UNIVERSITY OF LEEDS

This is a repository copy of *Does Adaptive Thermogenesis occur after weight loss in adults? A systematic review*.

White Rose Research Online URL for this paper:
https://eprints.whiterose.ac.uk/172561/

Version: Accepted Version

Article:

Nunes, CL, Casanova, N, Francisco, R et al. (4 more authors) (2021) Does Adaptive Thermogenesis occur after weight loss in adults? A systematic review. British Journal of Nutrition. pp. 1-43. ISSN 0007-1145

https://doi.org/10.1017/s0007114521001094

© The Authors 2021. This article has been published in a revised form in British Journal of Nutrition https://doi.org/10.1017/S0007114521001094. This version is free to view and download for private research and study only. Not for re-distribution, re-sale or use in derivative works. Uploaded in accordance with the publisher's self-archiving policy.

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

White Rose university consortium
Universities of Leeds, Sheffield & York

eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk/

Accepted manuscript

Does Adaptive Thermogenesis occur after weight loss in adults? A systematic review

Catarina L. Nunes[1], Nuno Casanova[2], Ruben Francisco[1], Anja Bosy-Westphal[3], Mark Hopkins[2], Luís B. Sardinha[1], Analiza M. Silva[1]

Running title: Adaptive thermogenesis - Systematic Review

Affilitations:

[1] Exercise and Health Laboratory, CIPER, Faculdade Motricidade Humana, Universidade Lisboa, Estrada da Costa, 1499-688 Cruz-Quebrada, Portugal;

[2] School of Food Science and Nutrition, Faculty of Environment, University of Leeds, Leeds, UK;

[3] Department of Human Nutrition, Institute of Human Nutrition and Food Sciences, Christian-Albrechts University, Kiel, Germany.

Correspondent author:
Analiza M. Silva, Ph.D.

Laboratório de Exercício e Saúde, Faculdade de Motricidade Humana da Universidade de Lisboa

Estrada da Costa, 1499-002, Cruz-Quebrada, Portugal

Telephone: + 351 21 4149172

Email: analiza@fmh.ulisboa.pt

Key words: Energy balance, metabolic adaptation, metabolic compensations, behavioral compensations, weight loss.

THE NUTRITION SOCIETY
Advancing Nutritional Science

This peer-reviewed article has been accepted for publication but not yet copyedited or typeset, and so may be subject to change during the production process. The article is considered published and may be cited using its DOI
10.1017/S0007114521001094
The British Journal of Nutrition is published by Cambridge University Press on behalf of The Nutrition Society

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 with or without a weight stabilization phase. Studies published until May 15th, 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>18years; sample size≥10 participants; intervention period ≥1week; published in English; objective measures of total daily energy expenditure(TDEE), resting energy expenditure(REE) and sleeping energy expenditure(SEE). The systematic review was registered at PROSPERO(2020 CRD42020165348). A total of 33 studies comprising 2528 participants, were included. AT was observed in 27 out of 33 studies. Twenty-three studies showed significant values for AT for REE(82.8%), 4 studies for TDEE(80.0%) and 2 studies 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. Overall, 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 stabilization/neutral energy balance. Therefore, more high-quality studies are warranted not only to disclose the existence of AT, but to understand its clinical implications on weight management outcomes.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

INTRODUCTION

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 behavioral compensatory responses that occur during periods of negative energy balance. Some of these proposed compensatory responses include reductions in EE (8), PA behaviors (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) interventions. However, some studies have reported contrasting findings as they have not observed a significant value for AT (28, 32, 40).

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 resting energy expenditure (REE), total daily energy expenditure (TDEE), and sleeping energy expenditure (SEE) during or after WL induced by diet and/or exercise, bariatric surgery or pharmacological therapy, followed by weight stabilization in adults.

METHODOLOGY

This systematic review was conducted according to the 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 May 15th, 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 weight loss; 2) Observational with follow-up or experimental study; 3) Conducted in adults (>18 years); 4) A total sample size of at least 10 participants; 5) Intervention period of at least 1-week; 5) Published in English; 6) Objective measures of total daily EE, REE and SEE (indirect calorimetry, metabolic chamber, doubly labeled water) and 7) Objective measures of FM and FFM (Dual-energy X-ray Absorptiometry,

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

DXA; Air displacement plethysmography; Bioelectrical impedance analysis; and/or multicompartment molecular models (e.g. 4-compartment models, including combination of several techniques such as DXA, 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 breastfeeding; 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 May 15th, 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 caloric restriction, bariatric surgery, physical activity or exercise, pharmacotherapy); ii) terms representing the outcomes of interest (e.g. adaptive thermogenesis, metabolic adaptation, energy metabolism, resting energy expenditure, metabolic compensation); iii) terms representing the population of interest (e.g. adults); and iv) terms representing body composition components of interest (e.g. fat mass, 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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

strategy example for PubMed is provided as a supplementary file (Supplementary file 1).

Study selection and data processing

Based on the initial abstracts retrieved, duplicates were removed, and 25 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 33 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 supplementary material (Supplementary file 2).

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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, 69 were excluded (Supplementary file 3) and 33 were included in this systematic review. The PRISMA flow chart of the study selection is presented in Figure 1.

Figure 1.

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

- Resting energy expenditure (REE) – 29 studies;
- Total daily energy expenditure (TDEE) – 7 studies;
- Sleeping energy expenditure (SEE) – 2 studies;

Some articles included more than 1 intervention type and/or assessed AT in more than one EE component.

From the included studies, 6 (20.7%) were randomized controlled trials (RCT), 2 (6.9%) were randomized trials without a control group (RT), 12 (41.4%) were non-randomized trials (NRT), 3 (10.3%) were retrospective observational (RO) studies and 10 (34.5%) were considered prospective observational (PO) studies. A summary of the results reported in each study, divided by study type and %WL is presented in table 1.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Resting Energy Expenditure (REE)

A total of 29 studies reporting changes in REE were included in this review (12, 13, 16-40, 47, 48) (Table 2), divided in: RCT=4 (13.8%); NRT=12 (41.4%); RT=2 (6.9%); PO=8 (27.6%); RO=3 (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 3 studies had a mean BMI<30kg/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 10 studies reporting a WL > 10% (16-21, 25-27, 33) and 7 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 5 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 x PAL): ~67% (20, 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 >1.2g/kg) (17, 18, 33). A ketogenic diet was used by Gomez-Arbealez et al. (19). Karl and colleagues used 4 types of diets differing in carbohydrate (CHO) content: 55%, 60%, 70% or 80% CHO (24). Jonge et al. also divided the sample in 4 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 6.1MJ/day 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 resting energy expenditure (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 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, Pourhassan and Muller, used the sum of 7 tissue-level components obtained by magnetic resonance imaging (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 15 studies (16-18, 20-25, 27-31, 33). Only 3 studies did not report a significant AT after WL (19, 26, 32). Byrne et al. (20), which compared a continuous energy restriction (CER) versus an intermittent energy restriction (IER), only reported AT for the CER group (~209kJ/d), which lost ~8.4% of their initial weight. For the IER group, AT was not significant despite a greater WL (~-12.9%). Jonge et al. compared 4 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 2 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 disappeared or was attenuated after a period of

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

weight stabilization (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 1 article reported an exercise-only intervention (40), its results will be analyzed with combined diet and exercise interventions, comprising 7 articles (12, 13, 16, 23, 40, 47, 48).

