What is the effect of diet and/or exercise interventions on behavioural compensation in non-exercise physical activity and related energy expenditure of free-living adults? A systematic review

Analiza M. Silva¹*, Pedro B. Júdice¹, Eliana V. Carraça¹, Neil King², Pedro J. Teixeira¹ and Luís B. Sardinha¹

¹Exercise and Health Laboratory, Interdisciplinary Centre for the Study of Human Performance (CIPER), Faculdade Motricidade Humana, Universidade Lisboa, 1499-002 Cruz Quebrada, Portugal

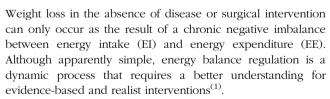
(Submitted 24 November 2017 – Final revision received 24 February 2018 – Accepted 16 March 2018)

Abstract

MS British Journal of Nutrition

Non-exercise physical activity (NEPA) and/or non-exercise activity thermogenesis (NEAT) reductions may occur from diet and/or exercise-induced negative energy balance interventions, resulting in less-than-expected weight loss. This systematic review describes the effects of prescribed diet and/or physical activity (PA)/exercise on NEPA and/or NEAT in adults. Studies were identified from PubMed, web-of-knowledge, Embase, SPORTDiscus, ERIC and PsycINFO searches up to 1 March 2017. Eligibility criteria included randomised controlled trials (RCT), randomised trials (RT) and non-randomised trials (NRT); objective measures of PA and energy expenditure; data on NEPA, NEAT and spontaneous PA; ≥10 healthy male/female aged >18 years; and ≥7 d length. The trial is registered at PROSPERO-2017-CRD42017052635. In all, thirty-six articles (RCT-10, RT-9, NRT-17) with a total of seventy intervention arms (diet, exercise, combined diet/exercise), with a total of 1561 participants, were included. Compensation was observed in twenty-six out of seventy intervention arms (fifteen studies out of thirty-six reporting declines in NEAT (eight), NEPA (four) or both (three)) representing 63, 27 and 23% of diet-only, combined diet/exercise, and exercise-only intervention arms, respectively. Weight loss observed in participants who decreased NEAT was double the weight loss found in those who did not compensate, suggesting that the energy imbalance degree may lead to energy conservation. Although these findings do not support the hypothesis that prescribed diet and/or exercise results in decreased NEAT and NEPA in healthy adults, the underpowered trial design and the lack of state-of-the-art methods may limit these conclusions. Future studies should explore the impact of weight-loss magnitude, energetic restriction degree, exercise dose and participant characteristics on NEAT and/or NEPA.

Key words: Energy balance: Physical activity: Energy expenditure: Behavioural compensation: Weight loss: Free-living physical activity



Metabolic and behavioural compensations have been observed in response to diet and/or exercise interventions designed to induce changes in the energy balance components⁽²⁻⁴⁾. It is recognised that weight loss induced from a negative energy balance reduces over time, as energetic

demands are attenuated, mitigating an indefinite exposure to energy balance deficit⁽⁵⁾. Although metabolic adaption to weight loss occurs^(5,6), behavioural compensations, that is compensation for an energy balance intervention through behaviour changes, may also occur. Indeed, behavioural compensation resulting from creating a negative energy balance includes a reduction in voluntary EE and/or an increase in EI in the absence of a strict control⁽⁷⁾. To better clarify voluntary EE, important concepts should be addressed, such as physical activity EE (PAEE) that represents the overall energy expended to move the body, further divided into structured physical

Abbreviations: ACC, accelerometer; DLW, doubly labelled water; EE, energy expenditure; EI, energy intake; ExEE, exercise energy expenditure; HR, heart rate; NEAT, non-exercise activity thermogenesis; NEPA, non-exercise physical activity; NRT, non-randomised trial; PA, physical activity; PAEE, physical activity energy expenditure; RCT, randomised controlled trial; REE, resting energy expenditure; RT, randomised trials; SMR, sleeping metabolic rate; TEE, total energy expenditure; TEF, thermic effect of food.

* Corresponding author: A. M. Silva, email analiza@fmh.ulisboa.pt



²Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, QLD 4059, Australia



activity (PA) (exercise) or non-exercise activity thermogenesis (NEAT). Non-exercise PA (NEPA) refers to the physical motion of the body in activities that do not pertain to volitional exercise, including all activities of daily living (fidgeting, maintaining posture and ambulation), whereas NEAT defines the EE associated with these activities⁽⁸⁾. However, the role of NEPA and/or NEAT on compensation from exercise and/or diet-induced weight loss is less well understood.

A recent systematic review with meta-analysis indicated no mean changes in NEPA during exercise training⁽⁹⁾. However, the authors reported that session duration, intervention length, age and sex influenced changes in NEPA during exercise training⁽⁹⁾. Washburn *et al.*⁽¹⁰⁾ indicated that more data from adequately powered trials using objective measurements are required to improve the understanding of the effects of exercise-induced weight loss on NEAT and NEPA. Measurement of EI and EE, including all components of EE, objective measurement of PA and accurate measurement of changes in body energy stores, must be included in such studies.

Relatively few studies have investigated the effect of energy restriction on free-living NEPA and NEAT, possible owing to the cost and burden of measuring PA accurately in participants' habitual environment. Furthermore, many of the findings are contradictory. No changes in posture allocation (time spent reclining or sitting v. standing or ambulating) were observed when obese people lost weight⁽¹¹⁾, whereas other studies only found trends towards decreases in PA among non-obese weight-reduced men^(12,13). In contrast, other groups found a decrease in PA and corresponding EE during an energy restriction diet, with inclusion of exercise training^(14,15). Three randomised controlled trials (RCT) under the Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE) study found that energy restriction significantly decreased NEAT, but not NEPA⁽¹⁶⁾.

Dhurandhar et al. (17) provided a systematic review with metaanalysis using a mathematical modelling approach concluding that there is substantial compensation in both dietary and exercise interventions designed to induce weight loss. The authors identified a possible range of behavioural and metabolic compensations that can be very difficult to quantify, but which may reduce the expected amount of weight loss after a given intervention (17). The extent to which this compensation is due to changes in NEPA or NEAT is unclear. There is insufficient evidence to definitively answer the question of whether diet or exercise-induce weight loss leads to compensatory reductions in NEAT and NEPA, as a result of increases in sedentary behaviour, decreases in overall PA or both. So far no systematic review has covered both exercise and diet, and their combined and independent effects on compensatory activity. The aim of this systematic review is to describe the effects of diet and/or exercise energy balance interventions on behavioural compensation in NEPA and/or related decreases in NEAT of free-living adults.

Methods

Criteria for study eligibility: studies and participants

In this review, articles reporting changes in compensatory behaviours occurring during or as a result of diet and/or exercise interventions, designed to intervene in one or more components of the energy balance equation, were retrieved. To be included, studies had to fulfil all of the following criteria: (1) adult samples (>18 years), regardless of sex; (2) n>10 participants; (3) an intervention period of at least 1 week; (4) be published in English language; (5) include objective measures of total EE (TEE) and/or PA (doubly labelled water (DLW), indirect calorimetry, accelerometer (ACC), pedometer, inclinometer); and (6) be a clinical trial. In turn, studies involving participants taking medication or having diseases/conditions known to affect metabolism/ weight (cancer, thyroid disease, diabetes, bariatric surgery, pregnancy, total parenteral nutrition, HIV/AIDS, organ transplant, Prader-Willi Syndrome, polycystic ovary syndrome, chronic obstructive pulmonary disease or acute illnesses, such as infections or traumatic injury) were excluded. The current review is registered on PROSPERO (PROSPERO 2017 CRD42017052635).

Information sources and search strategy

A comprehensive search of peer-reviewed articles published until 1 March 2017 (including online ahead of print publications) was conducted in the following electronic databases: Pubmed, PsycINFO, Embase, CINAHL, Cochrane Library, ERIC and SPORTDiscus. Searches included all meaningful combinations of the following sets of terms: (i) terms concerning the population of interest (e.g. adults, obese, overweight); (ii) terms concerning the intervention(s) of interest (e.g. diet or energetic restriction, PA or exercise, weight or body fat loss/change, behaviour change or lifestyle intervention); (iii) terms representing the outcomes of interest (e.g. NEPA, spontaneous PA, NEAT, compensatory response/behaviour); and (iv) terms concerning the study design (e.g. trial, experimental, treatment). A complete list of search strategies can be obtained from the authors, whereas a search strategy example for Pubmed is provided as an additional file (online Supplementary material SI). Other sources included manual cross-referencing of literature cited in prior reviews and retrieved studies, and hand-searches of the content of key scientific journals.

Study selection and data processing

All abstracts identified from the literature searches were screened for potential inclusion eligibility by one author (P. B. J.). Of all abstracts, duplicates were removed and twenty-three added from other sources. In all, seventy-five full-text articles were retrieved, and thirty-six met all inclusion criteria and were included in the present review (Fig. 1). A data extraction form was developed, based on the PRISMA statement for reporting systematic reviews⁽¹⁸⁾. Data extraction was conducted by two authors (P. B. J. and E. V. C.) and included information about the article (e.g. authors, year), participants (e.g. demographics, BMI), study design, intervention characteristics (e.g. aim, length, follow-up, arms), outcome measures and main results.

The articles were grouped by study design as RCT (Table 1), randomised trials (RT, Table 2) and non-randomised trials (NRT, Table 3), whereas in the results text, articles were further presented by intervention type: diet-only, exercise-only and combined diet and exercise. Across studies, heterogeneity was observed in



https://doi.org/10.1017/S000711451800096X Published online by Cambridge University Press

various parameters, including (i) study characteristics (sample size, completion rate, trial length, with or without behavioural intervention, methodology for NEPA/NEAT); (ii) participant characteristics (sex, age, BMI, ethnicity, activity level); (iii) diet (degree of energy restriction) or exercise prescriptions (mode, frequency, intensity, duration); (iv) assessment of NEPA/NEAT (ACC, heart rate (HR), activity diary, indirect calorimetry, DLW); and (v) main outcomes (compensation or non-compensation in NEPA and related energy expenditure, NEAT). If the outcome measure was PA assessed through activity monitors, then NEPA was used. If the outcome was non-exercise EE measured using DLW or assessment from accelerometry or other methods, NEAT was used. When PAEE was referred to as NEAT, an assumption that volitional exercise during the intervention was not performed was made. This terminology was used consistently throughout the manuscript to adequately differentiate these two concepts/outcomes. Considering this heterogeneity, a meta-analysis was found inappropriate. Results based on the extracted data were instead synthesised and presented grouped by study design (Tables 1–3) and intervention type (in the text).

Frequencies, medians, range and proportions were assessed using SPSS (version 24; IBM SPSS Statistics for Windows).

Quality assessment

Study quality was assessed with the Quality Assessment Tool for Quantitative Studies⁽⁵²⁾ (online Supplementary material SII). evaluating six key methodological domains: study design, blinding, representativeness (selection bias), representativeness

(withdrawals/dropouts), confounders and data collection. Each domain was classified as strong, moderate or weak methodological quality. A global rating was determined based on the scores of each component. Two authors independently rated the six domains and overall quality (P. B. J., E. V. C.). Discrepancies were discussed until a consensus was reached. Inter-rater agreement was good (Cohen's $\kappa = 0.68$). Quality assessment of all studies included in the review is provided as the online Supplementary material SIII.

Results

The initial search identified 1412 (1389 citations identified by database search and twenty-three through other sources) unique records, of which 314 were removed owing to duplication. From the remaining 1098 records, 1023 citations were excluded based on the screening of titles and abstracts. Full-text articles for the remaining seventy citations were retrieved and reviewed. A total of thirty-nine articles did not satisfy the inclusion criteria and were excluded; thus, thirty-six articles were considered (Fig. 1).

A total of thirty-six articles (10 (28%) RCT, 9 (25%) RT and 17 (47%) NRT) with a total of seventy intervention arms (diet, exercise, diet plus exercise), comprising 1561 participants, met the inclusion criteria.

Behavioural compensation in NEPA or related decreases in NEAT were observed in twenty-six out of seventy intervention arms (fifteen out of thirty-six studies), whereas the remaining forty-four showed no compensation. From those who

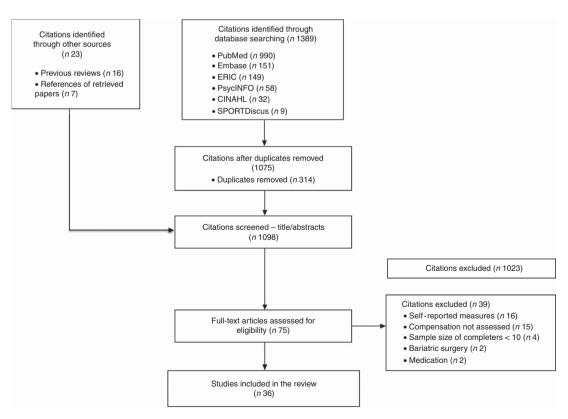


Fig. 1. Flow diagram.



compensated (fifteen studies), fifteen intervention arms were diet-only interventions, eight were exercise-only interventions and three were diet plus exercise interventions.

