31]	NRT	*n* 45 women BMI from 28·7 to 46·8 kg/m^2 Age from 22 to 46 years	Diet only: low calorie diet (3·3–4·2 MJ/d)	12·7 (SD 2·2) weeks	Body composition – 4C model BODPOD, DXA (Hologic Inc). MRI REE: indirect calorimetry (Vmax Spectra 29n)	pREE was based on the sum of eight body compartments (brain, heart, liver, kidneys, skeletal muscle mass, bone mass, adipose tissue and residual mass) × the specific tissue metabolic rate AT was assessed after WL	WL = 9·5 (SD 3·4) kg (~–4 %) Decreases in leptin and T3	AT was 230 (SD 650) kJ/d Correlations with T3 concentrations
Doucet *et al.*[32]	RCT	*n* 35 (15 males) Age = 44·3 (SD 1·7) years (males) and 41·4 (SD 1·1) years (females)	Diet + pharmacological therapy: two groups: 60 mg/d fenfluramine (*n* 27) Non-macronutrient-specific energy restriction of approximately 2·9 MJ/d	15 weeks + 2–4 weeks follow-up	Body composition: hydrodensitometry %BF: Siri formula REE – indirect calorimetry	Predictive equation using FM and FFM AT was considered as the difference between the changes in pREE from the reference equations and the changes in mREE AT was calculated after WL and after a follow-up period	Significant WL and FM	Non-significant AT after the weight stabilisation
Dulloo *et al.*[33]	NRT	*n* 32 males Age: 25 (SD 4) years Weight: 69·4 (SD 5·8) kg	Diet only: Control period: 15·1 MJ/d: 13 % PRO, 37 % fat, 50 % CHO. Semistarvation: 6·1 MJ/d: 25 % PRO, 17 % fat and 58 % CHO	12 weeks baseline + 24 weeks semistarvation + 12 weeks refeeding	Body composition: hydrodensitometry. BMR – rate of oxygen consumption	Total thermogenic economy (adaptive reduction in BMR) assessed by an equation using ΔFFM and ΔFM AT was calculated after WL and after the refeeding period	Each man lost ~25 % of his initial body weight	12 weeks: AT = –1491 (SD 514) kJ/d S24 weeks: AT = –1706 (SD 477) kJ/d Refeeding: AT = –693 (SD 464) kJ/d Huge variability in BMR reductions
Exercise only and combined exercise and diet interventions								
Martins *et al.*[16]	O (retrospective)	*n* 171 females BMI = 28·3 (SD 1·3) kg/m^2 Age = 35·2 (SD 6·3) years	Diet + exercise: aerobic exercise training OR resistance training (3 × week)	2 years of follow-up	Body composition: 4C model (BODPOD, DXA (DPX-L Lunar) and isotope dilution) REE: indirect	AT was tested with *t* tests by comparing mREE with pREE. pREE was achieved by a predictive equation using age, sex, race, FM	WL = –12·2 (SD 2·6) kg (–15·7 % (SD 2·9) %); no metabolic adaptation was seen at 1- and 2-year follow-up in all participants	AT = –226 (SD 439) kJ/d AT is minimal when measurements are taken under conditions of weight stability and does not predict weight

Table 2. (*Continued*)