Participants' characteristics. A total of 678 participants were involved (151 males). Only 1 study comprised participants with a BMI<25kg/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 5 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 that 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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Harris-Benedict equation to estimate REE (pREE), dividing mREE by pREE to calculate a ratio (48).

Adaptive thermogenesis. AT was reported in 6 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 ± 2.7 kg). Despite having AT after WL, 1 study reported an attenuation after 1-2y of follow up (16). The values for AT ranged between 126-418 kJ/d except for 2 studies (12, 13). These studies reported significant weight losses (WL = -58.3±24.9 kg (12) and WL = -57.6 ± 23.8 kg (13)) and showed a larger AT (~837-1255 kJ/d which increased during follow up for ~2092kJ/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 (75 males) underwent bariatric surgery. Baseline characteristics were similar among studies, with all including participants with obesity (mean BMI>30kg/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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 4 of the 6 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 to 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 5 studies reporting changes in TDEE were included in this review (34, 50-53), with 2 RCTs (40%) and 3 prospective observational studies included (60%) (Table 3).

From those, 1 was related to a diet-only intervention (50), 2 to a diet-only vs. a combined diet and exercise intervention (51, 52) and 2 to bariatric surgery (34, 53). Due to the small number of studies, all intervention types were analyzed together.

Participants' characteristics. The 5 studies comprised 164 participants (53 males). Participants from the studies related to lifestyle interventions had a BMI ranging from 25 to 30kg/m^2 (50-52). For studies that used bariatric surgeries, BMI was above 40kg/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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 were assessed by doubly labeled 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 4 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 ± 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 (SEE)

Only two studies reporting changes in SEE were found (50, 51) (Table 4). One had a RCT design and 1 was a prospective observational study.

Participants' characteristics. The 2 studies comprised 75 individuals with a mean BMI between 25 and 30 kg/m^2 (30 males). Both studies reported a WL >10%.

Intervention type. Marlatt et al. generated a caloric deficit of 25% based on each participant's energy needs (50), while Lecoultre et al. used two different approaches: i)

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 stabilization phase. Overall, significant values for AT were reported in 27 of the 33 included studies. Most studies reported a large variability between subjects (for example, when a standard deviation is higher than the respective mean) with regard to the magnitude of WL and/or AT.

<u>Resting Energy Expenditure</u>

The majority of the studies aimed to assess AT in REE. From those, 23 out of 29 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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

catecholamines after WL (22). 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 are 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 weight loss (~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 bodyweight 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,

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 utilized. 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 1 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 to lifestyle interventions. Interestingly, despite large WL (~-20%), two studies did not report a significant value for AT (36, 39). Altogether, the findings from

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 1 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 (~209-251kJ/d) after a 4-week weight stabilization period (16). However, it is important to acknowledge that weight stability does not imply the presence of a neutral energy balance, as in this study participants were under a very low caloric ketogenic diet (3.3MJ/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 stabilization, participants had lost an extra 0.8kg of FM while gaining 0.9kg 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 heterogenous results. Therefore, in order to examine whether AT is present after WL, measurements should be conducted under conditions of neutral energy balance.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 current literature, the most common method is the use of regression models to predict REE. This method includes the utilization 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 4-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 DXA), 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 2-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 nitrogen, glycogen and sodium 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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

composition of FFM (losses of high-metabolic rate organs vs skeletal muscle vs body water) may dramatically influence the prediction of REE. Therefore, using 2-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 to 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 behaviors 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 (versus 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 metabolizable 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 standardization 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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

measurements of FM and FFM, variables such 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 stabilization 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 27 out of 33 studies, the methodological quality of each study needs to be taken into consideration, since well-designed studies (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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

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 27 out of 33 studies, suggesting that WL may lead to a greater than predicted decrease in EE. Overall, these findings suggest that although weight loss 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 stabilization 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.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

FUNDING

C.L.N. was supported with a PhD scholarship from the Portuguese Foundation for Science and Technology (SFRH/BD/143725/2019).

CONFLICTS OF INTEREST

The authors reported no conflicts of interest.

AUTHORSHIP

CLN and AMS contributed to the conception and design. CLN, NC and RF contributed to data acquisition, analysis and interpretation. CLN and NC wrote the systematic review. AB, MH, LB and AMS revised it critically for important intellectual content. All the authors approved the final version of the manuscript.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

REFERENCES

1. Hall KD, Guo J. Obesity Energetics: Body Weight Regulation and the Effects of Diet Composition. Gastroenterology. 2017;152(7):1718-27.e3.

2. Edholm OG, Adam JM, Healy MJ, Wolff HS, Goldsmith R, Best TW. Food intake and energy expenditure of army recruits. Br J Nutr. 1970;24(4):1091-107.

3. Casanova N, Beaulieu K, Finlayson G, Hopkins M. Metabolic adaptations during negative energy balance and their potential impact on appetite and food intake. Proc Nutr Soc. 2019;78(3):279-89.

4. Melby CL, Paris HL, Foright RM, Peth J. Attenuating the Biologic Drive for Weight Regain Following Weight Loss: Must What Goes Down Always Go Back Up? Nutrients. 2017;9(5).

5. Wadden TA, Neiberg RH, Wing RR, Clark JM, Delahanty LM, Hill JO, et al. Four-year weight losses in the Look AHEAD study: factors associated with long-term success. Obesity (Silver Spring). 2011;19(10):1987-98.

6. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63.

7. Heymsfield SB, Harp JB, Reitman ML, Beetsch JW, Schoeller DA, Erondu N, et al. Why do obese patients not lose more weight when treated with low-calorie diets? A mechanistic perspective. Am J Clin Nutr. 2007;85(2):346-54.

8. Thomas DM, Bouchard C, Church T, Slentz C, Kraus WE, Redman LM, et al. Why do individuals not lose more weight from an exercise intervention at a defined dose? An energy balance analysis. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2012;13(10):835-47.

9. Levine JA, Eberhardt NL, Jensen MD. Role of nonexercise activity thermogenesis in resistance to fat gain in humans. Science (New York, NY). 1999;283(5399):212-4.

10. Dulloo AG, Jacquet J, Montani JP, Schutz Y. Adaptive thermogenesis in human body weight regulation: more of a concept than a measurable entity? Obesity reviews : an official journal of the International Association for the Study of Obesity. 2012;13 Suppl 2:105-21.

11. Major GC, Doucet E, Trayhurn P, Astrup A, Tremblay A. Clinical significance of adaptive thermogenesis. Int J Obes (Lond). 2007;31(2):204-12.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

12. Fothergill E, Guo J, Howard L, Kerns JC, Knuth ND, Brychta R, et al. Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. Obesity (Silver Spring). 2016;24(8):1612-9.

13. Johannsen DL, Knuth ND, Huizenga R, Rood JC, Ravussin E, Hall KD. Metabolic slowing with massive weight loss despite preservation of fat-free mass. J Clin Endocrinol Metab. 2012;97(7):2489-96.

14. Tremblay A, Major G, Doucet É, Trayhurn P, Astrup A. Role Of Adaptive Thermogenesis In Unsuccessful Weight-Loss Intervention. Future Lipidology. 2007;2(6):651-8.

15. Tremblay A, Royer MM, Chaput JP, Doucet E. Adaptive thermogenesis can make a difference in the ability of obese individuals to lose body weight. Int J Obes (Lond). 2013;37(6):759-64.