Detailed information about the included studies is presented in Tables 1–3, divided by design type – that is NRT, RT and RCT.

Studies will be further detailed by intervention type (diet-only, exercise-only and combined diet and exercise), as follows.

Intervention arms that decreased NEAT (i.e. twenty-one arms) presented a higher median value of weight loss (available in eighteen intervention arms: average of -10 kg) compared with those who showed no changes (available in thirty-eight intervention arms; average of -5 kg). Similar medians were observed for trial length, BMI and age. A similar trend was found when observing weight-loss medians for diet-only, exercise-only and combined diet and exercise, with higher weight loss found in the groups that reduced NEAT. In studies that showed reductions in NEPA, similar median weight loss, BMI, trials length and age were observed compared with those studies that reported no changes in NEPA. However, in dietonly interventions, weight loss observed in participants who decreased NEPA was double the weight loss found in those who did not compensate. The median study length of exerciseonly studies that showed decreases in NEAT was half the median length of trials that present no changes in NEAT. Compared with exercise-only studies without changes in NEAT or NEPA, the median exercise frequency was half in studies that showed reductions in NEAT, whereas the median exercise duration was double in trials that decreased NEPA. Studies with or without behavioural intervention had similar proportion of cases between compensators and non-compensator groups. In exercise-only and combined diet and exercise, studies with prescribed strength exercise are absent of cases with behavioural compensation (Table 4).

Diet-only interventions

The twenty-four diet-only interventions arms (i.e. fourteen diet-only trials) comprised approximately 39% of the total number of studies included in this review, with a total of five NRT (36%), six RT (43%) and three RCT (21%).

Study characteristics

Sample size. Diet-only interventions comprised a total of 400 participants with a median sample size of 18 (range 5–66). NRT included a median sample size of 23 (range 6–66), RT of 17 (range 5–57) and RCT of 15 (range 15–33).

Completion rate. Compliance to prescribed diet was only reported by DeLany et al. (28) as 55% and by Wang et al. (33) as 100%. Since Leibel et al. (43) performed a laboratory-based study, full compliance with protocol was achieved. The remaining trials did not report compliance.

Trial length. The median length of the studies was 5.6 (range 2–12) months, varying from 3.5 (range 2–6) for NRT, 4 (range 2–6) for RT and 8 (range 6–12) for RCT.

Behavioural intervention. A total of five studies included behavioural therapy^(14–16,22,35) comprising 36% of the diet-only studies included in this review.

Energy restriction. EI was restricted by $25^{(15,22)}$, 10, 20, 25 and $30\%^{(16)}$, $33\%^{(35)}$, 51% of weight maintenance⁽³⁷⁾ and 75% of resting EE (REE)⁽¹⁴⁾. EI was prescribed as $3724\,\mathrm{kJ/d}^{(15,22)}$, approximately $2092\,\mathrm{kJ/d}$ in the first 4 weeks followed by 4 weeks at approximately $3515\,\mathrm{kJ/d}^{(29)}$, $3347\,\mathrm{kJ/d}^{(51)}$, approximately $2929\,\mathrm{kJ/d}$ in the first 4 weeks and approximately $3347\,\mathrm{kJ/d}$ in the next 8 weeks⁽⁴⁹⁾, and according to body weight ($<90.7\,\mathrm{kg}$, $5021-6276\,\mathrm{kJ/d}$; $>90.7\,\mathrm{kg}$ and $<113.4\,\mathrm{kg}$, $6276-7531\,\mathrm{kJ/d}$; and $>113.4\,\mathrm{kg}$, $7531-8368\,\mathrm{kJ/d}^{(28)}$. EI was also prescribed as a reduction of $2929\,\mathrm{kJ/d}^{(34)}$, $3347\,\mathrm{kJ/d}^{(43)}$ and $1682\,\mathrm{kJ/d}^{(33)}$. EI was not reported in one study⁽²⁷⁾.

Participant characteristics

Age. The median age across the fourteen studies was 40.5 years (range 25.0-58.6), with values of 35.5 years (range 25-51) for NRT, 46.3 years (range 36.6-58.6) for RT and 39.2 years (range 34.7-55.2) for RCT.

Sex. Seven studies included women only $^{(14,27,29,33,37,49,51)}$, one study included men only $^{(34)}$ and six studies included a combined sample of women and men $^{(15,16,22,28,35,43)}$.

BMI. Four studies included overweight/obese individuals $^{(33,35,43,49)}$. Non-obese individuals were included in four studies $^{(15,16,22,37,51)}$. Obese-only individuals were included in five studies $^{(14,27-29,34)}$. In the studies that provided data on this parameter, BMI was $31\cdot2\,\mathrm{kg/m^2}$ (range $27\cdot4-43\cdot6$), with a median of $31\cdot4\,\mathrm{kg/m^2}$ (range $28\cdot1-38\cdot3$) for NRT, $35\cdot0\,\mathrm{kg/m^2}$ (range $31\cdot7-43\cdot6$) for RT and $27\cdot8\,\mathrm{kg/m^2}$ (range $27\cdot4-27\cdot9$) for RCT.

Ethnicity. Two studies described ethnic groups as Caucasian, Black, Asian and Hispanics $^{(15,22)}$, and four studies reported participants as Caucasian and Black $^{(27,28,33,51)}$. One study included Caucasian only $^{(37)}$ and seven studies did not report ethnic groups $^{(14,16,29,34,35,43,49)}$.

Physical activity level. Only six studies characterised the level of PA of the participants as sedentary^(14–16,22,33,35).

Methods for assessing non-exercise activity thermogenesis. Among RCT, Martin et al. (16) assessed NEAT by subtracting the sum of REE from indirect calorimetry and thermic effect of food (TEF) (assumed as 0.1 TEE) from TEE by DLW. Redman *et al.*⁽¹⁵⁾ assessed NEAT (referred to as activity-related EE) as the residual value of the regression between measured TEE obtained from DLW and measured sleeping metabolic rate (SMR) using indirect calorimetry. In RT, DeLany et al. (28) assessed NEAT (referred to as PAEE, as exercise was not prescribed) as TEE from DLW minus the sum of REE by indirect calorimetry with TEF (assumed as 0·1TEE). Kempen et al. (29) assessed NEAT (referred to as PAEE, as exercise was not prescribed) by subtracting the sum of SMR from indirect calorimetry and the TEF (assumed as 0·1TEE) from TEE by DLW. Racette et al. (14) assessed NEAT (referred to as PAEE, as exercise was not prescribed) with DLW for TEE, indirect calorimetry for REE and TEF as TEE - (REE+TEF). Wang et al. (33) used ACC for nonexercise PAEE. Weigle⁽³⁴⁾ used a 24-h EE in a metabolic ward to assess NEAT (referred to as non-resting EE = 24EE - REE). In NRT, Leibel et al. (43) assessed NEAT (referred to as non-resting EE) calculated as TEE from DLW minus the sum of REE and TEF obtained using a respiratory chamber. Weinsier et al. (51) determine NEAT (referred to as PAEE, as exercise was not





Table 1. Randomised controlled trials (ten studies)

Studies	Sample	Intervention	Length + follow-up	Measures	Results	Behavioural response
Church et al. ⁽¹⁹⁾	Control: 94 women Age = 57 (6) BMI = 32 (4) Exercise-only interventions: (a) 139 women Age = 58 (7) BMI = 31 (4) (b) 85 women Age = 57 (6) BMI = 32 (4) (c) 93 women Age = 56 (6) BMI = 31 (4) Control: no intervention Exercise-only interventions: 3-4 supervised sessions per week at 50 % VO _{2max} . In week 1, all exercisers expended 17 kJ/kg per week (KKW). Thereafter: (a) This group remained at 17 KKW (b) This group increased to 33 KKW (c) Training sessions alternated between recumbent cycle-ergometer and treadmill (c) 93 women Age = 56 (6) BMI = 31 (4)		6 Months	Participants wore a pedometer daily except when exercising	Monitoring of steps per day indicated that outside physical activity remained constant throughout the trial for all exercise groups No significant differences were found between groups at 6 months In the 17 and 33 KKW groups the actual weight loss closely matched the predicted weight loss. In the 50 KKW group the actual weight loss was lower than predicted	No compensation: no change in NEPA
Hollowell et al. ⁽²⁰⁾	Control: 4 women; 4 men Age = 51 (7) BMI = 31 (3) Exercise-only interventions: (a) Low amount/moderate intensity: 5 women; 3 men Age = 57 (6) BMI = 29 (3) (b) Low amount/vigorous intensity: 10 women; 10 men Age = 54 (6) BMI = 30 (3) (c) High amount/vigorous intensity: 5 women; 9 men Age = 51 (6) BMI = 30 (2)	Exercise-only interventions: 3–5 times per week (a) Low amount/moderate intensity: 40–55 % VO ₂ peak to achieve EE of 5029 kJ/week (b) Low amount/ vigorous intensity: 65–85 % VO ₂ peak to achieve EE of 5029 kJ/week (c) High amount/vigorous intensity: 65–85 % VO ₂ peak to achieve EE of 8381 kJ/week ous		RT3 accelerometer (Stayhealthy, Inc.) worn for 7 d at baseline and end of intervention Only days with 9720 total minutes of data in a 24-h period included All minute records from the RT3 file corresponding to the prescribed exercise were eliminated. The 30 min of RT3 data immediately before and after exercise were also eliminated The high-amount group showed a significantly greater increase in non-exercise PAEE increased with increasing exercise volume. There was no significant difference in change of non-exercise PAEE among groups. Change in body weight was not reported.		No compensation: no change in NEAT
Kozey-Keadle et al. ⁽²¹⁾	39 women; 19 men Control: 10 participants Age = 43 (10) BMI = 35 (5) Interventions: (a) Exercise (EX): 16 participants Age = 44 (10) BMI = 35 (5) Reduce Sedentary time (rST): 14 participants Age = 45 (10) BMI = 35 (4) EX + rST: 16 participants Age = 42 (11) BMI = 35 (4)	Control: maintain habitual behaviour Interventions: EX: Supervised aerobic exercise, 5 d/week, at a moderate intensity (40–65 % VO ₂ peak), 30–40 min rST: Strategies to increase NEPA and pedometer with weekly goal provided. Benefits of reducing ST discussed EX+rST: combination of EX and rST	12 Weeks	Active PAL worn for a 7-d period at weeks 3, 6, 9 and 12 of the intervention	For the EX group, ST did not decrease significantly and NEPA did not change from baseline to week 12 Yet, the changes were variable, with approximately 50% of participants increasing ST and decreasing NEPA The rST group decreased ST and increased NEPA as expected EX-rST significantly decreased ST and increased time in NEPA from baseline to week 12 The control group increased ST Body weight changes not reported	No overall compensation: no change in NEPA
Martin et al. ⁽²²⁾	46 (26 women; 20 men) non- obese participants Age = 37 (2) BMI = 28 (0·4)	Control: healthy weight maintenance diet matching 100 % of energy requirements Interventions: (a) LCD: low-energy diet to achieve 15 % reduction in body mass (3724 kJ/d) (b) CR: 25 % energy restriction from baseline energy requirements (c) CR + EX: 12.5 % CR + 12.5 % increase in EE by structured aerobic exercise, 5 d/week	6 Months	SPA was measured in a metabolic chamber TEE was measured by DLW SMR was assessed by a metabolic cart	SPA did not decrease in any groups from baseline to month 6, not even when dieting groups were combined and compared with controls Percent activity in a respiratory chamber and PAL did not change from baseline to month 6 All groups lost weight throughout the intervention period (marginal in the controls)	No compensation: no change in NEPA
Martin et al. (16)	3 sites-study PBRC: 19 women; 15 men; Control (n 11); CR-25 % (n 12); LCD (n 11) Age = 39 (7) BMI = 28 (2)	Control: healthy weight maintenance diet matching 100 % of energy requirements Diet-only interventions: PBRC (a) CR-25 %: 25 % energy restriction from baseline energy requirements	PBRC: 6 months TUFTS and WUSM: 12 months	DLW over 14 d at baseline, 3 and 6 months (PBRC), and 3, 6, 9 and 12 months (TUFTS and WUSM) Indirect calorimeter using a metabolic cart to measure REE PAEE = TEE - (REE + 0·1TEE)	PBRC: significant decreases in PAEE and PAL observed in the CR and LCD groups at months 3 and 6 Accelerometry data suggest that participants decreased time spent in higher-intensity activity in favour of lower-intensity activity	Compensation: reduction in NEAT No compensation: no change in NEPA