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
		Three groups: diet only diet + aerobic training diet + resistance training			calorimetry (Delta Trac II)	and FFM AT was measured after a 4-week period of weight stabilisation		regain up to 2 years follow-up
Ten Haaf *et al.*[47]	O (retrospective)	*n* 254 (88 males) BMI = 31·7 (SD 4·4) kg/m^2 Age = 51 (SD 14) years Two groups: Younger adults (*n* 122) BMI = 31·0 (SD 4·4) kg/m^2 Age = 40 (SD 9) years Older adults (*n* 132) BMI = 32·5 (SD 4·3) kg/m^2 Age = 62 (SD 5) years	Diet + exercise: All subjects went through a hypocaloric diet (30 % lipids, 52 % CHO, and 18 % PRO). A subgroup completed an exercise programme	8–13 weeks	Body composition: air displacement plethysmography (BodPod) + Siri Equation REE: indirect calorimetry (Vmax Encore n29)	pREE achieved by a linear regression with baseline data of FFM, FM, age, sex and FFM × age interaction. AT = pREE-mREE and corrected for measured *v.* predicted REE differences at baseline AT was calculated after WL	Young adults: WL = –2·8 (SD 3·3) kg; FM = –3·0 (SD 3·6) kg. Older adults: WL: –3·2 (SD 3·0) kg; FM = –3·4 (SD 3·3) kg	Significant AT in older adults (–278 (SD 774) kJ/d) but not in younger adults Whole sample: –176 (SD 715) kJ/d
Marzullo *et al.*[48]	NRT	*n* 100 (50 males) BMI = 45·1 (SD 4·8) kg/m^2 Age = 40·4 (SD 12·7) years	Diet + exercise: 75 % of mREE. 30 % lipids, 52 % CHO, 18 % PRO Aerobic PA – 2 sessions of 30 min for 5 d/week	4 weeks	Body composition: bioimpedance (BIA 101/S Akern); Thyroid ultrasonography; REE – indirect calorimetry (SensorMedics)	pREE was calculated by the Harris-Benedict formula and was employed to calculate the mREE/pREE ratio as a proxy of thermogenic potential, set as normal at 100 % AT was calculated after WL	Significant WL (–5·5 (SD 1·8) %) Significant reductions for FM and FFM only for men	REEm/REEp = 91·8 (SD 10·2) % (< 100 %) Association between REE and thyroid hormones
Fothergill *et al.*[12]	O (prospective)	*n* 14 (6 males) BMI = 49·5 (SD 10·1) kg/m^2 Age = 34·9 (SD 10·3) years	Diet + exercise: Restricted diet (~70 % of their baseline energy requirements) Physical activity: 6 × a week, 90 min/d of supervised vigorous circuit training and/or aerobic training	6 years follow-up	Body composition: DXA (iDXA, GE Lunar) REE – indirect calorimetry (TrueOne Metabolic cart) TEE – doubly labelled water	pREE calculated through linear regression equation as a function of FFM, FM, age and sex. Differences between mREE and pREE defined the magnitude of metabolic adaptation which was considered to be present if the REE residuals were significantly different from zero AT was calculated after WL and after the follow-up period	Severe WL WL = –58·3 (SD 24·9) kg Decreases in FM and FFM Increases of PA Significant decreases in leptin, T4 and TAG At 6 years, 41·0 (SD 31·3) of the lost weight was regained	Presence of AT after 30 weeks of competition (–1150 (SD 866) kJ/d) and after 6 years (–2088 (SD 866) kJ/d)
McNeil *et al.*[23]	RT w/ no CG	*n* 93 women BMI = 32·1 (SD 4·3) kg/m^2 Age = 58·1 (SD 4·8) years 2 groups: Diet-only (*n* 65) Diet + exercise (*n* 28)	Diet: REE × 1·4 and then 3·3 MJ was subtracted from this result 30 % lipids and 15 % proteins Supervised resistance training 3 × week	6 months	Body composition: DXA (General Electric Lunar Prodigy) REE: indirect calorimetry TEE: doubly labelled water	pREE by a multiple regression analysis using age, FFM, leptin and PYY AT was achieved by comparing pREE with mREE via a repeated-measures ANOVA AT was calculated after the WL intervention	Both interventions decreased weight and FFM Diet only: WL = –4·8 (SD 4·6) kg Diet + exercise: WL = –6·7 (SD 4·5) kg Significant time × group interaction for FM. Greater decrease in FM for diet + exercise group. Decreases in leptin and increases in PYY at both groups. Leptin and PYY were not significant predictors of the differences between pREE and mREE	Greater predicted *v.* measured REE was noted post-intervention (data not shown, –126 kJ/d) Participants with higher energy restriction saw greater decreases in their mREE *v.* pREE This significant effect disappeared after correcting for the degree of energy restriction
Hopkins *et al.*[40]	NRT	*n* 30 women BMI = 30·6 (SD 3·6) kg/m^2 Age = 40·6 (SD 9·1) years	Exercise only: Supervised aerobic exercise designed to expend 10·5 MJ/week	12 weeks	Body composition: air displacement plethysmography (BODPOD). REE – indirect calorimetry (GEM)	pREE by a regression equation from a reference population using FM and FFM AT was achieved when residuals between pREE and mREE were different from zero	Small but significant WL (84·3 (SD 10·3) to 83·7 (SD 10·7) (week 6) and to 83·0 (SD 11·2) (week 12)) No significant loss of FFM Decrease in leptin	Non-significant AT Highly variability between subjects

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Table 2. (*Continued*)