16. Martins C, Gower BA, Hill JO, Hunter GR. Metabolic adaptation is not a major barrier to weight-loss maintenance. Am J Clin Nutr. 2020.

17. Thom G, Dombrowski SU, Brosnahan N, Algindan YY, Rosario Lopez-Gonzalez M, Roditi G, et al. The role of appetite-related hormones, adaptive thermogenesis, perceived hunger and stress in long-term weight-loss maintenance: a mixed-methods study. European Journal of Clinical Nutrition. 2020;74(4):622-32.

18. Nymo S, Coutinho SR, Torgersen LH, Bomo OJ, Haugvaldstad I, Truby H, et al. Timeline of changes in adaptive physiological responses, at the level of energy expenditure, with progressive weight loss. Br J Nutr. 2018;120(2):141-9.

19. Gomez-Arbelaez D, Crujeiras AB, Castro AI, Martinez-Olmos MA, Canton A, Ordoñez-Mayan L, et al. Resting metabolic rate of obese patients under very low calorie ketogenic diet. Nutr Metab (Lond). 2018;15:18.

20. Byrne NM, Sainsbury A, King NA, Hills AP, Wood RE. Intermittent energy restriction improves weight loss efficiency in obese men: the MATADOR study. Int J Obes (Lond). 2018;42(2):129-38.

21. Rosenbaum M, Leibel RL. Models of energy homeostasis in response to maintenance of reduced body weight. Obesity (Silver Spring). 2016;24(8):1620-9.

22. Müller MJ, Enderle J, Pourhassan M, Braun W, Eggeling B, Lagerpusch M, et al. Metabolic adaptation to caloric restriction and subsequent refeeding: the Minnesota Starvation Experiment revisited. Am J Clin Nutr. 2015;102(4):807-19.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

23. McNeil J, Schwartz A, Rabasa-Lhoret R, Lavoie JM, Brochu M, Doucet É. Changes in leptin and peptide YY do not explain the greater-than-predicted decreases in resting energy expenditure after weight loss. J Clin Endocrinol Metab. 2015;100(3):E443-52.

24. Karl JP, Roberts SB, Schaefer EJ, Gleason JA, Fuss P, Rasmussen H, et al. Effects of carbohydrate quantity and glycemic index on resting metabolic rate and body composition during weight loss. Obesity (Silver Spring). 2015;23(11):2190-8.

25. Camps SG, Verhoef SP, Westerterp KR. Leptin and energy restriction induced adaptation in energy expenditure. Metabolism. 2015;64(10):1284-90.

26. Pourhassan M, Bosy-Westphal A, Schautz B, Braun W, Glüer CC, Müller MJ. Impact of body composition during weight change on resting energy expenditure and homeostasis model assessment index in overweight nonsmoking adults. Am J Clin Nutr. 2014;99(4):779-91.

27. Camps SG, Verhoef SP, Westerterp KR. Weight loss, weight maintenance, and adaptive thermogenesis. Am J Clin Nutr. 2013;97(5):990-4.

28. Bosy-Westphal A, Schautz B, Lagerpusch M, Pourhassan M, Braun W, Goele K, et al. Effect of weight loss and regain on adipose tissue distribution, composition of lean mass and resting energy expenditure in young overweight and obese adults. Int J Obes (Lond). 2013;37(10):1371-7.

29. de Jonge L, Bray GA, Smith SR, Ryan DH, de Souza RJ, Loria CM, et al. Effect of diet composition and weight loss on resting energy expenditure in the POUNDS LOST study. Obesity (Silver Spring). 2012;20(12):2384-9.

30. Goele K, Bosy-Westphal A, Rumcker B, Lagerpusch M, Muller MJ. Influence of changes in body composition and adaptive thermogenesis on the difference between measured and predicted weight loss in obese women. Obes Facts. 2009;2(2):105-9.

31. Bosy-Westphal A, Kossel E, Goele K, Later W, Hitze B, Settler U, et al. Contribution of individual organ mass loss to weight loss-associated decline in resting energy expenditure. Am J Clin Nutr. 2009;90(4):993-1001.

32. Doucet E, St-Pierre S, Alméras N, Després JP, Bouchard C, Tremblay A. Evidence for the existence of adaptive thermogenesis during weight loss. Br J Nutr. 2001;85(6):715-23.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

33. Dulloo AG, Jacquet J. Adaptive reduction in basal metabolic rate in response to food deprivation in humans: a role for feedback signals from fat stores. Am J Clin Nutr. 1998;68(3):599-606.

34. Wolfe BM, Schoeller DA, McCrady-Spitzer SK, Thomas DM, Sorenson CE, Levine JA. Resting Metabolic Rate, Total Daily Energy Expenditure, and Metabolic Adaptation 6 Months and 24 Months After Bariatric Surgery. Obesity (Silver Spring). 2018;26(5):862-8.

35. Bettini S, Bordigato E, Fabris R, Serra R, Dal Pra C, Belligoli A, et al. Modifications of Resting Energy Expenditure After Sleeve Gastrectomy. Obes Surg. 2018;28(8):2481-6.

36. Browning MG, Rabl C, Campos GM. Blunting of adaptive thermogenesis as a potential additional mechanism to promote weight loss after gastric bypass. Surg Obes Relat Dis. 2017;13(4):669-73.

37. Tam CS, Rigas G, Heilbronn LK, Matisan T, Probst Y, Talbot M. Energy Adaptations Persist 2 Years After Sleeve Gastrectomy and Gastric Bypass. Obes Surg. 2016;26(2):459-63.

38. Carrasco F, Papapietro K, Csendes A, Salazar G, Echenique C, Lisboa C, et al. Changes in resting energy expenditure and body composition after weight loss following Roux-en-Y gastric bypass. Obes Surg. 2007;17(5):608-16.

39. Coupaye M, Bouillot JL, Coussieu C, Guy-Grand B, Basdevant A, Oppert JM. One-year changes in energy expenditure and serum leptin following adjustable gastric banding in obese women. Obes Surg. 2005;15(6):827-33.

40. Hopkins M, Gibbons C, Caudwell P, Hellstrom PM, Naslund E, King NA, et al. The adaptive metabolic response to exercise-induced weight loss influences both energy expenditure and energy intake. Eur J Clin Nutr. 2014;68(5):581-6.

41. Muller MJ, Bosy-Westphal A. Adaptive thermogenesis with weight loss in humans. Obesity (Silver Spring). 2013;21(2):218-28.

42. Muller MJ, Enderle J, Bosy-Westphal A. Changes in Energy Expenditure with Weight Gain and Weight Loss in Humans. Curr Obes Rep. 2016;5(4):413-23.

43. Rosenbaum M, Leibel RL. Adaptive thermogenesis in humans. Int J Obes (Lond). 2010;34 Suppl 1(0 1):S47-55.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

44. Trexler ET, Smith-Ryan AE, Norton LE. Metabolic adaptation to weight loss: implications for the athlete. Journal of the International Society of Sports Nutrition. 2014;11(1):7.

45. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.

46. Armijo-Olivo S, Stiles CR, Hagen NA, Biondo PD, Cummings GG. Assessment of study quality for systematic reviews: a comparison of the Cochrane Collaboration Risk of Bias Tool and the Effective Public Health Practice Project Quality Assessment Tool: methodological research. J Eval Clin Pract. 2012;18(1):12-8.