Table 1. Continued

Studies	Sample	Intervention	Length + follow-up	Measures	Results	Behavioural response
	TUFTS: 33 women; 12 men; CR-10% (n 12); CR-30% (n 33) Age = 35 (5) BMI = 28 (2) WUSM: 15 women; 11 men; Control (n 9); CR-20% (n 18) Age = 55 (3) BMI = 27 (2)	(b) LCD: low-energy diet to achieve 15% reduction in body mass (3724 kJ/d) TUFTS (a) CR-10 %: 10 % energy restriction from baseline energy requirements (b) CR-30 %: 30 % energy restriction from baseline energy requirements WUSM (a) CR-20 %: 20 % energy restriction from baseline energy requirements		Accelerometers: Model 7164 (Actigraph); RT3 accelerometer (Stayhealthy, Inc.) used at the same periods	Significant weight loss in both groups. TUFTS: significant decreases in PAEE and PAL observed in both CR groups at months 6, 9 and 12. No significant weight loss in both groups WUSM: significant change in PAEE only in the CR group at month 6. Significant weight loss in both groups Greater weight loss was associated with larger decreases in PAEE	
Redman et al. ⁽¹⁵⁾	46 participants (women and men) Age = 37 (1) BMI = 28 (1) Control: 11 participants Interventions: (a) Low-energy diet group (LCD): 11 participants (b) Energy restriction group (CR): 12 participants (c) CR + exercise (EX) group: 12 participants	Control: healthy weight maintenance diet matching 100 % of energy requirements Interventions: (a) LCD: low-energy diet to achieve 15 % reduction in body mass (3724 kJ/d) (b) CR: 25 % energy restriction from baseline energy requirements (c) CR+EX: 12.5 % CR plus 12.5 % increase in energy expenditure by structured aerobic exercise, 5 d/week	6 Months	DLW over 14d at baseline, weeks 10–12 and weeks 22–24 SMR by metabolic chamber Activity-related EE calculated as the residual value of the regression between measured TEE and SMR	Activity-related EE decreased throughout the intervention period in LCD and CR, but not in CR+EX or controls Body weight decreased in all groups from baseline to 6 months	Compensation: NEAT decreased in the diet-only groups
Rosenkilde et al. ⁽²³⁾	Control: 17 men Age = 31 (6) BMI = 28 (3) Exercise-only interventions: (a) MOD: 18 men Age = 30 (7) BMI = 29 (2) (b) HIGH: 18 men Age = 28 (5) BMI = 28 (1)	Control: no intervention Exercise-only interventions: (a) MODERATE: Aerobic exercise (e.g. running, cycling) at moderate intensity, 30–60 min, 3 d/week (1255 kJ/d) (b) HIGH: Aerobic exercise (e.g. running, cycling) at high intensity, 30–60 min, 3 d/week (2510 kJ/d)	13 Weeks	Model GT1M (Actigraph) worn for 3 d, at baseline and at 6 and 11 weeks after randomisation Non-exercise PA was obtained by subtracting activity counts during prescribed exercise from total activity counts	When the exercise component was subtracted from total activity counts, no significant difference in NEPA was found between any of the groups Body weight decreased similarly in both exercise groups	No compensation: no change in NEPA
Turner <i>et al.</i> ⁽²⁴⁾	Control: 14 men Age = 53 (4) BMI = 28 (3) Exercise-only intervention: 15 men Age = 55 (5) BMI = 28 (3)	Control: no intervention Exercise-only intervention: Walking, running, cycling progressing from 30 min, 3 d/week, 50 % VO _{2max} at weeks 1–2 to 60 min, 4 d/week, 70 % VO _{2max} by week 24; supervised sessions approximately 10 %	24 Weeks	Actiheart (CamNtech Ltd) (combined HR and accelerometer) worn over 7 d, at baseline, weeks 2, 9 and 18 and at 2 weeks in detraining. Non-prescribed PAEE was calculated by subtracting prescribed PAEE from overall PAEE	Prescribed exercise had no detrimental effect on time spent in non-prescribed PA and PAEE There was a trend for greater non-prescribed PAEE in the exercise group and no change in the controls. Significant change in body mass only in the exercisers	No compensation: no change in NEAT or NEPA
Whybrow et al. ⁽²⁵⁾	6 men Age = 30 (6) BMI = 24 (2) 6 women Age = 25 (6) BMI = 23 (2)	Cross-over design with: Control phase: no additional exercise Exercise-only phases: (a) MOD, two 40-min sessions, in cycle ergometer, to expend 28-6 kJ/kg (b) HIGH, three 40-min sessions, cycle ergometer, to expend 57-1 kJ/kg	14 d	TEE was assessed by DLW over 14d Non-exercise EE = TEE – ExEE	Non-exercise EE was not significantly different between study conditions No significant changes in body weight in all phases	No compensation: NEAT was not affected by the treatment condition
Willis et al. (26)	Control: 9 women; 9 men Age = 23 (3) BMI = 30 (4) Exercise-only interventions: (a) 1674 kJ: 19 women; 18 men Age = 23 (3) BMI = 31 (6) (b) 2510 kJ: 18 women; 19 men Age = 23 (3) BMI = 31 (4)	Control: no intervention Exercise-only interventions: (a) Aerobic exercise training 5 d/week at 1674 kJ/session (b) Aerobic exercise training 5 d/week at 2510 kJ/session	10 Months	REE was assessed by indirect calorimetry. TEE was assessed using DLW over a 14-d period. Both assessed at baseline and 10 months Non-ExEE = (0.9TEE – REE) – net ExEE (EXEE – REE) NEPA and sedentary time were assessed by an accelerometer (model GT1M; Actigraph)	Within the exercise groups, there were no significant effects of group, time or group—time interaction for NEPA No significant within- or between-group differences in change in non-exercise EE Activity counts were higher in the 2510-kJ group Body weight decreased in exercise groups and slightly increased in controls	No compensation: no changes in NEPA or NEAT

NEPA, non-exercise physical activity; PAEE, physical activity energy expenditure; NEAT, non-exercise activity thermogenesis; Ex, exercise; PAL, physical activity level; LCD, low-energy diet; CR, energy restriction; SPA, spontaneous physical activity; SRI, self-regulatory intervention; TEE, total energy expenditure; DLW, doubly labelled water; SMR, sleep metabolic rate; PA, physical activity; HRR, heart rate reserve; EE, energy expenditure; EXEE, exercise energy expenditure; HR_{max}, maximal heart rate; RM, repetition maximum; REE, resting energy expenditure; DO, diet-only; D-PA, diet plus physical activity; TEF, thermic effect of food; NR, non-reported; AT, aerobic training; RT, resistance training; PBRC, Pennington Biomedical Research Center; TUFTS, Tufts University; WUSM, Washington University School of Medicine.

Table 2. Randomised trials with no control group (nine studies)

Studies	Sample	Intervention	Length + follow-up	Measures	Results	Behavioural response
Brehm et al. ⁽²⁷⁾	Low-carbohydrate diet (low-carb): 20 women Age = 45 (2) BMI = 33 (0.5) Energy-restricted, low-fat diet: 20 women Age = 41 (3) BMI = 34 (0.5)	Low-carb: Ad libitum low-carb diet Low-fat: energy-restricted, low-fat diet	4 Months	Pedometer records (number of steps per day)	Estimates of PA were stable in the dieters during the study and did not differ between groups Both groups lost weight throughout the intervention	No compensation: no changes in NEPA
DeLany et al. ⁽²⁸⁾		Diet alone (DO): prescribed energy restriction of 5021–6276 kJ/d for those weighing < 90.7 kg, 6276–7531 kJ/d for those weight ≥90.7 but <113.4 kg, and 7531–8786 kJ/d for those weighing >113.4 kg Diet plus PA (D-PA): prescribed energetic restriction + moderate-intensity PA, similar to brisk walking, prescribed and progressing to 60 min, 5 d/week		TEE measured with DLW at baseline and 12 months; TEE assessed at baseline and 6 months using DLW REE was measured at baseline, 6 and 12 months by indirect calorimetry Multisensor physical activity monitors worn during DLW periods and at 12 months PAEE = TEE – (REE + 0.01 × TEE) (but ExEE not determined)	Although counselled to maintain PA levels, over half of the DO group showed an increase in steps 40 % of the D-PA group showed an increase of less than 500 steps/d, and 27 % showed no increase or non-significant decrease No significant change in PAEE between groups Both groups decreased body weight	No compensation: no changes in NEAT NEPA increased in the DO group
Kempen et al. ⁽²⁹⁾	Diet: 10 women Age = 37 (2) BMI = 32 (1) Diet + exercise: 10 women Age = 39 (5) BMI = 32 (1)	Diet: 4 weeks of a low-energy diet (approximately 2092 kJ/d); 4 weeks of a mixed, balanced diet (approximately 3515 kJ/d) Diet + exercise: 90 min sessions, 3 d/week, aerobic dancing and fitness (cardiac + strength training), at 50–60 %	8 Weeks	SMR measured on calorimeter TEE assessed by DLW at baseline and weeks 7-8 PAEE = TEE - (SMR+0·1TEE) (diet group) PAEE = TEE - (SMR+0·1TEE+ExEE) (Ex+diet group) ExEE assessed by HR monitor	TEE decreased in both groups	Compensation: decrease in NEAT in the diet plus exercise arm No compensation: no change in NEAT in the diet-only arm
Nicklas <i>et al.</i> ⁽³⁰⁾	DIET + EX: 15 women; 5 men Age = 70 (3) BMI = 33 (3) SRI + DIET + EX: 16 women; 5 men Age = 71 (4) BMI = 34 (2)	VO _{2max} DIET + EX: hypoenergetic diet (2510 kJ/d deficit) and treadmill walking, 4 d/week, at 65–70 % HRR, progressing from 15–20 min at 50 % HRR at week 1 to 30 min at 65–70 % HRR by the end of the week 6 SRI + DIET + EX: hypoenergetic diet (–2510 kJ/d deficit) + exercise + self-regulatory intervention (SRI) to promote SPA		SPA was measured by tri-axial accelerometer worn for 7 d at baseline, 5 and 10 months, and operationalised as minutes of light PA	PA increased in both groups during the weight-loss phase Adjusted changes in minutes of light activity tended to be significantly greater in the SRI+DIET+EX group compared with the DIET+EX group Both groups reduced body weight during the intervention and regained during follow-up. Greater weight loss and lower regain found in the SRI+DIET+EX group	No compensation: NEPA increased
Racette et al. ⁽¹⁴⁾	Low-fat non-exercise: 7 obese women Age = 37 (4) BMI = NR Low-carb non-exercise: 6 obese women Age = 41 (6) BMI = NR Low-fat exercise: 5 obese women Age = 40 (4) BMI = NR Low-carb exercise: 5 obese women Age = 36 (5) BMI = NR	Diet-only group: Low-fat non-exercise: 15 % fat; 60 % carb; 25 % protein to approach 75 % of participant's REE or low-carb non-exercise: 50 % fat; 25 % carb; 25 % protein to approach 75 % of participant's REE Diet + Exercise Group: Low-fat exercise: supervised programme of aerobic exercise; 3d/week, 45 min/session, at 60–65 % VO _{2max} + low-fat diet or low-carb exercise: supervised programme of aerobic exercise, 3 d/week, 45 min/session, at 60–65 % VO _{2max} + low carb diet	12 Weeks	TEE by DLW over a 2-week period at baseline and end of intervention REE and TEF measured by indirect calorimetry PAEE = TEE – (REE + 0-01 × TEF) EXEE assessed by HR monitor Heart rate monitor worn on 3 d during DLW period (n 14)	The addition of aerobic exercise during the reducing diet proved to be an effective	Compensation: NEPA and NEAT decreased in the diet-only group No compensation: no change in NEPA and NEAT in the diet plus exercise group

