Results of a 2x2 factorial randomized controlled trial investigating a digital toolkit for weight loss maintenance in European adults: The NoHoW trial

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R. James Stubbs[1]; Cristiana Duarte[2]; Clarissa Dakin[1] PhD; António L Palmeira[3]; Falko F Sniehotta[4]; Graham W Horgan[5]; Sofus Larsen[6]; Marta M Marques[7]; Jorge Encantado[8]; Elizabeth H Evans[2]; Jake Turicchi[1]; Ruari O'Driscoll[1]; Sarah E Scott[1]; Beth Pearson[1]; Lauren Ramsey[1]; Marie-Louise Mikkelsen[5]; Inês Santos[3]; Marcela Matos[9]; Pedro J Teixeira[8]; Berit L Heitmann[6]

[1]School of Psychology, Faculty of Medicine and Health, University of Leeds, Leeds, United Kingdom. Leeds GB
[2]Department of Psychology, Faculty of Science, Durham University, Durham, United Kingdom. Durham GB
[3]Centro de Investigação em Desporto, Educação Física, Exercício e Saúde (CIDEFES), Universidade Lusófona and Centro de Investigação, Formação, Inovação e Intervenção em Desporto (CIFI2D), Universidade do Porto, Porto, Portugal. Porto PT
[4]Division of Public Health, Social and Preventive Medicine, Centre for Preventive Medicine and Digital Health (CPD), Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany. Mannheim DE
[5]Biomathematics & Statistics Scotland, Aberdeen, United Kingdom. Aberdeen GB
[6]Research Unit for Dietary Studies, The Parker Institute, Bispebjerg and Frederiksberg Hospital, The Capital Region, Denmark. Copenhagen DK
[7]Comprehensive Health Research Centre (CHRC), NOVA Medical School, Universidade Nova de Lisboa, Lisboa, Portugal. Lisboa PT
[8]Interdisciplinary Center for the Study of Human Performance (CIPER), Faculdade de Motricidade Humana, Universidade de Lisboa, Cruz Quebrada, Portugal. Cruz Quebrada PT
[9]Center for Research in Neuropsychology and Cognitive and Behavioural Intervention (CINEICC), Universidade de Coimbra, Coimbra, Portugal. Coimbra PT

Corresponding Author:
R. James Stubbs
School of Psychology, Faculty of Medicine and Health, University of Leeds, Leeds, United Kingdom.
School of Psychology, Faculty of Medicine and Health, University of Leeds, Leeds, United Kingdom.
Leeds
GB

Abstract

Background: Digital approaches to weight management have potential to produce cost-effective and scalable weight management solutions.

Objective: The core components of effective weight management interventions encourage self-regulation of energy balance behaviors which could be enhanced using aspects of emotion regulation.

Methods: The NoHoW trial studied 1627 participants in a 2×2 factorial, randomised, single blind, controlled trial. The trial evaluated a digital toolkit for weight management subsequent to initial ?5% weight loss in the prior 12 months (weight loss maintenance (WLM)) involving: (i) self-regulation and motivation (M), (ii) contextual behavioural elements of emotion regulation (E), or (iii) these intervention components in combination (M+E), compared to an active control (generic toolkit content, regular self-weighing, and wearable tracking device (Fitbit®) use). We hypothesized that the combined intervention would be more effective for WLM compared to the self-regulatory or emotion regulatory interventions alone, which individually would also be more effective than the active control group. The primary outcome was weight change from baseline and secondary outcomes were health biomarkers, physical activity, sleep, dietary intake and self-reported psychological processes at 12 months from baseline.
Linear models evaluated weight change from 0 -12 months using (i) intention to treat (ITT), (ii) participants who completed 12 months (completers), and (iii) participants who had measurements at 12 months and completed ?80% of toolkit modules (per protocol). Explanatory terms were recruitment centre, gender, M intervention, E intervention and two-way interactions between these terms. Age group, BMI group and pre-trial weight loss were included as additional covariates. Predefined subgroups analyses were carried out for men and women separately.

Results: For the ITT (76% retention at 12 months) and the completer populations, the M arm, the E arm and the E+M arms did not significantly affect weight outcomes compared to the active control. Analyses of gender differences showed a small but

clinically negligible effect of the self-regulation/motivation arm on weight in men only, for the ITT, per protocol and completer populations. There were no significant effects of the interventions on biomarkers, body composition or health outcomes. Regardless of imputation method for missing weight data, due to participant drop-out there was a tendency for pre-trial weight loss to be regained on average.