47. Ten Haaf T, Verreijen AM, Memelink RG, Tieland M, Weijs PJM. Reduction in energy expenditure during weight loss is higher than predicted based on fat free mass and fat mass in older adults. Clin Nutr. 2018;37(1):250-3.

48. Marzullo P, Minocci A, Mele C, Fessehatsion R, Tagliaferri M, Pagano L, et al. The relationship between resting energy expenditure and thyroid hormones in response to short-term weight loss in severe obesity. PLoS One. 2018;13(10):e0205293.

49. Müller MJ, Bosy-Westphal A, Klaus S, Kreymann G, Lührmann PM, Neuhäuser-Berthold M, et al. World Health Organization equations have shortcomings for predicting resting energy expenditure in persons from a modern, affluent population: generation of a new reference standard from a retrospective analysis of a German database of resting energy expenditure. Am J Clin Nutr. 2004;80(5):1379-90.

50. Marlatt KL, Redman LM, Burton JH, Martin CK, Ravussin E. Persistence of weight loss and acquired behaviors 2 y after stopping a 2-y calorie restriction intervention. Am J Clin Nutr. 2017;105(4):928-35.

51. Lecoultre V, Ravussin E, Redman LM. The fall in leptin concentration is a major determinant of the metabolic adaptation induced by caloric restriction independently of the changes in leptin circadian rhythms. J Clin Endocrinol Metab. 2011;96(9):E1512-6.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

52. Redman LM, Heilbronn LK, Martin CK, de Jonge L, Williamson DA, Delany JP, et al. Metabolic and behavioral compensations in response to caloric restriction: implications for the maintenance of weight loss. PLoS One. 2009;4(2):e4377.

53. Novaes Ravelli M, Schoeller DA, Crisp AH, Shriver T, Ferriolli E, Ducatti C, et al. Influence of Energy Balance on the Rate of Weight Loss Throughout One Year of Roux-en-Y Gastric Bypass: a Doubly Labeled Water Study. Obes Surg. 2019;29(10):3299-308.

54. MacLean PS, Bergouignan A, Cornier MA, Jackman MR. Biology's response to dieting: the impetus for weight regain. American Journal of Physiology - Regulatory, Integrative and Comparative Physiology. 2011;301(3):R581-600.

55. Rosenbaum M, Goldsmith RL, Haddad F, Baldwin KM, Smiley R, Gallagher D, et al. Triiodothyronine and leptin repletion in humans similarly reverse weight-loss-induced changes in skeletal muscle. Am J Physiol Endocrinol Metab. 2018;315(5):E771-e9.

56. Beckman LM, Beckman TR, Earthman CP. Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass procedure: a review. J Am Diet Assoc. 2010;110(4):571-84.

57. Drummen M, Tischmann L, Gatta-Cherifi B, Fogelholm M, Raben A, Adam TC, et al. High Compared with Moderate Protein Intake Reduces Adaptive Thermogenesis and Induces a Negative Energy Balance during Long-term Weight-Loss Maintenance in Participants with Prediabetes in the Postobese State: A PREVIEW Study. The Journal of Nutrition. 2019;150(3):458-63.

58. Fuller NJ, Jebb SA, Laskey MA, Coward WA, Elia M. Four-component model for the assessment of body composition in humans: comparison with alternative methods, and evaluation of the density and hydration of fat-free mass. Clin Sci (Lond). 1992;82(6):687-93.

59. Smith-Ryan AE, Mock MG, Ryan ED, Gerstner GR, Trexler ET, Hirsch KR. Validity and reliability of a 4-compartment body composition model using dual energy x-ray absorptiometry-derived body volume. Clin Nutr. 2017;36(3):825-30.

60. Wilson JP, Mulligan K, Fan B, Sherman JL, Murphy EJ, Tai VW, et al. Dual-energy X-ray absorptiometry-based body volume measurement for 4-compartment body composition. Am J Clin Nutr. 2012;95(1):25-31.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

61. Müller MJ, Bosy-Westphal A. Effect of Over- and Underfeeding on Body Composition and Related Metabolic Functions in Humans. Curr Diab Rep. 2019;19(11):108.

62. Elia M. Organ and tissue contribution to metabolic rate In: Kinney JM, Tucker HN, editors. Energy metabolism: Tissue determinants and cellular corollaries. New York: Raven Press; 1992.

63. Müller MJ, Wang Z, Heymsfield SB, Schautz B, Bosy-Westphal A. Advances in the understanding of specific metabolic rates of major organs and tissues in humans. Curr Opin Clin Nutr Metab Care. 2013;16(5):501-8.

64. Bosy-Westphal A, Braun W, Schautz B, Müller MJ. Issues in characterizing resting energy expenditure in obesity and after weight loss. Front Physiol. 2013;4:47.

65. Quercia I, Dutia R, Kotler DP, Belsley S, Laferrère B. Gastrointestinal changes after bariatric surgery. Diabetes Metab. 2014;40(2):87-94.

66. Damms-Machado A, Friedrich A, Kramer KM, Stingel K, Meile T, Küper MA, et al. Pre- and postoperative nutritional deficiencies in obese patients undergoing laparoscopic sleeve gastrectomy. Obes Surg. 2012;22(6):881-9.

67. Lefebvre P, Letois F, Sultan A, Nocca D, Mura T, Galtier F. Nutrient deficiencies in patients with obesity considering bariatric surgery: a cross-sectional study. Surg Obes Relat Dis. 2014;10(3):540-6.

68. Gregory DM, Twells LK, Lester KK, Midodzi WK, Pedersen MR, Pace D, et al. Preoperative and Postoperative Assessments of Biochemical Parameters in Patients with Severe Obesity Undergoing Laparoscopic Sleeve Gastrectomy. Obes Surg. 2018;28(8):2261-71.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

69. Johnstone AM, Murison SD, Duncan JS, Rance KA, Speakman JR. Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine. Am J Clin Nutr. 2005;82(5):941-8.

70. Hall KD, Chow CC. Estimating changes in free-living energy intake and its confidence interval. The American Journal of Clinical Nutrition. 2011;94(1):66-74.

71. Racette SB, Das SK, Bhapkar M, Hadley EC, Roberts SB, Ravussin E, et al. Approaches for quantifying energy intake and %calorie restriction during calorie restriction interventions in humans: the multicenter CALERIE study. Am J Physiol Endocrinol Metab. 2012;302(4):E441-8.