Table 2. Continued

Studies	Sample	Intervention	Length + follow-up	Measures	Results	Behavioural response
Rangan et al. ⁽³¹⁾	Aerobic training (AT): 14 women, 14 men. Age = 52 (9) BMI = 31 (3) Resistance Training (RT): 20 women; 8 men. Age = 51 (12) BMI = 30 (3) AT/RT: 16 women; 10 men Age = 48 (11) BMI = 31 (3)	AT: Treadmill, elliptical or cycle ergometer exercise progressed over 8–10 weeks to reach a volume of approximately 7.4 km/ week RT: 3 d/week, 3 sets, 8–12 reps, 8 exercises for major muscle groups AT/RT: full combination of both exercise prescriptions	8 Months	RT3 accelerometer (Stayhealthy, Inc.) worn for 7 d at baseline and end of intervention All known exercise data were removed from the raw accelerometer files. The 30 min of RT3 data immediately before and after exercise were also eliminated	No significant change in non-exercise PAEE in any of the exercise training groups Change in body weight not reported	No compensation: no change in NEAT
Schutz et al. (32)	55 normal-weight and overweight women Age = 27 (1) BMI = 25 (5)	Prescribing additional PA (walking only) of 30 min/d Prescribing additional PA (walking only) of 60 min/d Prescribing additional PA (walking only) of 90 min/d	8 Weeks	Uniaxial accelerometer to measure PA	Compensation increased progressively as length of prescription increased The average compensation rate calculated as the ratio between expected steps/d (from baseline steps/d) by the observed steps/d from prescribed walking was 25 % with substantial inter-individual variation	Compensation: decrease in NEPA for the 60- and 90- min walking arms
Wang <i>et al.</i> ⁽³³⁾	34 women Age = 50-70 BMI = 25-40 Diet (n 11) Diet + LO-EX (n 12) Diet + HI-EX (n 11)	Diet: hypoenergetic diet (reduction of 1682 kJ/d) Diet + LO-EX: hypoenergetic diet (reduction of 1443 kJ/d) + treadmill walking, 3 d/week, progressing from 15–20 min at 45–50 % of HRR on week 1 to 55 min at 45–50 % HRR Diet + HI-EX: hypoenergetic diet (reduction of 1443 kJ/d) + treadmill walking, 3 d/week, progressing from 15–20 min at 45–50 % of HRR on week 1 to 30 min at 70–75 % HRR	20 weeks 12-month follow-up	REE measured via indirect calorimetry PAEE measured by RT3 accelerometer (Stayhealthy, Inc.)	Decreases in non-exercise PAEE during intervention Significant reductions in body weight in all groups The amount of weight regained after 6 and 12 months was inversely associated with decreases in PAEE	Compensation: NEAT decreased in all the intervention arms
Weigle et al. (34)	Diet: 5 men Age = 53 (9) BMI = 37 (3) Diet plus vest for weight replacement: 5 men Age = 49 (8) BMI = 35 (2)	Diet-only group received a 2929-kJ liquid diet Diet (2929-kJ liquid diet) plus a vest into which weights were inserted twice weekly to replace the weight lost	17 weeks	Waist motion sensor pedometer worn the entire intervention period 24-h in a metabolic ward	PA declined slowly and equally in both groups. Significant weight loss in both groups	Compensation: decreases in NEPA and NEAT in both intervention arms

PA, physical activity; NEPA, non-exercise physical activity; DO, diet-only; D-PA, diet plus physical activity; TEE, total energy expenditure; DLW, doubly labelled water; REE, resting energy expenditure; PAEE, physical activity energy expenditure; NEAT, non-exercise activity thermogenesis; SMR, sleep metabolic rate; Ex, exercise; SRI, self-regulatory intervention; SPA, spontaneous physical activity; HRR, heart rate reserve; NR, non-reported; TEF, thermic effect of food; AT, aerobic training; RT, resistance training; LO-Ex, low exercise; HI-Ex, high exercise.

Table 3. Non-randomised trials (seventeen studies)

Studies	Sample	Intervention	Length + follow-up	Measures	Results	Behavioural response
Bonomi et al. ⁽³⁵⁾	66 overweight and obese subjects: 56 women; 10 men Age = 51 (12) BMI = 38 (7)	Intervention consisted in 67% energy restriction	12 Weeks	PA was measured using a tri-axial accelerometer	Body weight decreased by 14 kg and activity counts increased Significantly less sedentary time and increased time spent walking and bicycling were observed Significant reduction in body weight	No compensation: NEPA increased
Colley et al. ⁽³⁶⁾	13 obese women Age = 41 (12) BMI = 34 (5)	Structured moderate-intensity walking programme with a weekly target of 6276 kJ/ week. A 4-week supervised phase (including 3–4 sessions/week) was followed by a 4-week unsupervised phase	8 Weeks	RT3 accelerometer (Stayhealthy, Inc.) worn for 14 d at baseline and weeks 3–4 TEE by DLW used on 7 participants at baseline and weeks 3–4 REE by indirect calorimetry NEAT = TEE-(REE + 0.1TEE + EXEE)	Accelerometer data showed no change in the time spent in sedentary, light or moderate activity from baseline to the intervention (week 4) NEAT decreased 22% from baseline to the intervention (week 4) Change in body weight not reported	Compensation: NEAT decreased
De Groot et al. ⁽³⁷⁾	13 overweight women (10 re-evaluated at 1 month follow-up; 8 re-evaluated at 1-year Follow-up) Age = 39 (6) BMI = 28 (2)	Slimming programme with low-energy diet tailored to each individual energy requirement (51% of weight maintenance intake), followed by a weight maintenance diet, adjusted for weight lost – prescribed until 1 year of follow-up	8 Weeks 1-Year follow-up	Metabolic chamber used to measure TEE and PAEE Actometer and Doppler metre counts	No difference was found between TEE before and 1 month after slimming PA increased 12 % during intervention but remained below baseline PA. 1 year after, reduced level of PA as in the 1-month follow-up was observed Spontaneous PA decreased during slimming and tended to increase afterwards	Compensation: reductions in NEPA during the slimming period
Di Blasio et al. ⁽³⁸⁾	34 post-menopausal women Age = 56 (4) BMI = 27 (4)	Walking programme at moderate intensity, 4 d/ week, progressing from 40 min at RPE 11 (on 15-category RPE scale) at month 1 to 50 min at RPE 13 at month 3	13 Weeks	SenseWear Pro ₂ armband worn for 3 consecutive days (2 weekdays and 1 weekend day), at baseline and end of intervention Measurements included both training and non-training days	No significant change in TEE or non-exercise PAEE in the complete sample, but two subgroups were identified: 44 % showed reduced non-ex PAEE and TEE of non-ex training days (GROUP-, non-responders), whereas 56 % increased their non-ex PAEE and TEE (GROUP+, responders) Change in body weight not reported	Compensation: reduction in NEAT in the non- responders subgroup
Goran et al. ⁽³⁹⁾	5 women Age = 63 (5) BMI = 24 (NR) 6 men Age = 68 (7) BMI = 24 (NR)	Cycle ergometer, 3 d/week. Progression from a target EE of 628 kJ/session at 60 % VO ₂ max to 1255 kJ/session, at 85 % VO ₂ max	8 Weeks	DLW over 10 d at baseline and in the last 10 d of the training programme REE by indirect calorimetry ExEE by HR monitor Non-ex PAEE = TEE – (REE + 0.1TEE + EXEE)	Non-exercise EE declined throughout the intervention No significant change in body mass	Compensation: decrease in NEAT
Herrmann et al. ⁽⁴⁰⁾	74 healthy, overweight/ obese, sedentary men and women Responders Age = 23 (3) BMI = 31 (4)	Intervention: Treadmill walking or jogging, 5 d/week, 1674 or 2510 kJ/session Comparison between participants with weight loss <5% (non-responders) v. ≥5% (responders)	10 Months	REE was assessed by indirect calorimetry. TEE was assessed using DLW over a 14-d period (at baseline and at 10 months) Non-Ex PAEE = (0.9 TEE-REE) net ExEE (i.e. ExEE-REE)	Non-exercise EE and NEPA increased in responders and decreased in non-responders Sedentary time decreased in both groups, but only in men was significant	Compensation: NEAT and NEPA decreased in the non-responders group

Table 3. Continued

Studies	Sample	Intervention	Length + follow-up	Measures	Results	Behavioural response
Hunter et al. ⁽⁴¹⁾	Non-responders Age = 22 (5) BMI = 31 (5) 7 women; 8 men Age = 67 (4) BMI = 25 (4)	Supervised resistance training (RT), 3 times per week for approximately 45 min/session Subjects were instructed to complete two sets of 10 repetitions in all exercises at an intensity of 65–80 % of 1 RM with a 2-min rest between each set	26 Weeks	NEPA and sedentary time were assessed by an accelerometer (model GT1M; Actigraph) TEE assessed by DLW at baseline and last 2 weeks of RT. PAEE = TEE - REE - 0·1TEE Adjusted PAEE = PAEE - Average ExEE Average ExEE assessed by indirect calorimetry in a previous study ARTE index was used to derive free-living PA (min/d) from PAEE	TEE and TEE minus the average exercise EE significantly increased Free-living PA (via ARTE index) increased and PAEE showed a tendency to raise No significant weight change	No compensation: no changes in NEAT and NEPA
Keytel et al. ⁽⁴²⁾	Control: 10 women Age = 55 (5) BMI = 27 (4) Exercise: 9 women Age = 58 (7) BMI = 25 (3)	Control: no exercise Exercise: Walking, 3 d/week, 70–75 % HR _{max} , beginning with 3 km walking on a sport's field and progressing to walking or jogging 3–6 km on the road	8 Weeks	Total daily energy expenditure (TEE) was calculated from HR minus EE regression equations and 24-h HR monitoring, at baseline and end of intervention	No significant differences in TEE either between exercise and control, or before or after exercise training No significant differences in TEE on exercise ν . non-exercise days Change in body weight not reported	No compensation: no change in NEAT
Leibel et al. ⁽⁴³⁾	18 obese (11 women and 7 men); Age = 29 (10) BMI = (NR) 23 non-obese (7 women and 16 men) Age = 26 (10) BMI = (NR)	Diet intervention: liquid formula (3347 kJ/d 40 % fat (maize oil), 45 % carbohydrate (glucose polymer), and 15 % protein (casein hydrolysate)). The energy intake was adjusted until the body weight was constant for at least 14 d 3 groups lost weight (non-obese 10 % loss, <i>n</i> 11; obese 10 % loss, <i>n</i> 9; obese 20 % loss, <i>n</i> 12)	Weight loss phase ranged from 4 to 7 weeks for the non- obese and from 6 to 14 weeks for the obese	TEE determined by DLW REE and TEF measured by indirect calorimetry in a respiration chamber Non-resting EE = TEE – (REE + TEF) PA monitor by using a wall- mounted radar detector in the metabolic chamber	Non-resting EE was significantly lower at weights 10 and 20% below the initial weight than at the initial weight The percentage of time spent in motion during a 23-h period did not differ (n 8)	Compensation: reduction in NEAT No compensation: no change in NEPA
Matsuo et al. ⁽⁴⁴⁾	90 women Age = 52 (7) BMI = 28 (3)	Combined diet and exercise intervention: Diet: twelve 90-min lectures + individual counselling Exercise: three 60-min lectures. For a sub-sample, additional supervised aerobic exercise sessions (90 min/session, 24 sessions)	14 Weeks	Uniaxial accelerometer worn for 7 d at baseline and end of intervention PAEE did not discriminate between training and spontaneous PA, but one group did not have supervised exercise sessions	Significant increases were observed in daily TEE/body weight and PAEE/body weight A significant correlation was observed between PAEE before and after the intervention Significant decreases in body weight	No compensation: no change in NEAT
McLaughlin et al. ⁽⁴⁵⁾	Eight men Age = 23 (1) BMI = 25 (5) Eight women Age = 24 (3) BMI = 22 (2)	Control phase: 8 d of usual activity Exercise phase: 8 d with imposed cycle ergometer to expend 2092 kJ plus REE on 4 alternate days of the week	16 d	HR monitoring with individuals HR/ EE calibration	No significant differences in non-exercise PAEE between exercise and control periods Body mass did not change	No compensation: no change in NEAT
Meijer et al. ⁽⁴⁶⁾	16 women Age = 35 (4) BMI = 23 (2) 16 men Age = 37 (3) BMI = 23 (2)	Running programme: 1 supervised + 3 non-supervised sessions, for a total distance of 15–25 km/week after 8 weeks and 25–40 km/week after 20 weeks Training included long slow-distance running (at 70 %–80 % HR _{max}), running at a higher	5 Months	Accelerometer for 7 consecutive days at baseline and 20 weeks DLW for TEE assessment SMR by indirect calorimetry Non-ExEE assessed from non- exercise activities	Accelerometer counts excluding training-related increased approximately 15% in men, but this change was not significant In men, a discrepancy was observed between the increase of TEE and the expenditure due to ExEE and non-ExEE activities. When	No compensation: no change in NEAT and NEPA