Conclusions: The current study highlights some possible design aspects of the digital behaviour change intervention that could be improved to enhance intervention effectiveness. Clinical Trial: ISRCTN88405328.

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R James Stubbs[1]*, Cristiana Duarte[2], Clarissa Dakin[1,] António L Palmeira[3], Falko F Sniehotta[4] , Graham W Horgan[5], Sofus C Larsen[6, 7] Marta M Marques[8], Jorge Encantado[9], Elizabeth H Evans[10], Jake Turicchi[1], Ruari O'Driscoll[1], Sarah E Scott[1], Beth Pearson[1], Lauren Ramsey[1], Marie-Louise Mikkelsen[6], Inês Santos[3], Marcela Matos[11] Pedro J Teixeira[9], Berit L Heitmann [6, 12, 13].

1 School of Psychology, Faculty of Medicine and Health, University of Leeds, Leeds, United Kingdom.

2 School of Education, Language and Psychology, York St John University, York, United Kingdom.

3 Centro de Investigação em Desporto, Educação Física, Exercício e Saúde (CIDEFES), Universidade Lusófona and Centro de Investigação, Formação, Inovação e Intervenção em Desporto (CIFI2D), Universidade do Porto, Porto, Portugal.

4 Division of Public Health, Social and Preventive Medicine, Centre for Preventive Medicine and Digital Health (CPD), Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany.

5 Biomathematics & Statistics Scotland, Aberdeen, United Kingdom.

6 Research Unit for Dietary Studies, The Parker Institute, Bispebjerg and Frederiksberg Hospital, The Capital Region, Denmark.

7 The Research Unit for General Practice and Section of General Practice, Department of Public Health, University of Copenhagen, Copenhagen, Denmark.

8 Comprehensive Health Research Centre (CHRC), NOVA Medical School, Universidade Nova de Lisboa, Lisboa, Portugal.

9 Interdisciplinary Center for the Study of Human Performance (CIPER), Faculdade de Motricidade Humana, Universidade de Lisboa, Cruz Quebrada, Portugal.

10 Department of Psychology, Faculty of Science, Durham University, Durham, United Kingdom.

11 Center for Research in Neuropsychology and Cognitive and Behavioural Intervention (CINEICC), Universidade de Coimbra, Coimbra, Portugal.

12 The Boden Group, Faculty of Medicine and Health, Sydney University, Sydney, NSW 2006, Australia.

13 Section for Clinical Practice, Department of Public Health, University of Copenhagen, 1014 Copenhagen, Denmark.

Corresponding author: *Professor James Stubbs, School of Psychology, Faculty of Medicine and health, University of Leeds, Leeds, United Kingdom. E-mail: r.j.stubbs@leeds.ac.uk.

Short title: The NoHoW trial

Abstract

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Linear models evaluated weight change from 0 -12 months using (i) intention to treat (ITT), (ii) participants who completed 12 months (completers), and (iii) participants who had measurements at 12 months and completed ≥80% of toolkit modules (per protocol). Explanatory terms were recruitment centre, gender, M intervention, E intervention and two-way interactions between these terms. Age group, BMI group and pre-trial weight loss were included as additional covariates. Predefined subgroups analyses were carried out for men and women separately.

Results: For the ITT (76% retention at 12 months) and the completer populations, the M arm, the E arm and the E+M arms did not significantly affect weight outcomes compared to the active control. Analyses of gender differences showed a small but clinically negligible effect of the self-regulation/ motivation arm on weight in men only, for the ITT, per protocol and completer populations. There were no significant effects of the interventions on biomarkers, body composition or health outcomes. Regardless of imputation method for missing weight data, due to participant drop-out there was a tendency for pre-trial weight loss to be regained on average.

Conclusions: The current study highlights some possible design aspects of the digital behaviour change intervention that could be improved to enhance intervention effectiveness.

Trial registration number: ISRCTN88405328.

Keywords: emotion regulation, information and communication technologies, motivation, obesity, self-regulation, weight loss maintenance.