72. Shook RP, Hand GA, O'Connor DP, Thomas DM, Hurley TG, Hébert JR, et al. Energy Intake Derived from an Energy Balance Equation, Validated Activity Monitors, and Dual X-Ray Absorptiometry Can Provide Acceptable Caloric Intake Data among Young Adults. The Journal of Nutrition. 2018;148(3):490-6.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

	%WL		REE		TDEE		SEE
			WL	WM	WL	WM	WL
RCT	<10%	Marzullo et al, 2018 (48)	↓				
		de Jonge et al, 2012 (29)	↓				
		Karl et al, 2015 (24)	↓	✗			
	10 – 15%	Doucet et al, 2001 (32)	↓	↓ Men ✗ Women			
		Byrne et al, 2018 (20)	↓	✗			
		Redman et al, 2009 (52)			↓ CR and LCD ✗ Exercise	✗ (CR)	
		Lecoultre et al, 2011(51)			↓ CR and LCD ✗ Diet and Exercise		↓ (CR)
NRT	<5%	Hopkins et al, 2014 (40)	✗				
		Bosy Westphal et al, 2009 (31)	↓				
	5 a 10%	Müller et al, 2015 (22)	↓				
		Camps et al, 2013 (27)	↓				
		Goele et al, 2009 (30)	↓				
		Camps et al, 2015 (25)	↓				
	10-20%	Bosy-Westphal et al, 2013(28)		↓ (weight regainers)			
		Thom et al 2020(17)	↓				
		Nymo et al, 2018 (18)	↓				
	>20%	Gomez-Arbelaez et al, 2018 (19)	✗				
		Rosenbaum et al, 2016 (21)	↓				
		Dulloo et al, 1998 (33)	↓				
RT	<10%	McNeil et al, 2015 (23)	↓				
Observational	<10%	Ten Haaf et al, 2018 (47)	↓				
	10-20%	Pourhassan et al, 2014 (26)	✗				
		Marlatt et al, 2017 (50)			✗		↓
		Martins et al, 2020 (16)	↓				
		Coupaye et al, 2005 (39)	✗				
	20-30%	Wolfe et al, 2018 (34)	↓	✗	↓	✗	
		Tam et al 2016 (37)	↓	✗			
		Browning et al, 2016 (36)	✗				
		Ravelli et al 2019 (53)			↓	✗	
	>30%	Bettini et al, 2018 (35)	↓				
		Carrasco et al, 2007 (38)	↓				
		Johannsen et al, 2012 (13)	↓				
		Fothergill et al, 2016 (12)	↓	↓			

Table 1. Summary of the results

Legend: 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

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 2. Resting Energy Expenditure (REE)

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Diet-only intervention								
Martins et al, 2020 (16)	O (retrospective)	n=171 females BMI=28.3±1.3 kg/m^2 Age=35.2±6.3y 3 groups: Diet only Diet + aerobic training Diet + resistance training	Diet: ~3.3 MJ/d: 20–22% fat, 20–22% protein 56–58% CHO	2y 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 stabilization	WL= −12.2 ± 2.6 kg (−15.7% ± 2.9%); No metabolic adaptation was seen at 1- and 2-y follow-up in all participants	AT= −226 ± 439 kJ/d AT is minimal when measurements are taken under conditions of weight stability
Thom et al 2020(17)	NRT	N=15 females BMI=39.4± 4.3 Age=46.3±9.5y	Diet only: 3.5–3.7 MJ/d; 59% CHO, 13% fat, 26% protein, 2% fiber	6mo + 18mo 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 ± 6.3 kg (~13,5%); Significant reductions in TAT (-11.5 ± 4.9kg) with preservation of SMM. Reductions in Leptin and GLP-1. Increases in Ghrelin.	AT=−628 ± 678 kJ/d Large inter-individual variability in adaptive thermogenesis.
Nymo et al, 2018 (18)	NRT	N=31 (18 males) BMI = 36.7±4.5 kg/m^2 Age = 43±10y	Diet only: VLCD 2.3-2.8MJ/d 42 % CHO, 36% PRO, 18% Fat and 4% fiber.	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 stabilization.	WL: (week 9) -18.7±4.1kg FM and FFM was 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, 2018 (19)	NRT	N=20 (8 males) BMI = 35.5±4.4 kg/m^2 Age = 47.2±10.2y	Diet only: ketogenic diet; VLCD (2.5-3.3MJ/day), <50g/d HC and only 10g olive oil per day. Protein 0.8-1.2g/kg/day	4mo	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±6.9; (~-21%) Significant reductions for FM and FFM. Severe reductions for leptin.	Non-significant AT.
Byrne et al, 2018 (20)	RCT	N=36 males Age: 25-54y. 2 groups: - Continuous energy restriction (CER) n=19 BMI = 34.3±3.0 kg/m^2 Age = 41.2±5.5y - Intermittent energy restriction (IER) n=17 BMI 34.1±4.0 kg/m^2 Age = 39.5±8.4y	Diet only: ~67% of individual weight maintenance energy requirements IER: 2 weeks of ER + 2 weeks EB CER: Continuous ER	CER: 28weeks IER: 42weeks + 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±3.7kg (~-8.4%); IER: WL: -14.1±5.6kg (~-12.9%) Significant reductions for FM in both groups.	Significant AT only for CER group (~-209kJ/d). No information about AT after weight maintenance phase.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 2. Continued

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Rosenbaum et al, 2016 (21)	NRT	N=17 (3 males) BMI = 44.6 ±11.2 kg/m^2 Age = 28.4±8.8y	Diet only 3.3 MJ/d liquid formula diet; 40% fat, 45% CHO, 15% protein + mineral supplementation	7-13weeks to achieve 10% WL + 8-14weeks to achieve 20%	Body composition: DXA; TEE - Doubly labeled 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±870kJ/d 20%WL = -778±983 kJ/d
Müller et al, 2015 (22)	NRT	N=32 men BMI: 20.7-29.3 kg/m^2 Age: 20–37 y	Diet-only: CR: 50% of energy needs. Protein intake: 49±6g/d. food and drinks provided	6weeks (1week overfeeding, 3weeks CR, 2weeks overfeeding)	Body composition: MRI (ECHOMRI-AH) REE: Indirect Calorimetry (Vmax Spectra, SensorMedics); PA: 24h heart rate and accelerometry.	pREE was based on the **sum of 7 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±0.873kg (~-8%); Decreases in FM (~-18%) Leptin decreased. No associations between hormones and AT.	AT= -301±481kJ/d. Considerable between-subject variance in AT and weight- loss. Non-significant after refeeding
McNeil et al, 2015 (23)	RT w/ no CG	N=93 women BMI = 32.1±4.3 kg/m^2 Age = 58.1±4.8y 2 groups: Diet-only (n=65) Diet + exercise (n=28)	Diet: REE x 1.4 and then ~3.3MJ was subtracted from this result. 30% lipids and 15%proteins. resistance training 3x week	6mo	Body composition: DXA (General Electric Lunar Prodigy) REE: indirect calorimetry TEE: doubly-labeled 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±4.6kg Diet + Exercise: WL=-6.7±4.5kg Leptin and PYY were not significant predictors of the differences between pREE and mREE.	Greater predicted vs. measured REE was noted post-intervention (data not shown, ~126kJ/d). This significant effect disappeared after correcting for the degree of caloric restriction.
Karl et al, 2015 (24)	RCT	N=91 (39 males) BMI = 28-38 kg/m^2 Age = 45-65y	Diet only: Phase 1 - 5weeks 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.	22weeks (5weeks phase 1 + 12 weeks phase 2 + 5weeks phase 3) + 12mo 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 4 groups lost weight (~-7,5%) ~80% WL was FM No difference in CHO content	Existence of AT after WL (-226kJ/d [95%CI: -314 kJ/d, -138kJ/d]) but not after 5weeks of weight stabilization.
Camps et al, 2015 (25)	NRT	N=82 (23 males) BMI = 31.9±3.0 kg/m^2 Age = 41±8y;	Diet-only: VLCD 2.1 MJ/d; 51.9g 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 labeled 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 ± 4.1% Reductions in FM and FFM. Reductions in Leptin	mREE/pREE= 0.96±0.07. Six percent of the variation in REEm/REEp after the diet was explained by the decrease in leptin.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 2. Continued