Table 3. Continued

Studies	Sample	Intervention	Length + follow-up	Measures	Results	Behavioural response
		speed (80–95 $\%$ HR $_{\rm max}$), and interval training (95–100 $\%$ HR $_{\rm max}$)			expressing TEE normalised for body mass or FFM, this difference disappeared Change in body mass not reported	
Meijer et al. ⁽⁴⁷⁾	Control: 4 women; 3 men. Age = 57 (3) BMI = 25 (1) Exercise: 8 women; 7 men. Age = 59 (4) BMI = 26 (3)	Supervised exercise, twice a week: a group session of 60-min with various aerobic exercises on 1 d and an individual session of 90 min consisting of 9 exercises using cardioand weight-stack machines on day 2; at 50 % HR reserve	12 Weeks	Tri-axial accelerometer worn for 14 d at baseline, 6 and 12 weeks	At week 6, no significant differences in non- exercise PA between training days and non- training days At week 12, after adjusting for training activity, physical activity on training days was significantly lower than on non-training days No change in body mass in both groups	Compensation: reduction in NEPA
Meijer et al. ⁽⁴⁸⁾	Control: 5 women; 6 men. Age = 59 (4) BMI = 26 (3) Exercise: 11 women; 11 men. Age = 63 (8) BMI = 29 (4)	Supervised exercise, twice a week: a group session of 60 min with various aerobic exercises on 1 d and an individual session of 90-min consisting of 9 exercises using cardio-and weight-stack machines on day 2. Intensity 50 % HR reserve	12 Weeks	Tri-axial accelerometer worn for 14 d at baseline, 6 and 12 weeks	At week 6, no significant differences in non- exercise accelerometer data between training days and non-training days At week 12, after adjusting for training activity, physical activity on training days was significantly lower than on non-training days No change in body mass in both groups	Compensation: reduction in NEPA
Van Dale et al. ⁽⁴⁹⁾	Diet: 6 women Age = 20–45 BMI = 30 (1) Diet + Exercise: 6 women Age = 20–45 BMI = 30 (1)	Diet (D): low energy formula diet first 4 weeks (approximately 2929 kJ/d); combination of the diet with normal food on the next 8 weeks (approximately 3347 kJ/d) Diet + Exercise (DE): low-energy formula diet first 4 weeks (approximately 2929 kJ/d); combination of the diet with normal food on the next 8 weeks (3602 kJ/d) plus 4 exercise sessions, 2-h aerobic training and 2-h fitness training per week at 55 % VO _{2max}	12 Weeks	HR memory system measured 24- h EE at baseline, weeks 4 and Wrist accelerometer Actometer worn over 5 full consecutive days, including 2 d of training and weekend days	PA increased 27 % in the DE group but not in the D group The adoption of regular structured exercise did not result in a negative compensatory reduction in NEPA No significant weight loss in both groups	No compensation: increases in NEPA
Van Etten et al. ⁽⁵⁰⁾	Control: 8 men Age = 35 (6) BMI = 24 (NR) Exercise: 18 men Age = 33 (6) BMI = 24 (NR)	Control: no exercise Exercise: supervised RT, 2 non-consecutive days/week, 3 sets, 15 reps, 10 exercises	18 weeks	Tri-axial accelerometer worn for 7 d, at baseline and intervention's end DLW over a 2-week period on 12 exercisers Indirect calorimetry for SMR HR monitor used to determine EXEE Non-ex PAEE = TEE- SMR - 0.1TEE - EXEE	Non-training PA measured by accelerometer did not change between groups Non-training EE measured did not change between groups Body mass did not change in both groups	No compensation: no change in NEAT and NEPA
Weinsier et al. ⁽⁵¹⁾	18 white and 14 black women Age = 38 (7) BMI = 29 (2)	Energy-restricted diet without exercise: diet provided a fixed proportion of carbohydrate, fat and protein (55, 22 and 23 %, respectively) and had an energy content of 3347 kJ/d No attempt was made to alter the subjects' self-selected patterns of PA	Length necessary to achieve the weight loss of 10 kg (average 24 weeks)	REE measured in a chamber calorimeter TEE measured by DLW over 14 d PAEE was assessed as	Free-living PA was similar between the groups. Free-living PAEE did not change significantly after weight loss Free-living PA increased an average of 30 % above-rest, but not above-sleep. However, reported activities did not change from before to after weight loss	No compensation: no change in NEAT or NEPA

PA, physical activity; NEPA, non-exercise physical activity; TEE, total energy expenditure; DLW, doubly labelled water; REE, resting energy expenditure; NEAT, non-exercise activity thermogenesis; Ex, exercise; ExEE, Exercise energy expenditure; PAEE, physical activity energy expenditure; NR, non-reported; TEF, thermic effect of food; RM, repetition maximum; ARTE, activity-related time equivalent; FFM, fat-free mass; HR, heart rate; HR_{max}, maximal heart rate; RT, resistance training; SMR, sleep metabolic rate; RPE, rated perceived exertion.

Table 4. Diet-only, exercise-only, combined diet and exercise and all studies combined, according to the presence or absence of changes in non-exercise activity thermogenesis (NEAT) and non-exercise physical activity (NEPA) (Medians and ranges; numbers and percentages)

		Reducti	on (<i>n</i> 15)		No changes (n 21)				
	NEAT	(n 11)	NEP	A (n 7)	NEAT	「 (n 13)	NEPA (n 17)		
All studies (n 36)*	Median	Range	Median	Range	Median	Range	Median	Range	
Age (years)	39	23–66	39	23–63	43	22–71	41	22–71	
BMI (kg/m²)	30	23-37	29	25–37	30	23-44	30	23-44	
Study length (months)	5	2-12	4	2-10	5	0.3-10	6	0.3-12	
Weight loss (kg)	-10	-29-4	-8	-27-0	-5	-14-0	-7	-29-0	
Behavioural therapy (studies)									
n		3		1		3		6	
Diet-only studies									
Age (years)	39	25-59	44	39-53	38	33-51	38	25-59	
BMI (kg/m²)	28	27–37	35	28–37	31	28-44	28	27-44	
Study length (months)	6	3–12	4	2–4	5	0.3–10	6	0.3-12	
Weight loss (%)	-10	-29-3.5	-17	-27-8-3	-8	-14-0	-8	-29-0	
Behavioural therapy (studies)									
n		3		1		1		3	
Exercise-only studies		_							
Age (years)	49	23-66	40	23-63	48	22-67	50	22-67	
BMI (kg/m²)	29	23-34	26	25-31	29	23–35	30	23–35	
Study length (months)	3	2–10	6	3–10	6	0.3–10	6	0.3-10	
Weight loss (%)	-8	-8-7	-1	-8-0	-1	-9-0	-1	-9-1	
Behavioural therapy (studies)									
n		0		0		0		1	
Exercise duration (min/session)	53	45–60	75	60–90	45	20-120	45	20-120	
Exercise frequency (times/week)	3	2–10	6	3–10	6	0.3-10	6	0.3-10	
Aerobic exercise (%)		00	71		76		87		
Strength exercise (%)		0	0		18		13		
Combined aerobic and strength (%)		0	29		6		0		
Combined diet and exercise studies									
Age (years)	59	39–59		0	43	33-71	48	33–71	
BMI (kg/m²)	33	32–33		0	32	28–44	33	28–44	
Study length (months)	5	2–5		0	5	3–6	5	2–6	
Weight loss (%)	-12	-15-9		0	-9	-13-5	-9	-15-5	
Behavioural therapy (studies)									
n		0		0		2		3	
Exercise duration (min/session)	30	30–55		0	50	30–90	48	30–90	
Exercise frequency (times/week)	3	2–3		0	4	2–5	4	2–5	
Aerobic exercise (%)	-	6.7		0	-	00	=	100	
Strength exercise (%)		0		0	·	0		0	
Combined aerobic and strength (%)		3·3		0		0	0		

^{*} Discrepancy between the number of overall studies that showed reductions (15) or no changes (21) in NEAT and NEPA and the number of studies displayed in the row below, according—the presence or absence of changes in NEAT (11 v. 13, respectively) and NEPA (7 v. 17, correspondingly), is due to studies that determined both NEAT and NEPA.

prescribed) by subtracting the sum of REE by indirect calorimetry with TEF (assumed as 0·1TEE) from TEE obtained by DLW.

Methods for assessing non-exercise physical activity. In RCT, Martin et al. (16) assessed NEPA with ACC (model 716 (Actigraph) and RT3 accelerometer (Stayhealthy, Inc.)). In another trial under the CALERIE study, Martin et al. (22) used a metabolic chamber to assess NEPA by determining the percent time participants were active. In RT, DeLany et al. (28) assessed NEPA by counting steps/d using multisensor PA monitors (SenseWear-Pro3; BodyMedia Inc.). Racette et al. (14) assessed NEPA from HR monitors for PA assessment (excluding exercise data on exercise activity). Weigle (34) used a pedometer for assessing NEPA. In NRT, Bonomi et al. (35) assessed NEPA through a combined actometer and Doppler measures. Brehm et al. (27) used pedometers for assessing NEPA.

De Groot *et al.*⁽³⁷⁾ assessed NEPA using an actometer and Doppler metre counts. Leibel *et al.*⁽⁴³⁾ assessed NEPA using a

respiratory chamber equipped with a wall-mounted radar detector to monitor PA. Van Dale *et al.*⁽⁴⁹⁾ assessed NEPA using an actometer and HR monitor. Weinsier *et al.*⁽⁵¹⁾ determined NEPA by using the activity-related time equivalent (Arte) index for free-living PA (min/d).

Weight loss. Median weight loss was $-11.0 \,\mathrm{kg}$ (range $-29.2 \,\mathrm{to}$ 0·1) with a median of $-12.0 \,\mathrm{kg}$ (range $-29.2 \,\mathrm{to}$ 0·1) for NRT, $-13.0 \,\mathrm{kg}$ (range $-26.9 \,\mathrm{to}$ -6.1) for RT and $-8.4 \,\mathrm{(range}$ $-11.2 \,\mathrm{to}$ -3.5) for RCT.

Risk of bias. The quality of assessment tool rated one trial as weak⁽⁴³⁾, twelve as moderate^(14–16,22,27,29,33–35,37,49,51) and one trial as strong⁽²⁸⁾ (online Supplementary material SIII).

Main outcome. A total of fifteen out of twenty-four intervention arms (seven out of fourteen diet-only interventions) reported a significant decrease in NEAT or NEPA resulting from the prescribed diet.





Among the nine diet-only trials assessing NEAT, decreases were observed in six studies (fourteen diet-only trial arms) – specifically three intervention arms of an NRT⁽⁴³⁾, four intervention arms of RT^(14,33,34) and seven intervention arms of RCT^(15,16)

From the eleven studies assessing NEPA, behavioural compensation was observed in three diet-only interventions (four intervention arms), specifically one intervention arm of an $NRT^{(37)}$ and three intervention arms of $RT^{(14,34)}$.

Exercise-only interventions

The thirty-five exercise-only intervention arms (twenty studies) comprised approximately 56% of the total number of studies included in this review, with a total of eleven NRT (55%), two RT (10%) and seven RCT (35%).

Study characteristics

Sample size. Exercise-only studies comprised 917 participants with a median sample size of 28 (range 8-139). NRT included a median sample size of 20 (range 9-40), RT included a median sample size of 27 (range 26–28) and RCT included a median sample size of 35 (range 8-139).

Completion rate. Fourteen trials reported the percentage of exercise sessions attended as $>99^{(19,21)}$, $62.5^{(26,40)}$, $94^{(24)}$, 99%for moderate intensity and 96% for high intensity (23), 90% for aerobic training, 84% for combined aerobic and resistance training, but % was not available for resistance training (31). 100% for 30-min and 60-80% for 60- and 90-min groups (32), $86^{(38,48)}$, $>90^{(41)}$, $85^{(47)}$, $95^{(50)}$, $100^{(45)}$ and $64\%^{(26,40)}$, whereas one trial⁽³⁶⁾ reported the level of exercise EE (prescribed 6276 kJ/week; achieved 6000 kJ/week). Whybrow *et al.* (25) and Meijer et al. (46) reported good compliance, but no percent values were given. Compliance with the exercise protocol was not reported in three trials (20,39,42).

Trial length. The median duration of the studies was 5.3 (range 0.3–10) months, varying from 4.2 (range 0.3–10) for NRT, 8 months for the two RT and 5.2 (range 0.5-10) for the RCT

Behavioural intervention. Only the study of Kozey-Keadle et al. (21) included behavioural therapy.

Exercise mode. NRT included a variety of indoor or outdoor walking/running^(36,38,42,46), cycle ergometer exercise^(39,45), fitness classes and resistance training (47,48), resistance training only (41,50) and treadmill (40). RT intervention arms involved a combination of resistance and aerobic training (31) and daily walking⁽³²⁾. The remaining RCT intervention arms used laboratorybased aerobic exercise conducted on cycle ergometers/rowers/ steppers/Arc Trainer/treadmills^(19–21,23,25,26), or outdoor walking/ running⁽²⁴⁾.