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
						AT was calculated immediately after the WL programme		
Johannsen *et al.* 2012[13]	O (prospective)	*n* 16 (7 males) BMI = 49·4 (SD 9·4) kg/m^2 Age = 33 (SD 1 0) years	Diet + exercise: Restricted diet (~70 % of their baseline energy requirements) Physical activity: 6 × a week, 90 min/d of supervised vigorous circuit training and/or aerobic training.	30 weeks	Body composition: Dual-energy X-ray absorptiometry (GE Lunar). REE – Indirect Calorimetry (Max II metabolic cart); Total daily energy expenditure (TEE) – doubly labelled water	pREE calculated by an equation for predicting REE based on FFM, FM, age, and sex at baseline. AT was considered if the REE residuals were negative and different from zero. AT was assessed immediately after the WL programme.	6 weeks: WL = –15·0 (SD 4·9) kg (>–10 %) 30 weeks: WL = –57·6 (SD 23·8) kg (~–38 %) Decreases in leptin and T3. Increases in adiponectin	6 weeks: AT = –1021 (SD 967) kJ/d 30 weeks AT = –2109 (SD 715) kJ/d No association between changes in T3 and AT
Surgery								
Wolfe *et al.*[34]	O (prospective)	*n* 25 (3 males) BMI = 47 (SD 6) kg/m^2 Age = 45 (SD 11) years	Bariatric surgery (88 % Roux-em-Y gastric bypass, 8 % adjustable gastric banding and 4 % biliopancreatic bypass with duodenal switch)	24 months	Body composition: DXA (Discovery A, Hologic Lunar); REE: indirect calorimetry (Columbus Instruments); TDEE – DLW	Regression equation using baseline FFM as the independent variable to predict REE and TDEE. AT was calculated as the residuals between measured REE/TDEE and predicted REE/TDEE. AT was measured after 6 and 24 months	6 months: WL = –24 % (SD 5) %; FM = –37 % (SD 8) %; FFM = –11 (SD 4) %. 24 months: WL = –27 (SD 10·2) kg	Presence of AT at 6 months (REE = –674 (SD 582) kJ/d; but not at 24 months
Bettini *et al.*[35]	O (prospective)	*n* 154 (56 males) BMI = 45·5 (SD 7·2) kg/m^2 Age = 45·1 (SD 11·6) years	Sleeve gastrectomy	12 months	Body composition: bioimpedance (Soft Tissue Analyser, Akern); REE – indirect calorimetry (Vmax)	pREE was calculated through a predictive equation using FM, FFM and sex AT calculated as mREE minus pREE and was assessed after 12 months	Significant WL (~–30 %) Reductions in FM (~45 %) and FFM (~–14 %) Decreases of leptin and insulin	Significant AT (–833 (SD 996) kJ/d) No significant correlations between AT and metabolic variables
Browning *et al.*[36]	O (retrospective)	*n* 13 (3 males) BMI = 46·4 (SD 5·8) kg/m^2 Age = 46·2 (SD 12·7) years	Roux-em-Y gastric bypass (*n* 8) and laparoscopic adjustable gastric banding (*n* 5)	6 months	Body composition: DXA (Hologics discovery Wi) REE – indirect calorimetry (SensorMedics)	pREE from LBM, FM, age and sex using least squares linear regression. AT was calculated using the equation: (6-monthREEp – baseline REEp) – (6-month REEm – baseline REEm) AT was assessed after 6 months.	Significant WL; reductions on FM and FFM	Non-significant AT AT was highly variable across individuals, ranging from –598 to 891 kJ/d
Tam *et al*[37]	O (prospective)	*n* 35 (9 males) BMI = 42·1 (SD 6·5) kg/m^2 Age = 46 (SD 11) years	Gastric band (GB, *n* 8), sleeve gastrectomy (SG, *n* 13) or Roux-em-Y gastric bypass (RYGB, *n* 14)	24 months	Body composition: bioimpedance (Impedimed, HydexDF50) REE: indirect calorimetry (Medgem, Microlife)	AT was calculated as the difference between mREE and the pREE from fat-free mass, age and sex on the basis of equations established at baseline. AT was calculated after 6 weeks and 3, 6, 12 and 24 months	GB: WL = –16·1 (SD 3·2) % SG: WL = –30·7 (SD 2·6) % RYGB: WL = –32·9 (SD 2·7) % Similar and significative reductions on FFM (~–31 %)	For GB, AT occurred at 6 week (–469 (SD 285) kJ/d) and 3 month (–741 (SD 289) kJ/d) Insignificant after 6 months. For sleeve, AT was significant from week 6 to 24 months (–1448 (SD 247) kJ/d) For RYGB, AT was significant from week 6 to 24 months (–1167 (SD 259) kJ/d)
Carrasco *et al.*[38]	O (prospective)	*n* 31 (4 males) BMI 44·4 (SD 4·8) kg/m^2 Age = 37·3(SD 11·1) years	Roux-em-Y gastric bypass	6 months	Body composition: TBW – ^{2}H dilution REE: indirect calorimetry (Deltatrac) PA – physical activity survey. Cardio-frequency monitor (Polar Vantage NV)	pREE calculated through a regression equation among REE and FFM before surgery AT was calculated after 6 months	WL = –33·4(SD 7·6) kg BF ~–77 % of WL	AT = –348(SD 517) kJ/d Great dispersion of the difference between pREE and mREE

Table 2. (*Continued*)

Study	Study type	Sample	Intervention's description	Length ↓ follow-up	Measurements	AT definition and measurement	Results	AT
Coupaye *et al.*[39]	O (prospective)	*n* 36 females BMI = 47·2 (SD 8·5) kg/m^2 Age = 42·7 (SD 8·7) years	Laparoscopic adjustable gastric banding	12 months	Body composition: DXA (Hologic QDR 2000) REE – indirect calorimetry (Deltatrac II)	pREE – regression equations relating REE to LBM and FM at initial weight before surgery. AT = residual values (observed-minus-predicted values) different from zero. AT was calculated after 1 year	WL = −23·7 (SD 11·6) kg (−19 %); Decreases in leptin (−42 %)	Non-significant AT

O, observational; NRT, non-randomised trial; RCT, randomised clinical trial; RT, randomised trial; CG, control group; FM, fat mass; FFM, fat-free mass; WL, weight Loss; AT, adaptive thermogenesis; CHO, carbohydrates; PRO, protein; CR, caloric restriction; VLCD, very low calorie diet; LCD, low calorie diet; CER, continuous energy restriction; IER, intermittent energy restriction; TDEE, total daily energy expenditure; BF, body fat; GB, gastric banding; SG, sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass.

disappeared or was attenuated after a period of weight stabilisation (measured after the follow-up period)[24,27,29]. Those three studies had participants with similar characteristics and methodologies to assess pREE (although de Jonge *et al.* created a regression equation without using FM and FFM as variables). Furthermore, Camps *et al.* also used a different methodology to assess AT (mREE/pREE).

Exercise only and combined exercise and diet interventions. Since only one article reported an exercise-only intervention[40], its results will be analysed with combined diet and exercise interventions, comprising seven articles[12,13,16,23,40,47,48].

Participants' characteristics. A total of 678 participants were involved (151 males). Only one study comprised participants with a BMI < 25 kg/m^2[16]. Half of the studies reported a > 10 % WL[12,13,16], while the others reported moderate amounts of WL (< 10 %)[23,40,47,48].

Intervention type. The study related to an exercise-only intervention[40] consisted of a supervised aerobic exercise designed to create an energy deficit of ~10·5 MJ per week. The type of exercise was divided into aerobic[40,48], resistance training[23] or both[12,13,16]. One study did not add any information about the type of exercise[47].