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Pourhassan et al, 2014 (26) *(information only about WL group)*	O (prospective)	N=30 BMI = 33.6 ± 5.4 kg/m^2 Age = 36.9±8.4y	Diet-only: Very low-calorie diet	6mo	Body composition: Fuller 4C model. (BodPod + deuterium 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±4.9kg), which ~-72% was FM. Reductions in T3 and T4.	Non-significant AT (0.01 ± 0.93 MJ/d)
Camps et al, 2013 (27)	NRT	N=91 (22 males) BMI = 31.9±3.0 kg/m^2 Age = 40±9y	Diet-only: VLCD (2.1 MJ/d) 51.9 g PRO, 50.2 g CHO, 6.9 g lipids	8week + 44week follow up	Body composition - Siri's 3C model. BODPOD and deuterium diluition. 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.	8weeks: WL = -9.6±4.1kg (~-10%) 52weeks: WL = -6.0±5.7kg (~-7%)	8 weeks: AT = 0.967 ± 0.007 52 weeks: AT = 0.979 ± 0.007
Bosy-Westphal et al, 2013(28)	NRT	N=47 (11 males) 2 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 ± 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) x 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 ± 3.3kg. Weight regainers: WL = -9.0 ± 4.3kg. Decreases in T3 only for weight regainers after WL and follow up.	Significant AT only at weight regainers after WL (-0.39 ± 0.57 MJ/d).
de Jonge et al, 2012 (29)	RCT	N=811 (296 males) BMI from 25 - ≤40 kg/m^2 Age from 30–70 y	Diet-only: 4 types of caloric restriction: (i) 20% fat/15% PRO (ii) 20% fat/25% PRO (iii) 40% fat/15% PRO (iv) 40% fat/25% PRO	6months + 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±0.42 (iii) to -6.80±0.42 (ii). 24mo: From -3.26±0.56 (i) to -5.03±0.58 (ii).	6 months: Only groups (i) and (ii) reported significant values for AT. AT = −76 ± 28 kJ/d 24 months: +91 ± 42 kJ/d
Goele et al, 2009 (30)	NRT	N=48 women BMI = 35.4 ± 4.4 kg/m^2 Age = 31.5 ± 6.1y	Diet-only: 4.2 MJ/day (2 meals of a formula diet and a low-fat meal per day)	13.9 ± 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 ±3.9 kg (~-8.4%)	Significant AT in 26 of 48 women (–13.4 ± 5.0 kJ/kg FFM).
Bosy Westphal et al, 2009 (31)	NRT	N=45 women BMI from 28.7-46.8 kg/m^2 Age from 22-46y	Diet-only: Low calorie diet (3.3 – 4.2 MJ/d)	12.7 ± 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) x the specific tissue metabolic rate. AT was assessed after WL.	WL=9.5±3.4kg (~-4%) Decreases in Leptin and T3	AT was 230 ± 650 kJ/d Correlations with T3 concentrations.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 2. Continued

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Doucet et al, 2001 (32)	RCT	N=35 (15 males) Age = 44.3±1.7y (males) and 41.4±1.1y (females)	Diet + pharmacological therapy: 2 groups: 60mg/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 stabilization.
Dulloo et al, 1998 (33)	NRT	N= 32 males Age: 25 ± 4 y Weight: 69.4 ± 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	12w baseline + 24w semistarvation + 12weels 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 week: AT =-1491 ± 514 kJ/d S24 week: AT = -1706 ± 477 kJ/d Refeeding: AT =-693 ± 464 kJ/d Huge variability in BMR reductions
Exercise only and combined exercise and diet interventions								
Martins et al, 2020 (16)	O (retrospective)	n=171 females BMI=28.3±1.3 kg/m^2 Age=35.2±6.3y 3 groups: Diet only Diet + aerobic training Diet + resistance training	Diet + exercise: Aerobic exercise training OR resistance training (3x week)	2 years of 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** using age, sex, race, FM and FFM. AT was measured after a 4-week period of weight stabilization	WL= −12.2 ± 2.6 kg (−15.7% ± 2.9%); No metabolic adaptation was seen at 1- and 2-y follow-up in all participants	AT= −226 ± 439 kJ/d AT is minimal when measurements are taken under conditions of weight stability and does not predict weight regain up to 2 years follow-up.
Ten Haaf et al, 2018 (47)	O (retrospective)	N=254 (88 males) BMI=31.7 ± 4.4 kg/m^2 Age=51±14 y 2 groups: Younger adults (n=122) BMI=31.0 ± 4.4 kg/m^2 Age=40±9 y Older adults (N=132) BMI=32.5 ± 4.3 kg/m^2 Age=62±5 y	Diet + exercise: All subjects went through a hypocaloric diet (30% lipids, 52% CHO, and 18%PRO). A subgroup completed and exercise program.	8 to 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, gender and FFM*age interaction. **AT = pREE-mREE** and corrected for measured versus predicted REE differences at baseline. AT was calculated after WL	Young adults: WL=-2.8±3.3kg; FM=-3.0±3.6kg. Older adults: WL: -3.2±3.0kg; FM=-3.4±3.3kg.	Significant AT in older adults (-278±774 kJ/d) but not in younger adults. Whole sample: -176 ± 715 kJ/d
Marzullo et al, 2018 (48)	NRT	N=100 (50 males) BMI = 45.1±4.8 kg/m^2 Age = 40.4±12.7y	Diet + exercise: 75% of mREE. 30% lipids, 52% CHO, 18% PRO. Aerobic PA - 2 sessions of 30min for	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%.	Significant WL (-5.5±1.8%) Significant reductions for FM and FFM only for men.	REEm/REEp = 91.8±10.2% (<100%) Association between REE and thyroid hormones

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

			5days/week.			AT was calculated after WL.		

Table 2. Continued

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Fothergill et al, 2016 (12)	O (prospective)	N=14 (6 males) BMI = 49.5±10.1 kg/m^2 Age = 34.9±10.3y.	Diet + exercise: Restricted diet (~70% of their baseline energy requirements) Physical activity: 6x a week, 90min/d of supervised vigorous circuit training and/or aerobic training.	6y follow up	Body composition: DXA (iDXA, GE Lunar) REE - Indirect calorimetry (TrueOne Metabolic cart) TEE - double labeled 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±24.9kg. Decreases in FM and FFM. Increases of PA Significant decreases in leptin, T4 and TG. At 6y, 41.0±31.3 of the lost weight was regained.	Presence of AT after 30weeks of competition (-1150 ± 866 kJ/d) and after 6y (-2088 ± 866 kJ/d).
McNeil et al, 2015 (23)	RT w/ no CG	N=93 women BMI = 32.1±4.3 kg/m^2 Age = 58.1±4.8y 2 groups: Diet-only (n=65) Diet + exercise (n=28)	Diet: REE x 1.4 and then 3.3 MJ was subtracted from this result. 30% lipids and 15%proteins. Supervised resistance training 3x week	6mo	Body composition: DXA (General Electric Lunar Prodigy) REE: indirect calorimetry TEE: doubly-labeled 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±4.6kg Diet + Exercise: WL=-6.7±4.5kg Significant time x 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 vs. measured REE was noted post-intervention (data not shown, -126kJ/d). Participants with higher caloric restriction saw greater decreases in their mREE vs pREE. This significant effect disappeared after correcting for the degree of caloric restriction.
Hopkins et al, 2014 (40)	NRT	N=30 women BMI = 30.6±3.6 kg/m^2 Age = 40.6±9.1y	Exercise-only: Supervised aerobic exercise designed to expend 10.5 MJ/week	12weeks	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. AT was calculated immediately after the WL programme.	Small but significant WL (84.3±10.3 to 83.7±10.7 (week 6) and to 83.0±11.2 (week 12)) No significant loss of FFM Decrease in Leptin.	Non significant AT Highly variability between subjects
Johannsen et al, 2012 (13)	O (prospective)	N=16 (7 males) BMI = 49.4±9.4 kg/m^2 Age = 33±10y	Diet + exercise: Restricted diet (~70% of their baseline energy requirements) Physical activity: 6x a week, 90min/d of supervised vigorous circuit training and/or aerobic training.	30weeks	Body composition: Dual-energy x-ray absorptiometry (GE Lunar). REE - Indirect Calorimetry (Max II metabolic cart); Total daily energy expenditure (TEE) - Double labeled 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±4.9kg (>-10%) 30 weeks: WL=-57.6±23.8kg (~-38%) Decreases in leptin and T3. Increases in adiponectin.	6 weeks: AT = -1021 ± 967 kJ/d 30weeks AT= -2109 ± 715 kJ/d No association between changes in T3 and AT.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 2. Continued