Exercise supervision. All exercise sessions were supervised in thirteen NRT trials (39-41,47,48,50) and RCT (19-21,23-26), partially supervised in five NRT trials $^{(36,38,42,45,46)}$ or not reported in RT $^{(31,32)}$.

Exercise prescription (frequency). The median exercise frequency was 4.1 (range 2.0-7.0) d/week with daily week values of 3.4 (range 2.0-5.0) for NRT, 3.9 (range 2.5-5.0) for RT and 4.8 (range 3.5-7.0) for RCT.

Exercise prescription (intensity). Six NRT-prescribed intensity as a percentage of maximal VO_{2max} (53%⁽⁴⁵⁾, 85%⁽³⁹⁾), percentage of maximal HR (70-80 %HR_{max}, 70-75 %⁽⁴²⁾), by level of EE relative to body weight (moderate intensity: 28.6 kJ/kg and high intensity: 57·1 kJ/kg)⁽²⁵⁾, one based on HR reserve (50% HRR⁽⁴⁸⁾) and one based on ratings of perceived exertion (11-13 on a 15-point scale⁽³⁸⁾). Resistance training in the study by Hunter et al. (41) was conducted at 65-85% of one maximum repetition. Exercise intensity in RT/RCT studies that included aerobic exercise was prescribed as a percentage of maximal/ peak VO_2 in five trials $(50\%^{(19)})$; three sessions >70% and remaining self-selected $^{(23)}$, $70\%^{(24)}$; 65-80% – vigorous and $40-55 - \text{moderate}^{(20)}$, $75\%^{(31)}$), maximum HR (70-80\%^{(26)}), between 40 and 65% HR reserve⁽²¹⁾. Prescribed exercise intensity was not reported in four trials (36,46,47,50) and selfselected in an RT⁽³²⁾. Resistance training was performed at 8-12 repetition maximum (approximately 80%)(31), whereas Van Etten et al. (50) did not report intensity.

Exercise prescription (duration). Median session duration was approximately 55 min (20-120), with values of about 50 min (35–75) in NRT, 67 min (30–111) and 52 min (20–120). Four NRT-prescribed exercise duration was performed by time (50 min⁽³⁸⁾, 60 min aerobic plus 90 min aerobic/strength⁽⁴⁷⁾, 60 min aerobic plus 90 min aerobic/strength and 39 and 55 min⁽⁴⁰⁾, respectively, for the 1674 kJ/session and 2510 kJ/session), three based on level of exercise EE (1569-2092 kJ/ses $sion^{(36)}$, 1255 kJ/session⁽³⁹⁾, 2092 kJ/session⁽⁴⁵⁾) and two based on walking/running distance^(42,46). The median duration of exercise for the five trials prescribing exercise by time was 150 (range 60– 200) min/week. The median for trials prescribing exercise by EE was 4094 (range 1883-6276) kJ/week. Prescribed walking distance was 3-6 km/d⁽⁴²⁾, and running distance was 25-40 km/ week⁽⁴⁶⁾. One study dosed exercise by level of EE relative to body weight 28.6 or 57.1 kJ/kg⁽²⁵⁾) or absolute EE (2092 kJ/d above REE⁽⁴⁵⁾). In three trials, prescribed exercise duration was calculated as EE per body weight (19,20,31), four based on time (21,24,25,32) and two according to level of exercise EE (1255 and 2510 kJ/ session⁽²³⁾; 1674 and 2510 kJ/session⁽²⁶⁾). In three RCT, exercise time was prescribed for $60^{(24)}$, $40^{(21)}$ and $40 \, \text{min}^{(25)}$. Schutz et al. (32) involved three arms with different durations (30, 60 and 90 min). Willis *et al.*⁽²⁶⁾ prescribed 39 and 55 min for the $1674 \, \mathrm{kJ/}$ session and 2510 kJ/session; Rosenkilde et al. (23) prescribed 1255 and 2510 kJ/d; Church et al. (19) prescribed 17, 33 and 50 kJ/kg per week; and Rangan *et al.*⁽³¹⁾ and Hollowell *et al.*⁽²⁰⁾ dosed duration as 58.6 kJ/kg per week and 59 and 96 kJ/kg per week. Resistance training in the study of Van Etten et al. (50) consisted of three sets of fifteen reps over ten exercises, whereas for Hunter et al. (41) duration of 45 min, ten repetitions with 2 min of rest by set was used.

Participant characteristics

Age. Studies were generally conducted in adults with a median age of 44·1 years (22·1–66·8), specifically 49·0 years (range 22·1-66·8) for NRT, 38·7 years (range 27·0-52) for RT and 42.2 years (range 23-57.5) for RCT.

Sex. Five studies included women only (19,32,36,38,42), three studies included men only (23,24,50) and twelve studies included a combined sample of women and men^(20,21,25,26,31,39-41,45-48).

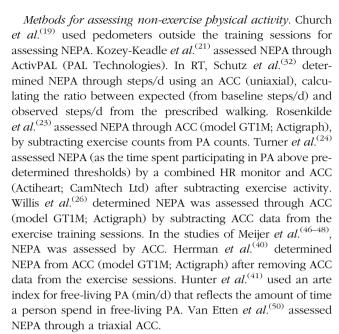


BMI. Nine studies included overweight/obese individuals $^{(19-21,24,26,31,38,40,48)}$. Non-obese participants were included in ten studies $^{(23,25,32,39,41,42,45-47,50)}$. Obese-only individuals were included in one study $^{(36)}$. Median BMI was $31\cdot2\,\mathrm{kg/m^2}$ (range $27\cdot4-43\cdot6$) in the studies that provided data on this parameter, with a median of $27\cdot0\,\mathrm{kg/m^2}$ (range $22\cdot8-33\cdot9$) for NRT, $27\cdot8\,\mathrm{kg/m^2}$ (range $22\cdot8-33\cdot9$) for RT and $42\cdot2\,\mathrm{kg/m^2}$ (range $23\cdot0-57\cdot9$) for RCT.

Ethnicity. Two studies described the ethnicity representation in the study sample as Caucasian^(23,41), whereas three studies included Caucasian, Black, Hispanics and Asians^(19,26,40). The remaining studies did not report ethnicity.

Physical activity level/fitness. In all, seventeen studies characterised the level of PA of the participants as sedentary or exercising <2–3 d/week^(19–21,23–26,31,36,40–42,45–48,50). Di Blasio *et al.*⁽³⁸⁾ reported that PA level ranged from sedentary to highly active and fitness level from poor to good. Two studies did not report PA level or fitness^(32,39).

Methods for assessing non-exercise activity thermogenesis. Hollowell et al. (20) used an ACC (RT3 accelerometer; Stayhealthy, Inc.) for assessing NEAT (although authors referred 'non-exercise PAEE') by excluding exercise EE (ExEE) (including the 30 min before and after exercise). Turner et al. (24) assessed NEAT (referred to as 'non-prescribed PAEE') through a combined HR monitor and ACC (Actiheart; CamNtech Ltd) by, respectively, subtracting the ExEE from the overall PAEE. Whybrow et al. (25) calculated non-exercise EE as the difference between TEE from DLW and ExEE by an individual calibrated HR monitor. Willis et al. (26) determined NEAT (referred as 'nonexercise EE') as (0.9 TEE-RMR)-net ExEE (ExEE-RMR), where TEE was assessed by DLW and REE and ExEE by indirect calorimetry. Rangan et al. (31) assessed NEAT (referred to as nonexercise PAEE) with ACC (RT3 accelerometer; Stayhealthy, Inc.) by removing exercise data EE. Across NRT, Colley et al. (36) assessed NEAT by subtracting the sum of exercise EE (using HR monitor), REE (indirect calorimetry) and TEF (assumed as 10% of TEE) from TEE obtained by DLW. Di Blasio et al. (38) used a SenseWear Pro 2 armband on training and non-training days to assess whether PAEE between responders and non-responders differed in non-exercise days. Goran & Poehlman⁽³⁹⁾ used DLW (TEE), indirect calorimetry (REE) and HR monitoring during exercise training to determine NEAT as TEE-(REE+0.1TEE+ ExEE). Herrman et al. (40) assessed NEAT (referred to as 'nonexercise EE') as (0.9 TEE-RMR)-net Exercise EE (exercise EE-RMR), where TEE was assessed by DLW and REE and ExEE by indirect calorimetry. Hunter et al. (41) used DLW (TEE) and indirect calorimetry (REE) to determine PAEE (as TEE-01TEE-REE) and adjusted PAEE (adjusted for energy cost of average ExEE). HR monitoring with individual HR/EE calibration was used by Keytel et al. (42) to assess 24-h daily EE between training and non-training days and between exercise and control group. McLaughlin et al. (45) calculated NEAT from HR monitor using HR/EE individual calibration between control and exercise periods. Meijer et al. (46) assessed TEE with DLW, SMR by indirect calorimetry and NEAT (referred as EE from nonexercise activities). Van Etten et al. (50) assessed NEAT (referred to as non-training EE) as TEE from DLW, minus SMR from indirect calorimetry minus ExEE from HR measurements.



Weight loss. Median weight loss was $-2.3 \,\mathrm{kg}$ (range $-9.1 \,\mathrm{to}$ 0.1) with a median and range of $-2.1 \,\mathrm{kg}$ (range $-9.1 \,\mathrm{to}$ 0.1) for NRT and $-2.4 \,\mathrm{kg}$ (range $-5.2 \,\mathrm{to}$ -0.8) for RCT (data not available for RT).

Risk of bias. Using the quality assessment tool, eight trials were rated as weak $^{(20,24,25,31,32,36,42,45)}$, eleven as moderate $^{(21,23,26,38-41,46-48,50)}$ and one trial as strong $^{(19)}$ (online Supplementary material SIII).

Main outcome. A total of seven out of twenty studies (eight in thirty-five intervention arms) reported a significant decrease in NEPA or NEAT, resulting from the prescribed exercise.

From the fourteen exercise-only interventions, reductions in NEAT were observed in four NRT (four intervention arms) $^{(36,38-40)}$.

In a total of twelve exercise-only trials, decreases in NEPA were observed in four studies, specifically three arms of $NRT^{(40,47,48)}$ and two arms of a $RT^{(32)}$.

Combined diet and exercise interventions

The 11 combined diet and exercise interventions arms (9 studies) comprised 25% of the total number of studies included in this review with a total of 2 NRT (22%), 5 RT (56%) and 2 RCT (22%).

Study characteristics

Sample size. Combined diet and exercise trials comprised a total of 244 participants with a median sample size of 23·8 (range 5–90). NRT included a median sample of 48 (range 6–90), RT of 20 (range 7–61) and two RCT, from the same large study (CALERIE), included twelve participants.

Completion rate. Two studies reported compliance to the exercise sessions (>90 $^{(33)}$ and 22 $^{(28)}$). Two studies reported compliance to diet (100 $^{(33)}$ and 55 $^{(28)}$). The remaining studies did not include data on compliance to either exercise or diet.

Trial length. The median duration of the studies was 4.4 months (range 2–0–6.0). Median duration was 2.8 months





(range 2.5-3.0) for NRT, 4.4 months (range 2.0-6.0) for RT and 6 months for the two RCT.

Behavioural intervention. A total of five studies included behavioural therapy^(14,15,22,30,44) comprising 44% of the combined diet and exercise studies included in this review.

Energy restriction. EI was reduced by 12.5 %(15,22) and 75% of RMR⁽¹⁴⁾. EI was prescribed as 5021 kJ/d⁽⁴⁴⁾, approximately 2092 kI/d in the first 4 weeks followed by 4 weeks at approximately 3515 kJ/d⁽²⁹⁾, about 2929 kJ/d in the first 4 weeks and about 3602 kJ/d in the next 8 weeks (49), and according to body weight (<90.7 kg, 5021-6276 kJ/d; >90.7 kg and $<113.4 \text{ kg}, 6276-7531 \text{ kJ/d}; \text{ and } >113.4 \text{ kg}, 7531-8368 \text{ kJ/d}^{(28)}$. EI was also prescribed as a reduction of 2510 kJ/d⁽³⁰⁾ and 1443 kJ/d⁽³³⁾.

Exercise mode. One study used indoor aerobic and strength training⁽²⁹⁾, indoor aerobic/fitness training^(44,49), treadmill/ walking^(30,33), treadmill/stairstep/rowing/bicycling⁽¹⁴⁾, walking/ running/bicycling^(15,22) and outdoor brisk walking⁽²⁸⁾.