Methodology to assess adaptive thermogenesis. A predictive equation to estimate REE was created in five studies[12,13,16,23,47]. Hopkins *et al.* also used a predictive equation to estimate REE but did not use their own sample but an independent population including women with overweight/obesity who did not participate in the intervention[40]. All of the mentioned studies calculated AT by comparing pREE with mREE using a statistical approach such as *t* test or ANOVA. Marzullo *et al.* used the Harris-Benedict equation to estimate REE (pREE), dividing mREE by pREE to calculate a ratio[48].

Adaptive thermogenesis. AT was reported in six studies[12,13,16,23,47,48]. Hopkins *et al.* study was the only study that did not report a significant value for AT[40], being the only exercise-only intervention in which participants lost a small amount of weight (−1·3 (SD 2·7) kg). Despite having AT after WL, one study reported an attenuation after 1–2 years of follow-up[16]. The values for AT ranged between 126 and 418 kJ/d except for two studies[12,13]. These studies reported significant weight losses (WL = −58·3(SD 24·9) kg[12] and WL = −57·6(SD 23·8) kg[13]) and showed a larger AT (~837–1255 kJ/d which increased during follow-up for ~2092 kJ/d)[12,13].

Bariatric surgery. For bariatric surgery, six studies were included in this review[34–39], with the study length ranging from 6 to 24 months.

Participants' characteristics. A total of 294 participants (seventy-five males) underwent bariatric surgery. Baseline characteristics were similar among studies, with all including participants with obesity (mean BMI > 30 kg/m^2). All of the

studies presented a mean WL of ~30 % except for those who underwent gastric banding (~15–20 %).

Intervention type. The following weight reduction surgeries were conducted: Roux-en-Y gastric bypass[34,36–38], sleeve gastrectomy[35,37], gastric band[34,36,38,39] and biliopancreatic bypass with duodenal switch[34].

Methodology to assess adaptive thermogenesis. A predictive equation was created and used for all the studies, calculating AT by comparing the pREE with a mREE using a statistical approach such as *t* test or ANOVA. Browning *et al.* calculated AT by a different approach ((6-monthREEp-baselineREEp)-(6-monthREEm-baselineREEm))[36].

Adaptive thermogenesis. A significant value for AT was reported in four of the six studies[36,39]. In two of these studies, AT only remained significant after 6 months, disappearing throughout time[34,37]. AT values were slightly lower for those who had gastric band surgery when compared with other surgeries such as sleeve gastrectomy or Roux-en-Y gastric bypass[37]. Studies in which participants underwent gastric banding did not report significant values for AT[36,39]. Both studies assessed AT by comparing the residuals (i.e. difference between measured REE and estimated based on the predictive equation) at baseline and after WL. A high variability between individuals was highlighted in two studies[36,38].

Total daily energy expenditure

A total of five studies reporting changes in TDEE were included in this review[34,50–53], with two randomised controlled trials (40 %) and three prospective observational studies included (60 %) (Table 3).

From those, one was related to a diet-only intervention[50], two to a diet-only *v.* a combined diet and exercise intervention[51,52] and two to bariatric surgery[34,53]. Due to the small number of studies, all intervention types were analysed together.

Participants' characteristics. The five studies comprised 164 participants (fifty-three males). Participants from the studies related to lifestyle interventions had a BMI ranging from 25 to 30 kg/m^2[50–52]. For studies that used bariatric surgeries, BMI was above 40 kg/m^2[34,53]. All of the studies reported a WL > 10 %.

Intervention type. Marlatt *et al.* created a caloric deficit of 25 % based on each participant's energy needs[50], while the other two authors used two different approaches: (i) a low calorie diet (~3·7 MJ/d) until each participant had reached a WL of 15 % of their initial weight or (ii) an individual diet based on individual EI targets[51,52].

Methodology to assess adaptive thermogenesis. TDEE was assessed by doubly labelled water method[34,52,53] or by a metabolic chamber[50,51]. A predictive equation was used to estimate TDEE (pTDEE) and AT was calculated by subtracting pTDEE from mTDEE.

Adaptive thermogenesis. AT was reported in four studies[34,51–53]. For lifestyle interventions, Redman *et al.* reported larger values for AT (~–1255 to –2092 kJ/d)[52], while Lecoultre reported lower values (–527 (SD 105) kJ/d)[51]. Marlatt *et al.* did not report any significant changes in TDEE[50]. Both studies that used weight reduction surgeries[34,53] reported a significant AT after 6 months, but not after 12 months[53] or 24 months[34]. Studies which did not find AT had a follow-up period and had similar methodologies to assess it, using a predictive equation with FM and FFM as variables and comparing the residual values.

Sleeping energy expenditure

Only two studies reporting changes in SEE were found[50,51] (Table 4). One had a randomised controlled trial design and one was a prospective observational study.

Participants' characteristics. The two studies comprised seventy-five individuals with a mean BMI between 25 and 30 kg/m^2 (thirty males). Both studies reported a WL > 10 %.

Intervention type. Marlatt *et al.* generated a energy deficit of 25 % based on each participant's energy needs[50], while Lecoultre *et al.* used two different approaches: i) a low calorie diet (~3·7 MJ/d) until each participant had reached a WL of 15 % of their initial weight or ii) an individual diet based on individual EI targets[51].

Methodology to assess adaptive thermogenesis. SEE was assessed in a respiratory chamber using microwave motion sensors. A predictive equation was created to estimate SEE (pSEE) and AT was calculated by subtracting pSEE from measured SEE.