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Surgery								
Wolfe et al, 2018 (34)	O (prospective)	N= 25 (3 males) BMI = 47±6 kg/m^2 Age = 45±11y	Bariatric Surgery (88% Roux-em-Y Gastric Bypass, 8% adjustable gastric banding and 4% biliopancreatic bypass with duodenal switch).	24mo	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 6mo and 24mo.	6mo: WL = -24%±5%; FM = -37%±8%; FFM = -11±4%. 24mo: WL = -27±10.2kg	Presence of AT at 6mo (REE = -674 ± 582 kJ/d; but not at 24mo.
Bettini et al, 2018 (35)	O (prospective)	N=154 (56 males) BMI =45.5 ± 7.2 kg/m^2 Age = 45.1 ± 11.6y	Sleeve Gastrectomy	12mo	Body composition: bioimpedance (Soft Tissue Analyzer, Akern); REE - Indirect Calorimetry (Vmax).	pREE was calculated through a **preditive equation** using FM, FFM and sex. **AT calculated as mREE minus pREE** and was assessed after 12mo**.**	Significant WL (~-30%) Reductions in FM (~45%) and FFM (~-14%) Decreases of Leptin and Insulin	Significant AT (-833 ± 996 kJ/day) No significant correlations between AT and metabolic variables.
Browning et al, 2016 (36)	O (retrospective)	N= 13 (3 males) BMI = 46.4±5.8 kg/m^2 Age = 46.2±12.7y	Roux-em-Y gastric bypass (n=8) and laparoscopic adjustable gastric banding (n=5)	6mo	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 - baselineREEp) - (6-month REEm - baselineREEm). AT was assessed after 6mo.	Significant WL; Reductions on FM and FFM.	Non-significant AT. AT was highly variable across individuals, ranging from -598 to 891 kJ/day.
Tam et al 2016 (37)	O (prospective)	N=35 (9 males) BMI=42.1±6.5 kg/m^2 Age=46±11 y	Gastric band (GB, n=8), sleeve gastrectomy (SG, n=13) or Roux-em-Y Gastric bypass (RYGB, n=14)	24mo	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 24mo.	GB: WL = -16.1±3.2% SG: WL = -30.7±2.6% RYGB: WL = -32.9±2.7 % Similar and significative reductions on FFM (~-31%)	For GB, AT occurred at 6 week (-469 ± 285 kJ/d) and 3mo (−741 ± 289 kJ/d) Insignificant after 6mo. For Sleeve, AT was significant from week 6 to 24mo (-1448 ± 247 kJ/d) For RYGB, AT was significant from week 6 to 24mo (- 1167 ± 259 kJ/d).
Carrasco et al, 2007 (38)	O (prospective)	N = 31 (4 males) BMI 44.4 ± 4.8 kg/m^2 Age = 37.3 ± 11.1 y	Roux-em-Y Gastric Bypass	6mo	Body composition: TBW - Deuterium 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 ± 7.6kg BF ~-77% of WL.	AT = -348 ± 517 kJ/d Great dispersion of the difference between pREE and mREE.
Coupaye et al, 2005 (39)	O (prospective)	N= 36 females BMI = 47.2 ± 8.5 kg/m^2 Age = 42.7 ± 8.7y	Laparoscopic adjustable gastric banding	12mo	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±11.6kg (-19%); Decreases in leptin (-42%)	Non significant AT

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

O – Observational; NRT - Non-randomized Trial; RCT – Randomized Clinical Trial; RT – Randomized 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 – Gastring Banding; SG – Sleeve Gastrectomy; RYGB – Roux-en-Y Gastric Bypass.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 3. Total Daily Energy Expenditure (TDEE)/24h 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, 2017 (50)	O (prospective)	N=29 (10 males) 2 groups: Caloric restriction n=18 BMI = 25.7 ± 1.6 kg/m^2 Control n=11 BMI = 25.7 ± 1.1 kg/m^2	Diet only 25% of their energy needs	2y	Body composition: DXA (Hologic QDR 4500A), EE: 24h respiratory chamber; TDEE: 14d 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 12mo and 24mo	After 2y of CR: WL: -9.0±0.6kg. 54% of the weight was regained 2y later.	No significant changes 24hEE were observed.
Lecoultre et al, 2011(51)	RCT	N= 46 (20 males) BMI = 27.8±0.7 kg/m^2 Age = 36.8±1.0y	Diet-only or diet + exercise: 4 groups: 25% calorie restriction; 12,5% calorie restriction + exercise LCD 3.7 MJ/d until a 15% reduction in BW 1 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 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 (6mo).	WL=-11.4±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 om for CR groups for 24hEE 527 ± 105 kJ/d).
Redman et al, 2009 (52)	RCT	N= 46 (20 males) BMI = 27.8±0.7 kg/m^2 Age = 36.8±1.0y	Diet-only or diet + exercise: 4 groups: 25% calorie restriction; 12,5% calorie restriction + exercise LCD 3.7 MJ/d until a 15% reduction in BW 1 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-day doubly labeled 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 6mo (after WL intervention)	Calorie restriction WL = -8.3±0.8 (-10%), Calorie restriction + exercise WL = -8.4±0.8 (-10%) LCD WL = -11.2±0.6 kg (-14%)	3months: Significant AT for CR group (-1552± 314 kJ/d) and for LCD (-2075 ± 285 kJ/d). 6months: Significant AT for LCD (-1151 ± 531 kJ/d)
Exercise only and combined exercise and diet interventions								
Lecoultre et al, 2011(51)	RCT	N= 46 (20 males) BMI = 27.8±0.7 kg/m^2 Age = 36.8±1.0y	Diet-only or diet + exercise: 4 groups: 25% calorie restriction; 12,5% calorie restriction + exercise LCD 3.7 MJ/d until a 15% reduction in BW 1 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 (6mo).	WL=-11.4±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.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 16:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 3. Continued