Exercise supervision. Exercise sessions were supervised in $NRT^{(44,49)}$ and $RT^{(14,30)}$, partially supervised in $RT^{(29)}$ and $RCT^{(15,22)}$, or not reported in two RT^(28,33).

Exercise prescription (frequency). The median exercise freguency was $3.7 \,\mathrm{d/week}$ (range 2.0-5.0) with $3.0 \,\mathrm{d/week}$ (range 2.0-4.0) for NRT, $3.6 \,\mathrm{d/week}$ (range 3.0-5.0) for RT and $5 \,\mathrm{d/mem}$ week in the two RCT.

Exercise prescription (intensity). Three trials prescribed intensity as a percentage of maximal VO_{2max} (NRT: 55%⁽⁴⁹⁾; RT: $50-60\%^{(29)}$; $60-65\%^{(14)}$), and two based on HR reserve $(65-70\%^{(30)}; 45-50\%; \text{ and } 70-75\%^{(33)})$. Prescribed exercise intensity was not reported in one trial (44) and was self-selected in three trials^(15,22,28).

Exercise prescription (duration). Exercise duration was prescribed by time in most studies (NRT: 90 min/session (44) and 60 min/session⁽⁴⁹⁾; RT: 30 min/session⁽³⁰⁾, 55 and $30 \, \text{min/session}^{(33)}$; $60 \, \text{min/session}^{(28)}$; $45 \, \text{min/session}^{(14)}$; $90 \, \text{min/session}^{(14)}$ session⁽²⁹⁾). Prescribed exercise duration was self-selected in two RCT^(15,22)

Participant characteristics

Age. Studies were generally conducted in adults with a median age of 44·1 years (range 22·1-66·8), specifically 49·0 years (range 22·1-66·8) for NRT, 38·7 years (range 27·0-52) for RT and 42.2 years (range 23-57.5) for the two RCT.

Sex. Five studies included women only (14,29,33,44,49), and four studies included a combined sample of women and men^(15,22,28,30).

BMI. Three studies included overweight/obese individuals (33,44,49), four studies included obese participants (14,28-30) and two trials included non-obese individuals (15,22). In the studies that provided data on this parameter, BMI was 32.3 kg/m² (range 27.5–43.6), with a median and range of 29.1 kg/m² (range 27.8–30.3) for NRT, 34.6 kg/m² (range 32.4– 43.6) for RT and 27.7 kg/m^2 (range 27.5-27.8) for the two RCT.

Ethnicity. Two studies include all ethnic groups - that is, Caucasian, Black, Asian and Hispanics (15,22); one study included Asians only⁽⁴⁴⁾; three studies included Caucasian and Black participants (28,30,33); and three studies did not report ethnic groups (14,29,49)

Participant activity level/fitness. Three studies characterised the level of PA of the participants as sedentary $^{(14,30,33)}$.

Methods for assessing non-exercise activity thermogenesis. Redman et al. (15) assessed NEAT (referred as activity-related EE) as the residual value of the regression between measured TEE obtained from DLW and measured SMR using indirect calorimetry, but ExEE was not assessed. DeLany et al. (28) assessed NEAT (referred to as PAEE) as TEE from DLW minus the sum of REE by indirect calorimetry with TEF (assumed as 0.1TEE) but ExEE was not calculated, restricting an accurate assessment of NEAT. Kempen et al. (29) assessed NEAT (referred to as non-exercised PA) by subtracting the sum of SMR from indirect calorimetry plus TEF (assumed as 0.1TEE) plus ExEE (from HR monitor) from TEE by DLW. Racette et al. (14) assessed NEAT (referred to as non-exercise PAEE) with DLW (for TEE), TEF and REE by indirect calorimetry and ExEE from HR monitors as TEE - (REE+TEF+ExEE). Wang et al. (33) used ACC (RT3 accelerometer; Stayhealthy, Inc.) for non-exercise PAEE (excluding exercise data on EE). Matsuo et al. (44) assessed NEAT using an ACC (Lifecorder; Suzuken Co. Ltd).

Methods for assessing non-exercise physical activity. Martin et al. (22) used a metabolic chamber to assess NEPA by determining the percent time participants were active. DeLany et al. (28) assessed NEPA through steps/d using a multisensor PA monitor. Nicklas et al. (30) used an ACC for assessing NEPA. Racette et al. (14) assessed NEPA from HR monitors for PA assessment (excluding exercise data on exercise activity). Van Dale et al. (49) assessed NEPA using an actometer and HR

Weight loss. Median weight loss was -9.8 kg (range -14.8 to -5.2) – specifically -9.2 kg (range -13.2 to -5.2) for NRT, $-10.4 \,\mathrm{kg}$ (range -14.8 to -6.6) for RT and $-8.8 \,\mathrm{kg}$ for the

Risk of bias. On the basis of the quality assessment tool, one trial was rated as weak⁽⁴⁴⁾, seven as moderate^(14,15,22,29,30,33,49) and one trial as strong⁽²⁸⁾ (online Supplementary material SIII).

Main outcome. A total of two out of nine combined diet and exercise interventions (three in eleven intervention arms) reported a significant decrease in NEPA or NEAT resulting from the prescribed diet plus exercise.

From the six combined diet and exercise trials that assessed NEAT, reductions were observed in three intervention arms of two RT^(29,33), whereas no behavioural compensation was observed in the five interventions that assessed NEPA.

Discussion

We systematically reviewed thirty-six studies with a variety of designs including NRT and RT to address whether the prescribed diet and/or exercise led to reductions in NEPA/NEAT in healthy adults. A reduction in NEAT has been hypothesised as a way to compensate for the increased EE of prescribed exercise and/or energy deficit from energetic restriction diets, resulting in less-than-expected negative energy balance and related weight loss⁽¹⁷⁾.

Overall, our review found decreases in NEPA or NEAT in fifteen out of thirty-six studies conducted in healthy adults using



diet-only intervention, combined diet and exercise intervention and exercise-only intervention (twenty-six out of a total of seventy intervention arms). Decreases in NEPA and/or NEAT were observed in seven out of fourteen diet-only interventions, two out of nine combined diet and exercise trials and seven out twenty exercise-only trials. In addition, it is important to highlight some other relevant findings. This review reported that the intervention arms that decreased NEAT were the ones presenting higher median values of weight loss (approximately 10 kg) compared with those who reported no changes in NEAT (approximately 5 kg). This observation suggests that reductions in NEAT may play a protective role when substantial body weight is lost.

Only seven of twenty exercise-only studies (eight out thirty-five intervention arms – 23%) included in this review reported a significant decrease in NEAT assessed by DLW/HR/metabolic chambers/cart^(36,38–40) or NEPA assessed by pedometer/ACC/actometer/doppler^(32,40,47,48). Studies that reported decreased NEPA/NEAT used a non-randomised design and were mainly conducted in sedentary overweight or obese adults. Age varied from young^(32,40), middle-aged^(36,38,47,48) to older adults⁽³⁹⁾. We observed that median age was similar between those who compensated compared with those who did not compensate, although Washburn *et al.*⁽¹⁰⁾ suggest that NEPA/NEAT may decrease in response to exercise training in older individuals.

In exercise-only studies that showed reductions in NEAT, the median duration of the studies was half the median duration of trials that did not present behavioural compensation. Apparently, compensation seems to occur in exercise studies of reduced duration. These results do not extend the findings observed by Riou *et al.* (53), reporting that the degree of energy compensation is near 84% for exercise interventions of a longer duration.

In contrast, seven out fourteen studies (fifteen out twenty-four intervention arms – 63%) testing the effects of diet-only interventions reported a significant decrease in NEAT assessed by DLW/HR/ ACC/metabolic chambers/cart($^{14-16,33,34,43}$) or NEPA assessed by pedometer/ACC/actometer/doppler(14,34,37). Studies that reported decreased NEPA/NEAT were conducted in sedentary overweight or obese adults and used a randomised design. Median age was below 40 years($^{14-16,37,43}$) in the majority of the trials, but middle-aged to older adults were studied(33,34).

Considering the combined effects of diet and exercise, only two out of nine studies (three out eleven intervention arms – 27%) testing the effects of diet plus exercise interventions showed a reduction in NEAT^(29,33) but not in NEPA by means of DLW/ACC/metabolic carts^(29,33). Studies that reported reductions in NEAT were conducted in sedentary overweight or obese adults and used a randomised design with a median age of 37 years⁽²⁹⁾ and approximately 60 years⁽³³⁾.

Reductions in NEAT/NEPA were observed in more than half of the diet-only intervention arms (approximately 63%), followed by diet plus exercise (27%) and exercise-only (23%) intervention arms. It is possible that diet-only interventions are more prone to cause reductions in NEAT/NEPA compared with exercise-only or diet plus exercise, but this

hypothesis has not been evaluated in a trial comparing changes in NEPA/NEAT in response to diet, exercise training protocols and combined diet and exercise training protocols. Moreover, in studies that involved exercise-only and diet plus exercise studies, the decrease in NEAT was absent in trials that prescribed resistance training. These observations suggest that exercise prescription may indeed have benefits for weight management interventions, although well-designed trials are required to definitively clarify the role of exercise dose on NEAT and NEPA.

Further, considering all the intervention arms that presented behavioural compensation in free-living PA, approximately 81% reduced NEAT and only 19% presented decrements in NEPA (twenty-one and nine intervention arms, respectively, out of twenty-six). Indeed, studies using methods to assess both NEAT and NEPA found reductions in the former but not in the latter⁽¹⁶⁾. These observations may be owing to methodological limitations in assessing NEPA in free-living conditions, although we only included those studies that used objective measures of PA. Indeed, obtaining accurate measures of NEPA and NEAT in free-living conditions is challenging, specifically during an energy balance intervention given the variable nature of human adaptive response. DLW method and activity monitors are the most common approaches (20,38,39,54). DLW is the state-of-the-art method for measuring TEE⁽⁵⁴⁾. When DLW is used in exercise training trials. NEAT is typically estimated using the measured or estimated REE and ExEE. Most of the studies assume that the TEF represents 10% of TEE without changes over the intervention. Therefore, NEAT is calculated as the difference between the TEE and the sum of REE, TEF (or the assumption of 0.1 TEE) and ExEE prescribed in exercise or combined diet and exercise interventions. In diet-only studies, authors refer to NEAT as PAEE, assuming that participants did not engage in exercise activities outside the energy-restricted intervention. A major drawback of determining NEAT is the involved cost, specifically owing to the use of DLW measurements, limiting the number of participants included in the studies. Nevertheless, DLW provides one value of TEE over a period of days, which means that for assessing NEAT when exercise is prescribed the related EE needs to be accounted for. In addition, DLW does not provide the type of non-Ex PA performed (i.e. sitting and ambulatory movement) or PA patterns. These limitations can partly be overcome using activity monitors, but estimates of EE from accelerometry are less accurate than those from DLW⁽⁵⁴⁾. Indeed, PAEE might be somewhat independent of measurements of body movement for wide ranges of PA amounts⁽⁵⁵⁾. Pontzer et al.⁽⁵⁵⁾ observed that after controlling for body composition and size TEE was positively related with PA, but the association was stronger over the lower range of PA, whereas TEE plateaued in individuals whose PA was considered in the upper range, supporting a constrained TEE model.

Limitations of the studies

There are important short-comings in the studies included in this systematic review. The methodological issues in assessing PA and EE, described previously, may limit the accuracy in

1343

evaluating the impact of diet and/or exercise training on NEAT/ NEPA. Considering the relevance of energy balance interventions for weight management, it is important to assess the effect of diet and/or exercise training on compensatory responses using accurate techniques. Only fourteen out of thirty-six studies (14–16,22,25,28,29,36,39–41,46,50,51) assessed NEAT using DLW, the state-of-the-art method for TEE measurements in freeliving individuals⁽⁵⁶⁾. In addition, for determining NEAT, REE measures through indirect calorimetry and accurate methods for assessing ExEE are required. Only two studies included in this review provided measures of exercise EE by indirect calorimetry (26,40), although REE was assessed with this technique in eleven studies along with DLW^(14,15,22,28,29,36,39,41,46,50,51)

Studies were not specifically designed and appropriately powered to detect differences in NEAT/NEPA between- or within-group with statistical significance in response to diet and/or exercise. The majority of these trials were conducted in small samples of <20 participants $^{(14,24,29,34,36,37,39,41,42,45,47,49,50)}$ In addition, in those studies that were specifically designed to address the effect of diet and/or exercise training on NEAT/ NEPA, small samples were used^(15,22,24,50).

Other limitations include the lack of studies that tested the impact of the degree of energy restriction, weight-loss magnitude and exercise dose.