Adaptive thermogenesis. Both studies reported significant and similar values for AT in SEE (~–335 to –377 kJ/d).

Discussion

The aim of this systematic review was to examine whether AT occurs after WL and/or a period of weight stabilisation phase. Overall, significant values for AT were reported in twenty-seven of the thirty-three included studies. Most studies reported a large variability between subjects (e.g. when a standard deviation is higher than the respective mean) with regard to the magnitude of WL and/or AT.

Resting energy expenditure

The majority of the studies aimed to assess AT in REE. From those, twenty-three out of twenty-nine reported a significant value for AT in REE[12,13,16–18,20–25,27–31,33–35,37,38,47,48].

The reduction in REE after WL occurs mainly due to the losses of FFM and FM[31,42]. Furthermore, it is known that WL is accompanied by hormonal changes such as a decrease in circulating leptin and thyroid hormones, and these changes may contribute to AT[11,54,55]. Also, other factors may potentially contribute to AT such as changes in sympathetic nervous system activity and concentrations of insulin and catecholamines after WL[22].

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Table 3 Total daily energy expenditure (TDEE)/24 h energy expenditure (24hEE)

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
Diet-only intervention								
Marlatt *et al.*[50]	O (prospective)	*n* 29 (10 males) Two groups: Caloric restriction *n* 18 BMI = 25·7 (SD 1·6) kg/m^2 Control *n* 11 BMI = 25·7 (SD 1·1) kg/m^2	Diet only 25 % of their energy needs	2 years	Body composition: DXA (Hologic QDR 4500A), EE: 24 h respiratory chamber; TDEE: 14 d DLW Sleeping metabolic rate: through PAL and/or Activity related energy expenditure	Predictive equation using BSA, age and sex to calculate pEE AT in 24hEE and SEE are expressed as changes in residual values AT was assessed at 12 and 24 months	After 2 years of CR: WL: –9·0 (SD 0·6) kg 54 % of the weight was regained 2 years later	No significant changes in 24hEE were observed
Lecoultre *et al.*[51]	RCT	*n* 46 (20 males) BMI = 27·8 (SD 0·7) kg/m^2 Age = 36·8 (SD 1·0) years	Diet only or diet + exercise: Four groups: 25 % calorie restriction; 12·5 % calorie restriction + exercise LCD 3·7 MJ/d until a 15 % reduction in BW one control group (weight maintenance diet)	6 months	Body composition: DXA (Hologics QDR 4500 A); 24hEE: metabolic chamber SEE: microwave motion sensors (02h–05h am)	Predicted values of 24 hSedEE and SEE: stepwise multivariate regression with FM, FFM, age, and sex as independent variables AT is calculated by m24hEE/mSEE minus p24hEE/SEE AT was calculated after the WL intervention (6 months)	WL = –11·4 (SD 0·6) %; Decreases in leptin (independent of the type of CR) Decreases in T3 and T4, related to the change in leptin, controlling for baseline leptin	AT was observed in 6 months for CR groups for 24hEE (–527 (SD 105) kJ/d)
Redman *et al.*[52]	RCT	*n* 46 (20 males) BMI = 27·8 (SD 0·7) kg/m^2 Age = 36·8 (SD 1·0) years	Diet only or diet + exercise: four groups: 25 % calorie restriction; 12·5 % calorie restriction + exercise LCD 3·7 MJ/d until a 15 % reduction in BW one control group (weight maintenance diet)	6 months	Body composition: DXA (Hologics QDR 4500 A) 24hSedEE: metabolic chamber SEE: microwave motion sensors (02h–05h am) TDEE: 14-d doubly labelled water; PA: PAL = TDEE/SMR OR mTDEE-mSMR	Predicted values of 24hSedEE and SEE: stepwise multivariate regression with FM, FFM, age and sex as independent variables AT is calculated by mTDEE minus pTDEE AT was calculated at 3 and 6 months (after WL intervention)	Calorie restriction WL = –8·3 (SD 0·8) (–10 %), calorie restriction + exercise WL = –8·4 (SD 0·8) (–10 %) LCD WL = –11·2 (SD 0·6) kg (–14 %)	3 months: Significant AT for CR group (–1552 (SD 314) kJ/d) and for LCD (–2075 (SD 285) kJ/d) 6 months: Significant AT for LCD (–1151 (SD 531) kJ/d)
Exercise only and combined exercise and diet interventions								
Lecoultre *et al.*[51]	RCT	*n* 46 (20 males) BMI = 27·8 (SD 0·7) kg/m^2 Age = 36·8 (SD 1·0) years	Diet only or diet + exercise: four groups: 25 % calorie restriction; 12·5 % calorie restriction + exercise LCD 3·7 MJ/d until a 15 % reduction in BW one control group (weight maintenance diet)	6 months	Body composition: DXA (Hologics QDR 4500 A); 24hSedEE: metabolic chamber SEE: microwave motion sensors (02h–05h am)	Predicted values of 24hSedEE and SEE: stepwise multivariate regression with FM, FFM, age and sex as independent variables AT is calculated by m24hEE/mSEE minus p24hEE/SEE AT was calculated after the WL intervention (6 months)	WL = –11·4 (SD 0·6) %; Decreases in leptin (independent of the type of CR Decreases in T3 and T4, related to the change in leptin, controlling for baseline leptin	Non-significant AT for the diet + exercise group

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Table 3 (*Continued*)