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Redman et al, 2009 (52)	RCT	N= 46 (20 males) BMI = 27.8±0.7 kg/m^2 Age = 36.8±1.0y	Diet-only or diet + exercise: 4 groups: 25% calorie restriction; 12,5% calorie restriction + exercise LCD 3.7 MJ/d until a 15% reduction in BW 1 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-day doubly labeled water; PA: PAL=TDEE/SMR OR mTDEE-mSMR.	Predicted values o 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 6mo (after WL intervention)	Calorie restriction WL = -8.3±0.8 (-10%), Calorie restriction + exercise WL = -8.4±0.8 (-10%) LCD WL = -11.2±0.6 kg (-14%)	Non-significant AT for the exercise group.
Surgery								
Ravelli et al 2019 (53)	O (prospective)	N=18 females BMI between 40 and 50 kg/m^2 Age = 20-45y	Roux-em-Y Gastric Bypass	12mo	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 kilograms (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 12months after surgery.	Significant weight loss at 6mo (≅−27%) and at 12mo (≅−33%). ~10% reduction of FFM and ~12% reduction of FM.	6mo: Presence of AT (−665 2092 kJ/day); 12mo: Non-significant AT
Wolfe et al, 2018 (34)	O (prospective)	N= 25 (3 males) BMI = 47±6 kg/m^2 Age = 45±11y	Bariatric Surgery (88% Roux-em-Y Gastric Bypass, 8% adjustable gastric banding and 4% biliopancreatic bypass with duodenal switch).	24mo	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 6mo and 24mo.	6mo: WL = -24%±5%; FM = -37%±8%; FFM = -11±4%. 24mo: WL = -27±10.2kg	Presence of AT at 6mo (TDEE=-950 ± 1423 kJ/d) but not at 24mo.

O – Observational study; RCT – Randomized Clinical Trial; EE – Energy Expenditure; TDEE – Total Daily Energy Expenditure; DLW – Double Labelled Water; SEE – Sleeping Energy Expenditure; CR – Caloric Restriction; LCD – Low Calorie Diet; WL – Weight Loss; FM – Fat Mass; FFM – Fat Free Mass.

Downloaded from https://www.cambridge.org/core. IP address: 92.7.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

Table 4. Sleeping Energy Expenditure (SEE)

Study	Study type	Sample	Intervention's description	Length + follow up	Measurements	AT definition and measurement	Results	AT
Marlatt et al, 2017 (50)	O (prospective)	N=29 (10 males) 2 groups: Caloric restriction n=18 BMI = 25.7 ± 1.6 kg/m^2 Control n=11 BMI = 25.7 ± 1.1 kg/m^2	Diet only 25% of their energy needs	2y + 2y follow up	Body composition: DXA (Hologic QDR 4500A), EE: 24h respiratory chamber; TDEE: 14d 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 2y of CR: WL: -9.0±0.6kg. 54% of the weight was regained 2y later.	Significant AT was observed between CR (-381 ± 75 kJ/d) and CG (-96 ± 96 kJ/d).
Lecoultre et al, 2011(51)	RCT	N= 46 (20 males) BMI = 27.8±0.7 kg/m^2 Age = 36.8±1.0y	Diet-only or diet + exercise: 4 groups: 25% calorie restriction; 12,5% calorie restriction + exercise LCD 3.7 MJ/d until a 15% reduction in BW 1 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 (6mo).	WL=-11.4±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 ± 71 kJ/d).

O – Observational Study; RCT – Randomized Clinical Trial; TDEE – Total Daily Energy Expenditure; 24hEE – 24h Energy Expenditure; SEE – Sleeping energy expenditure; WL – Weight loss; CR – Caloric Restriction; LCD – Low Calorie Diet; FM – Fat Mass; FFM – Fat Free Mass.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094

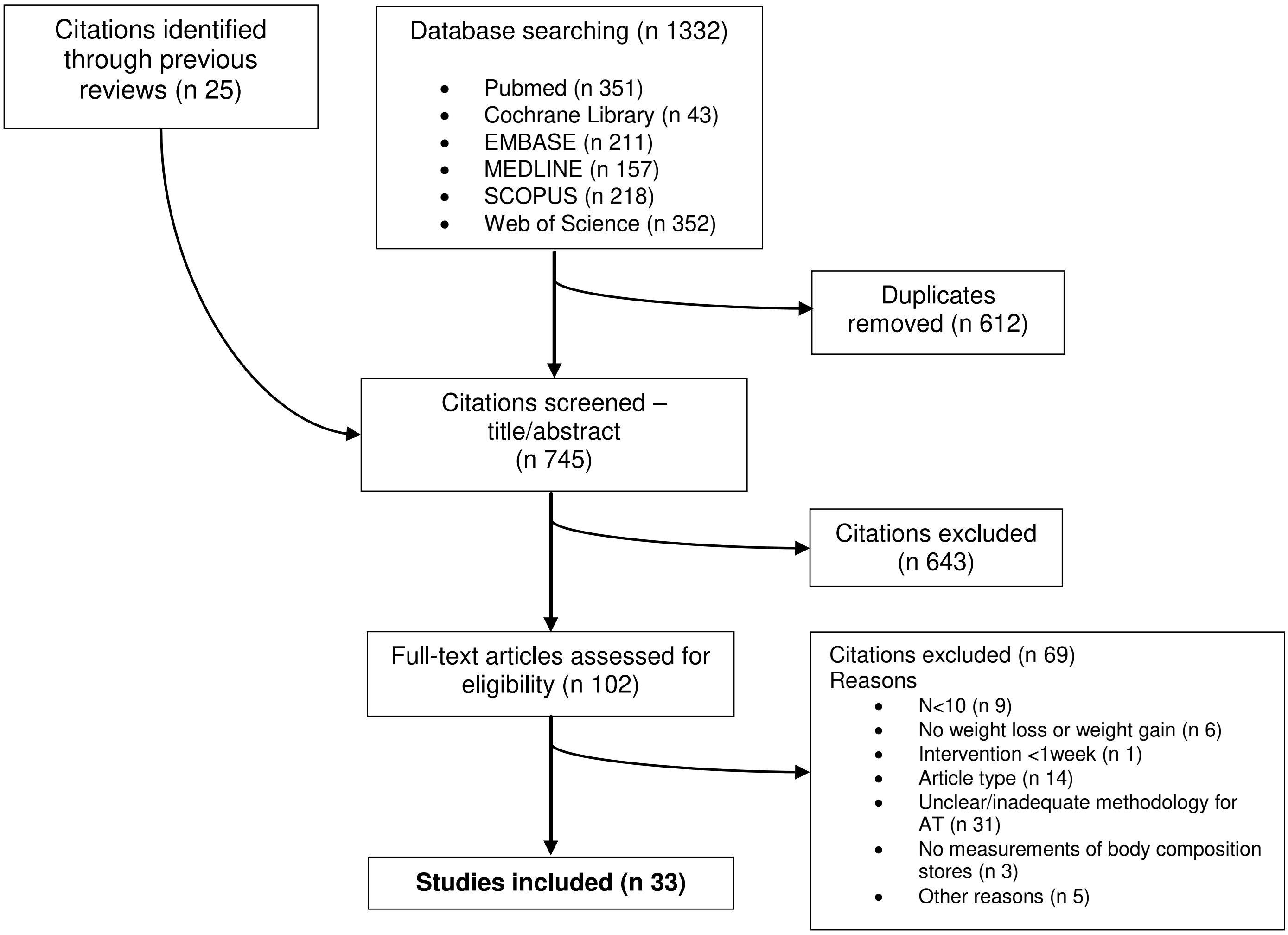

Figure 1. Flow diagram of studies' selection.

Downloaded from https://www.cambridge.org/core. IP address: 92.17.170.102, on 25 Mar 2021 at 11:46:49, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0007114521001094