Limitations of this review

The findings of our review are based on data coming essentially from weak to moderate study designs (NRT and RT with an elevated risk of bias).

Conclusions

Although the present systematic review did not find evidence to suggest that diet and/or exercise training has a significant effect, decreases in NEPA (four studies), NEAT (eight studies) or both (three studies) were observed in 63% of the total diet-only intervention arms, with only 23 and 27% of the declines observed in exercise-only or combined diet and exercise trial arms. We also reported that participants who decreased NEAT presented a median amount of weight loss that was almost double the amount of those participants who did not compensate, suggesting that behavioural compensation leading to reductions in NEAT may depend on the degree of energy stores used when substantial body weight is lost, thus conserving energy.

Nevertheless, additional RT designed to specifically evaluate the impact of diet and/or exercise on NEPA/NEAT should be conducted in overweight/obese adults. In particular, studies should be powered to detect clinically significant differences. In addition, measures of daily and exercise EE should be included for an accurate assessment of NEAT. Studies must also analyse the impact of the degree of energy restriction, weight-loss magnitude, exercise dose and participant characteristics in more detail.

Acknowledgements

The data sets generated for this analysis are available from the corresponding author on reasonable request.

The current work was supported by National funding from the Portuguese Foundation for Science and Technology within the R&D units 472 (UID/DTP/00447/2013). P. B. J. is supported by the Portuguese Foundation for Science and Technology with a post-doctoral scholarship (SFRH/BPD/115977/2016).

A. M. S., P. J. T., N. K. and L. B. S. designed the study. A. M. S. performed the literature searches. P. B. J. and E. V. C. conducted the title, abstract and full text screening and data. All authors contributed to the interpretation of the results and critically reviewed the manuscript. All authors read and approved the final manuscript.

The authors declare that there are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S000711451800096X

References

- 1. Hall KD, Heymsfield SB, Kemnitz JW, et al. (2012) Energy balance and its components: implications for body weight regulation. Am J Clin Nutr 95, 989-994.
- King NA, Caudwell P, Hopkins M, et al. (2007) Metabolic and behavioral compensatory responses to exercise interventions: barriers to weight loss. Obesity (Silver Spring) 15,
- 3. Dulloo AG, Jacquet J, Montani JP, et al. (2012) Adaptive thermogenesis in human body weight regulation: more of a concept than a measurable entity? Obes Rev 13, Suppl. 2, 105-121.
- Knuth ND, Johannsen DL, Tamboli RA, et al. (2014) Metabolic adaptation following massive weight loss is related to the degree of energy imbalance and changes in circulating leptin. Obesity (Silver Spring) 22, 2563-2569.
- Hall KD, Sacks G, Chandramohan D, et al. (2011) Quantification of the effect of energy imbalance on bodyweight. Lancet 378, 826-837.
- Thomas DM, Martin CK, Heymsfield S, et al. (2011) A simple model predicting individual weight change in humans. J Biol Dyn 5, 579-599.
- 7. Melanson EL, Keadle SK, Donnelly JE, et al. (2013) Resistance to exercise-induced weight loss: compensatory behavioral adaptations. Med Sci Sports Exerc 45, 1600-1609.
- Levine JA (2004) Nonexercise activity thermogenesis (NEAT): environment and biology. Am J Physiol Endocrinol Metab 286, E675-E685.
- Fedewa MV, Hathaway ED, Williams TD, et al. (2017) Effect of exercise training on non-exercise physical activity: a systematic review and meta-analysis of randomized controlled trials. Sports Med 47, 1171-1182.
- Washburn RA, Lambourne K, Szabo AN, et al. (2014) Does increased prescribed exercise alter non-exercise physical activity/energy expenditure in healthy adults? A systematic review. Clin Obes 4, 1-20.
- 11. Levine JA, Lanningham-Foster LM, McCrady SK, et al. (2005) Interindividual variation in posture allocation: possible role in human obesity. Science 307, 584-586.
- 12. Heyman MB, Young VR, Fuss P, et al. (1992) Underfeeding and body weight regulation in normal-weight young men. Am J Physiol 263, R250-R257.
- Velthuis-te Wierik EJ, Westerterp KR & van den Berg H (1995) Impact of a moderately energy-restricted diet on energy



metabolism and body composition in non-obese men. *Int J Obes Relat Metab Disord* **19**, 318–324.

- Racette SB, Schoeller DA, Kushner RF, et al. (1995) Effects of aerobic exercise and dietary carbohydrate on energy expenditure and body composition during weight reduction in obese women. Am I Clin Nutr 61, 486–494.
- Redman LM, Heilbronn LK, Martin CK, et al. (2009) Metabolic and behavioral compensations in response to caloric restriction: implications for the maintenance of weight loss. PLoS ONE 4, e4377.
- Martin CK, Das SK, Lindblad L, et al. (2011) Effect of calorie restriction on the free-living physical activity levels of nonobese humans: results of three randomized trials. J Appl Physiol (1985) 110, 956–963.
- Dhurandhar EJ, Kaiser KA, Dawson JA, et al. (2015) Predicting adult weight change in the real world: a systematic review and meta-analysis accounting for compensatory changes in energy intake or expenditure. Int J Obes (Lond) 39, 1181–1187.
- Liberati A, Altman DG, Tetzlaff J, et al. (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 6, e1000100.
- Church TS, Martin CK, Thompson AM, et al. (2009) Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. PLoS ONE 4, e4515.
- Hollowell RP, Willis LH, Slentz CA, et al. (2009) Effects of exercise training amount on physical activity energy expenditure. Med Sci Sports Exerc 41, 1640–1644.
- Kozey-Keadle S, Staudenmayer J, Libertine A, et al. (2014) Changes in sedentary time and physical activity in response to an exercise training and/or lifestyle intervention. J Phys Act Health 11, 1324–1333.
- Martin CK, Heilbronn LK, de Jonge L, et al. (2007) Effect of calorie restriction on resting metabolic rate and spontaneous physical activity. Obesity (Silver Spring) 15, 2964–2973.
- Rosenkilde M, Auerbach P, Reichkendler MH, et al. (2012) Body fat loss and compensatory mechanisms in response to different doses of aerobic exercise – a randomized controlled trial in overweight sedentary males. Am J Physiol Regul Integr Comp Physiol 303, R571–R579.
- Turner JE, Markovitch D, Betts JA, et al. (2010) Nonprescribed physical activity energy expenditure is maintained with structured exercise and implicates a compensatory increase in energy intake. Am J Clin Nutr 92, 1009–1016.
- Whybrow S, Hughes DA, Ritz P, et al. (2008) The effect of an incremental increase in exercise on appetite, eating behaviour and energy balance in lean men and women feeding ad libitum. Br J Nutr 100, 1109–1115.
- Willis EA, Herrmann SD, Honas JJ, et al. (2014) Nonexercise energy expenditure and physical activity in the Midwest Exercise Trial 2. Med Sci Sports Exerc 46, 2286–2294.
- Brehm BJ, Spang SE, Lattin BL, et al. (2005) The role of energy expenditure in the differential weight loss in obese women on low-fat and low-carbohydrate diets. J Clin Endocrinol Metab 90, 1475–1482.
- DeLany JP, Kelley DE, Hames KC, et al. (2014) Effect of physical activity on weight loss, energy expenditure, and energy intake during diet induced weight loss. Obesity (Silver Spring) 22, 363–370.
- Kempen KP, Saris WH & Westerterp KR (1995) Energy balance during an 8-wk energy-restricted diet with and without exercise in obese women. Am J Clin Nutr 62, 722–729.
- Nicklas BJ, Gaukstern JE, Beavers KM, et al. (2014) Selfmonitoring of spontaneous physical activity and sedentary

- behavior to prevent weight regain in older adults. *Obesity (Silver Spring)* **22**, 1406–1412.
- Rangan VV, Willis LH, Slentz CA, et al. (2011) Effects of an 8-month exercise training program on off-exercise physical activity. Med Sci Sports Exerc 43, 1744–1751.
- 32. Schutz Y, Nguyen DM, Byrne NM, *et al.* (2014) Effectiveness of three different walking prescription durations on total physical activity in normal- and overweight women. *Obes Facts* **7**, 264–273.
- 33. Wang X, Lyles MF, You T, *et al.* (2008) Weight regain is related to decreases in physical activity during weight loss. *Med Sci Sports Exerc* **40**, 1781–1788.
- Weigle DS (1988) Contribution of decreased body mass to diminished thermic effect of exercise in reduced-obese men. *Int J Obes* 12, 567–578.
- Bonomi AG, Soenen S, Goris AHC, et al. (2013) Weight-loss induced changes in physical activity and activity energy expenditure in overweight and obese subjects before and after energy restriction. PLOS ONE 8, e59641.
- Colley RC, Hills AP, King NA, et al. (2010) Exercise-induced energy expenditure: implications for exercise prescription and obesity. Patient Educ Couns 79, 327–332.
- De Groot LCPGM, Van Es AJH, Van Raaij JMA, et al. (1990)
 Energy metabolism of overweight women 1 mo and 1 y after an 8-week slimming period. Am J Clin Nutr 51, 578–583.
- Di Blasio A, Ripari P, Bucci I, et al. (2012) Walking training in postmenopause: effects on both spontaneous physical activity and training-induced body adaptations. Menopause 19, 23–32.
- Goran MI & Poehlman ET (1992) Endurance training does not enhance total energy expenditure in healthy elderly persons. Am J Physiol 263, E950–E957.
- Herrmann SD, Willis EA, Honas JJ, et al. (2015) Energy intake, nonexercise physical activity, and weight loss in responders and nonresponders: The Midwest Exercise Trial 2. Obesity (Silver Spring) 23, 1539–1549.
- Hunter GR, Byrne NM, Sirikul B, et al. (2008) Resistance training conserves fat-free mass and resting energy expenditure following weight loss. Obesity (Silver Spring) 16, 1045–1051.
- Keytel LR, Lambert MI, Johnson J, et al. (2001) Free living energy expenditure in post menopausal women before and after exercise training. Int J Sport Nutr Exerc Metab 11, 226–237.
- Leibel RL, Rosenbaum M & Hirsch J (1995) Changes in energy expenditure resulting from altered body weight. N Engl J Med 332, 621–628.
- 44. Matsuo T, Okura T, Nakata Y, et al. (2007) The influence of physical activity-induced energy expenditure on the variance in body weight change among individuals during a diet intervention. Obes Res Clin Pract 1, 109–117.
- McLaughlin R, Malkova D & Nimmo MA (2006) Spontaneous activity responses to exercise in males and females. *Eur J Clin Nutr* 60, 1055–1061.
- 46. Meijer GA, Janssen GM, Westerterp KR, et al. (1991) The effect of a 5-month endurance-training programme on physical activity: evidence for a sex-difference in the metabolic response to exercise. Eur J Appl Physiol Occup Physiol 62, 11–17.
- Meijer EP, Westerterp KR & Verstappen FT (1999) Effect of exercise training on total daily physical activity in elderly humans. Eur J Appl Physiol Occup Physiol 80, 16–21.
- Meijer EP, Westerterp KR & Verstappen FT (2000) Effect of exercise training on physical activity and substrate utilization in the elderly. *Int J Sports Med* 21, 499–504.
- Van Dale D, Schoffelen PFM, Ten Hoor F, et al. (1989) Effects of addition of exercise to energy restriction on 24-hour energy



- expenditure, sleeping metabolic rate and daily physical activity. Eur J Clin Nutr 43, 441-451.
- Van Etten LM, Westerterp KR, Verstappen FT, et al. (1997) Effect of an 18-wk weight-training program on energy expenditure and physical activity. J Appl Physiol (1985) 82, 298-304.
- Weinsier RL, Hunter GR, Zuckerman PA, et al. (2000) Energy expenditure and free-living physical activity in black and white women: Comparison before and after weight loss. Am J Clin Nutr 71, 1138-1146.
- Armijo-Olivo S, Stiles CR, Hagen NA, et al. (2012) 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. I Eval Clin Pract
- 53. Riou ME, Jomphe-Tremblay S, Lamothe G, et al. (2015) Predictors of Energy compensation during exercise interventions: a systematic review. Nutrients 7, 3677–3704.
- Westerterp KR (2009) Assessment of physical activity: a critical appraisal. Eur J Appl Physiol 105, 823-828.
- 55. Pontzer H, Durazo-Arvizu R, Dugas LR, et al. (2016) Constrained total energy expenditure and metabolic adaptation to physical activity in adult humans. Curr Biol 26, 410-417.
- Schoeller DA (1999) Recent advances from application of doubly labeled water to measurement of human energy expenditure. J Nutr 129, 1765-1768.