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
Redman *et al.*[52]	RCT	*n* 46 (20 males) BMI = 27·8 (SD 0·7) kg/m^2 Age = 36·8 (SD 1·0) years	Diet only or diet + exercise: four groups: 25 % calorie restriction; 12·5 % calorie restriction + exercise LCD 3·7 MJ/d until a 15 % reduction in BW one control group (weight maintenance diet)	6 months	Body composition: DXA (Hologics QDR 4500 A) 24hSedEE: Metabolic chamber SEE: microwave motion sensors (02h–05h am) TDEE: 14-d doubly labelled water; PA: PAL = TDEE/SMR OR mTDEE-mSMR	Predicted values of 24hSedEE and SEE: stepwise multivariate regression with FM, FFM, age and sex as independent variables AT is calculated by mTDEE minus pTDEE AT was calculated at 3 and 6 months (after WL intervention)	Calorie restriction WL = –8·3 (SD 0·8) (–10 %), Calorie restriction + exercise WL = –8·4 (SD 0·8) (–10 %) LCD WL = –11·2 (SD 0·6) kg (–14 %)	Non-significant AT for the exercise group
Surgery								
Ravelli *et al.*[53]	O (prospective)	*n* 18 females BMI between 40 and 50 kg/m^2 Age = 20–45 years	Roux-em-Y gastric bypass	12 months	Body composition: stable isotope dilution technique (Schoeller); TDEE: DLW	Predictive equation of TEEp, as a function of FM (kg), FFM (kg), age (years) and the number of steps (S) adjusted by current body weight (BW) in kg (S × W) in multiple linear regression AT was considered present when the residual values between mTEE and pTEE after surgery were negative AT was assessed at 6 and 12 months after surgery	Significant weight loss at 6 months (≅–27 %) and at 12 months (≅–33 %) ~10 % reduction of FFM and ~12 % reduction of FM	6 months: Presence of AT (–665 (SD 2092) kJ/d); 12 months: Non-significant AT
Wolfe *et al.*[34]	O (prospective)	*n* 25 (3 males) BMI = 47 (SD 6) kg/m^2 Age = 45 (SD 11) years	Bariatric surgery (88 % Roux-em-Y gastric bypass, 8 % adjustable gastric banding and 4 % biliopancreatic bypass with duodenal switch)	24 months	Body composition: DXA (Discovery A, Hologic Lunar); REE: indirect calorimetry (Columbus Instruments); TDEE – DLW	Regression equation using baseline FFM as the independent variable to predict REE and TDEE AT was calculated as the residuals between measured REE/TDEE and predicted REE/TDEE AT was measured after 6 and 24 months.	6 months: WL = –24 % (SD 5) %; FM = –37 % (SD 8) %; FFM = –11 (SD 4) %. 24 months: WL = –27 (SD 10·2) kg	Presence of AT at 6 months (TDEE = –950 (SD 1423) kJ/d) but not at 24 months

O, observational study; RCT, randomised clinical trial; TDEE, total daily energy expenditure; 24hEE, 24 h energy expenditure; SEE, sleeping energy expenditure; WL, weight loss; CR, caloric restriction; LCD, low calorie diet; FM, fat mass; FFM, fat-free mass.

Table 4. Sleeping energy expenditure

Study	Study type	Sample	Intervention's description	Length + follow-up	Measurements	AT definition and measurement	Results	AT
Marlatt *et al.*[50]	O (prospective)	*n* 29 (10 males) Two groups: Caloric restriction *n* 18 BMI = 25·7 (SD 1·6) kg/m^2 Control *n* 11 BMI = 25·7 (SD 1·1) kg/m^2	Diet only 25 % of their energy needs	2 years + 2 years follow-up	Body composition: DXA (Hologic QDR 4500A), EE: 24 h respiratory chamber; TDEE: 14 d DLW Sleeping metabolic rate: microwave motion sensors in a respiratory chamber (activity < 1 %)	Predictive equation using BSA, age and sex to calculate SEE AT in 24hEE and SEE are expressed as changes in residual values AT was assessed during follow-up	After 2 years of CR: WL: –9·0 (SD 0·6) kg. 54 % of the weight was regained 2 years later	Significant AT was observed between CR (–381 (SD 75) kJ/d) and CG (–96 (SD 96) kJ/d)
Lecoultre *et al.*[51]	RCT	*n* 46 (20 males) BMI = 27·8 (SD 0·7) kg/m^2 Age = 36·8 (SD 1·0) years	Diet only or diet + exercise: four groups: 25 % calorie restriction; 12·5 % calorie restriction + exercise LCD 3·7 MJ/d until a 15 % reduction in BW one control group (weight maintenance diet)	6 months	Body composition: DXA (Hologics QDR 4500 A); 24hSedEE: metabolic chamber Sleeping EE (SEE): microwave motion sensors (02h–05h am)	Predicted values of 24hSedEE and sleeping EE: stepwise multivariate regression with FM, FFM, age, and sex as independent variables AT is calculated by m24hEE/mSEE minus p24hEE/SEE AT was calculated after the WL intervention (6 months)	WL = –11·4 (SD 0·6) %; Decreases in leptin (independent of the type of CR) Decreases in T3 and T4, related to the change in leptin, controlling for baseline leptin	AT was observed in CR groups for SEE (–347 (SD 71) kJ/d)

O, observational study; RCT, randomised clinical trial; TDEE, total daily energy expenditure; 24hEE, 24 h energy expenditure; SEE, sleeping energy expenditure; WL, weight loss; CR, caloric restriction; LCD, low calorie diet; FM, fat mass; FFM, fat-free mass.

In this systematic review, some studies reported decreases in leptin[12,13,17,19,22,23,25,31,40] and in thyroid hormones[26,31]. The administration of exogenous leptin and triiodothyronine may restore baseline hormone concentrations[55] and reverse the effects of AT. However, the role of these hormones on AT is still a matter of debate[22] as not all studies observe a relationship.

Intervention's type and adaptive thermogenesis

Despite surgeries having a higher percentage of WL, they did not necessarily present higher values for AT, when compared with lifestyle interventions. Weight reduction surgeries differed in the degree of AT, with gastric banding being associated with a lower (or non-existent) AT and smaller amounts of WL (~10–20 %) compared with sleeve gastrectomy and gastric bypass (~30–40 %). No bariatric surgery's studies have included assessments of AT in SEE. Although it remains unknown why different surgeries may lead to different magnitudes of AT, its technical procedure could be a potential explanation. In sleeve or gastric bypass surgeries, part of the stomach is removed, while in gastric banding procedures the stomach remains intact, which alter the hormonal responses which may be linked to AT[56].

Although the studies performing bariatric surgeries reported the highest amounts of WL, the Biggest Loser's participants reported similar changes in body weight by creating a large energy deficit[12,13]. However, while in bariatric surgeries AT tended to disappear after a period of 6–24 months, on the Biggest Loser's studies, AT not only remained present but also increased their value after 6 years. However, as some of the participants lost weight on the 2 weeks prior to the 6-year follow-up measurements, the state of energy balance (energy deficit) could have influenced the assessments of AT.

For lifestyle interventions, it is important to consider that different methodologies (macronutrient composition, degree of energy restriction and inclusion of exercise) to achieve a negative energy balance were utilised. Therefore, heterogeneity in the results reported in these lifestyle interventions was to be expected.

Exercise-only studies usually report lower than expected magnitudes of WL mainly due to compensatory increases in EI and decreases in EE[8]. Therefore, there is a lack of exercise-only interventions including both a significant WL and assessments of AT. For this systematic review, only one study was included, which did not report a significant mean AT after a 12-week supervised exercise-only intervention[40], potentially explained by the smaller energy deficit.

Despite the large variability among studies, similar AT was found between bariatric surgeries and lifestyle interventions, regardless of total WL.

Relationship between the magnitude of weight loss and adaptive thermogenesis

It has been previously postulated that a relationship between total WL and degree of AT exists[13,23]. However, some studies have reported contradictory results[16,42]. If a relationship between magnitude of WL and degree of AT existed, it would be plausible that bariatric surgery would lead to a greater AT as total WL is usually larger. However, only Tam *et al.* reported higher values for AT (> 1255 kJ/d)[37], when compared with lifestyle interventions. Interestingly, despite large WL (~–20 %), two studies did not report a significant value for AT[36,39]. Altogether, the findings from this analysis suggest that the amount of WL is not associated with the magnitude of AT, corroborating the results from previous studies[16,42].

The influence of the state of energy balance on adaptive thermogenesis

An important consideration when examining the presence of AT is to understand the state of energy balance participants are at the time of the measurements. It has been shown that the state of energy balance may be associated with AT[57]. Notably, the majority of the included studies who did not report AT (in at least one group) had their participants EE measured under conditions of neutral energy balance (~70 %)[22,24,28,29,32,34,39,50,53]. Furthermore, some studies reported a minimal AT when measurements were taken under conditions of weight stability[16,24]. For instance, Martins *et al.* observed AT (~209–251 kJ/d) after a 4-week weight stabilisation period[16]. However, it is important to acknowledge that weight stability does not imply the presence of a neutral energy balance, as in the present study participants were under a very low energy-dense ketogenic diet (3·3 MJ/d)[16] which deplete glycogen stores. Therefore, participants could be in a negative energy balance and lose body fat while replenishing glycogen stores. Indeed, after 4 weeks of stabilisation, participants had lost an extra 0·8 kg of FM while gaining 0·9 kg of FFM.

Despite the potential influence of the state of energy balance on AT[57], most studies are not clear in reporting whether participants were assessed under similar states of energy balance, which could in part explain the conflicting and heterogeneous results. Therefore, in order to examine whether AT is present after WL, measurements should be conducted under conditions of neutral energy balance.

Methodological issues

The equivocal findings observed between studies may also be reflective of a lack of consistency regarding the definition and methods used to assess AT. In the present literature, the most common method is the use of regression models to predict REE. This method includes the utilisation of a previously validated equation or the development of an equation based on the baseline information from the population included in the study. Then, a comparison between measured and predicted REE is conducted to examine whether these are different. Therefore, examining the existence of AT is strongly dependent on the accuracy of the technique used to measure body composition. The four-compartment models, constructed from combinations of the reference methods[58], are considered the gold standard method to assess FM[59,60]. Since this model combines the use of several techniques, due to the assessment of bone mineral content (by dual-energy X-ray absorptiometry), total body water (isotopes dilution), body weight and body volume (air displacement plethysmography)[58], it requires considerable time and cost and only a few studies used it. Therefore, the most common methods used in weight management research

are two-compartment models, in which a stable density or hydration of FFM needs to be considered. Since FFM is composed of water, proteins, mineral and glycogen with different densities, any change in its composition during WL will alter the energy density of FFM. During WL, especially during an initial phase, a decrease in N, glycogen and Na leads to a negative water balance which changes the density of FFM, and thus compromising the FM obtained by densitometry methods[61].

Moreover, it is important to acknowledge that FFM represents a heterogeneous group of tissues with different metabolic rates[62,63]. This means that changes in the composition of FFM (losses of high-metabolic rate organs *v.* skeletal muscle *v.* body water) may dramatically influence the prediction of REE. Therefore, using two-compartment models to assess FM and FFM presents some limitations for the prediction of REE when comparing individuals before and after WL[64]. Interestingly, studies that assessed AT using MRI reported lower or non-significant values for AT[22,26,28,31]. This could be due to the ability to accurately assess tissue-organ components without relying on assumptions, also allowing to account for the specific metabolic rates associated with each tissue[62,63]. Therefore, the most accurate method to examine AT may be the estimation of REE based on the data collected from the MRI and the organ's specific metabolic rates[61]. However, MRI is not common in clinical practice due to the high time and cost investment[64], being used only in a limited number of studies[64]. Overall, the observed variability in AT between studies may be also due to the method used to assess it, as well its assumptions.

Also, it is important to state that AT in REE is generally considered as a greater than predicted decrease in REE after accounting for changes in body composition. However, when it comes to TDEE, AT is usually calculated using a similar method, which could lead to inaccurate calculations as this approach does not account for changes in PA behaviours that could influence EE independently of the presence of AT.

Lastly, comparing weight reduction surgeries, gastric banding seems to be the one associated with the lowest (or non-existent) AT. Although it remains unknown why different surgeries may lead to different magnitudes of AT, its technical procedure could be a potential explanation. This stomach removal in sleeve or gastric bypass surgeries (*v.* gastric banding procedures) may alter the concentration of hormones related to energy balance regulation or lead to different changes in body composition (different contributions of FM and FFM), and therefore influence AT. Moreover, after these types of surgeries, the digestibility and absorption after a meal are altered[65]. In fact, nutritional deficits are one of the major long-term complications of bariatric surgery[66,67]. Since the stomach undergoes a short cut, the gut receives less processed food, which may decrease absorption and stimulate defecation[68]. Therefore, the metabolisable energy of the food should also be taken into account.

Limitations

There are important limitations that need to be addressed. As expected, a large heterogeneity in the methods used to assess AT was found between studies, which could in part explain the equivocal results. Considering the quality assessment tool, it is important to state that the data included in this review ranged from weak to moderate study designs. Therefore, the need to establish a universal definition and assessment protocol of AT is warranted. Defining how AT is assessed will decrease the risk of bias and strengthen the comparisons between studies.

Recommendations for future studies

Due to the aforementioned limitations, the standardisation of the methods to assess AT is crucial in order to fully understand whether this compensatory response occurs during and/or after WL.

Firstly, a regression equation to predict REE should be created based on the population's baseline information and it should provide a good fit for the observations. The use of general predictive equations already published should be avoided since they were made using other population's characteristics. Moreover, apart from precise measurements of FM and FFM, variables such as age and sex may be included as they have been shown to influence REE[69]. Furthermore, residuals should be calculated before and after WL. If residuals are statistically different from zero at baseline, it means that participants already have a predicted REE different from the measured value. Therefore, residuals at baseline should be taken into account when assessing AT.

Previous research has demonstrated that AT may be associated with the state of energy balance[57]. Therefore, measurements of EE should be conducted in a similar state of energy balance. Furthermore, assessing AT in a neutral energy balance condition not only will assure a similar condition to baseline but will also eliminate the potential influence of an acute state of energy deficit. However, it is important to note that neutral energy balance and weight stabilisation are not synonyms. Since an energy deficit will inevitably lead to glycogen depletion, a neutral energy balance post-WL may lead to a short-term weight gain due to increases in water stores. Therefore, a neutral energy balance should be confirmed by not having FM changes during a period of time, although a small increase in FFM may occur. An alternative method to estimate the state of energy balance is to use the 'intake-balance' method. Based on changes in energy stores (i.e. changes in body weight[70] or composition[71,72]), it is possible to estimate the state of energy balance.

Despite AT being reported in twenty-seven out of thirty-three studies, the methodological quality of each study needs to be taken into consideration, since well-designed studies (online Supplementary File 2) reported lower or non-statistically significant values for AT. Furthermore, studies that assessed AT during a period of WL maintenance suggested that its magnitude cannot be a primary driver of weight regain[16]. In fact, when AT was measured under conditions of weight maintenance, values for AT were found to be reduced or statistically non-significant, comparing to when assessed during conditions of negative energy balance (Table 1). Also, studies comprising bariatric surgeries reported that AT tended to disappear throughout time. On the other hand, studies with poorer methodological designs that measured AT immediately after WL (under conditions of negative energy balance) must be interpreted carefully.

Although it remains unknown how much time would be needed to reverse the potential occurrence of AT under conditions of energy deficit, a period of several weeks in a true state of neutral energy balance could be necessary.

Conclusions

AT was found in (at least) one of the EE components in twenty-seven out of thirty-three studies, suggesting that WL may lead to a greater than predicted decrease in EE. Overall, these findings suggest that although WL may lead to AT in some of the energy expenditure components despite a high inter-individual variability, these values may be small or non-significant when higher-quality methodological designs are used. Furthermore, AT seems to be attenuated, or non-existent, after periods of weight stabilisation or neutral energy balance. Therefore, more high-quality studies are warranted not only to disclose the existence of AT in each energy expenditure component but to understand its clinical implications on weight management outcomes.

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Supplementary material

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