Introduction

Overweight and obesity remain significant societal challenges to the health and wellbeing of citizens, affecting more than half of the adult population [1]. The health care consequences and associated economic costs are well documented [2,3]. More than 40% of western adults report making at least one weight control attempt per year [4], most of which do not involve evidence-based behaviour change approaches [4]. Existing community-based programmes support initial weight loss (WL) but are subject to high attrition and to weight regain, limiting longer-term effectiveness [5-7]. The obesogenic environment and asymmetry of human energy balance (EB) regulation facilitates weight gain, while society stigmatises people suffering from overweight and obesity, leading to stress and negative emotions, which can undermine WL attempts [8-10]. The majority of WL attempts are therefore followed by some degree of weight regain [11] emphasizing the need to develop more effective weight loss maintenance (WLM) solutions. Long-term weight management, often referred to as weight loss maintenance (WLM) is even more challenging, weight relapse is common and obesity is therefore a chronic relapsing condition [12,13]. Effective support for WLM or the prevention of weight regain needs to address sustained changes in EB behaviors (diet, physical activity and weight control) and emotional/psychosocial challenges that may undermine cognitive self-management of EB behaviours [14]. It is likely that pathways of planned behaviour change involving self-management of EB are difficult to implement unless they become practiced and habitual. Dual process models of behaviour change suggest that such practice takes time to establish whereas existing habits, preferences, urges, desires and responsiveness to environmental cues have considerable capacity to undermine the implementation of new behaviour changes [15]. Models of behaviour change increasingly include both reflective and reactive elements, which if not aligned can deplete psychological resources and undermine maintenance of behaviour change [16]. Greaves et al. describe longer-term weight management as generating a tension between existing habits (EB behaviours), and incompatibility of new (weight management) behaviours with the fulfilment of pre-existing psychological needs [14]. This tension could be managed through self-regulation, renewed motivation and managing external influences to change habits, finding non-obesogenic approaches to meet psychological needs and changing self-concept [14]. It is likely that some of the factors that undermine longer-term WL, such as changes in EB physiology affecting energy expenditure, food reward-based processes or energy intake, may be outside of conscious recognition and control [17]. There is some evidence that aspects of self-regulation and motivation may improve the odds of changing EB behaviours and if those changes become habitual in the longer term, the chances of preventing weight regain may improve [18-

[20]. It is possible that changing habits can take 2–5 years [21]. However, it is likely that reactive processes (emotions, desires, impulses resulting from associative learning, and physiological resistance to WL) are powerful forces that can also undermine relatively transient and fragile attempts at changing EB behaviours during WL.

Self-regulation and motivation

Research identifying and linking specific behaviour change approaches to mechanisms of action of behaviour change interventions is still a developing field [22,23]. Core features of effective WLM interventions include reflective or cognitive behavior change techniques in line with self-regulation theories such as: 1) *self-monitoring* of weight and behavior; 2) *goal-setting*: agreement of clear weight targets/trigger points for weight control efforts; 3) feedback on behavior and weight; 4) *action plans* for weight control through dietary and physical activity behaviors and, 5) *plans* to cope with *risk factors* for weight regain and relapse prevention (e.g., problem solving) [18-20,24,25]. Many people also experience behavioural lapses and relapses as more pronounced situational or momentary events. Avoiding both gradual and more pronounced weight regains require behavioural strategies in which relapse coping and WLM become learned skills of self-regulation, autonomy and motivation as part of a longer-term process [12,26-28].

Physical activity and dietary WLM interventions based on current behaviour change theories characteristically achieve relatively modest effects of ~ 1.6 kg difference in weight regain compared to unsupported controls over 12 months [18,29,30]. Additional psychological processes, such as emotion regulation, potentially have additional beneficial effects on the behavioral changes that promote WLM [14].

Emotion regulation

Reactive processes (emotions, desires, habits resulting from associative learning and physiological states) may have a large impact on behaviour and behaviour change. These processes tend to be relatively rapid, automatic, impulsive (less conscious) and habitual in comparison to the slow, deliberative processes of motivation and self-regulation [15,31]. Such processes may undermine initial self-regulation of EB behaviours (particularly eating behaviours) in the face of a physiological system that resists longer-term WL [32]. Automatic components of self-regulation may also promote longer-term behaviour change if they are engaged and developed [33,34]. People with overweight and obesity commonly experience stigma, which enhances psychosocial stress and negatively impacts on physical and mental wellbeing [35-37]. Stigma impacts affect via shame, self-criticism and unfavourable

social comparisons, creating feelings of inferiority and inadequacy in relation to others [38]. The relationship between stress, emotion and food intake can derail strategies of planned behaviour and promote further weight gain [39]. Limited evidence suggests that acceptance, self-compassion and mindfulness-based approaches could potentially help some people in coping with obesity-related eating behaviours [40,41]. We hypothesised that self-monitoring, self-regulation and autonomous motivation in WLM could be supported favourably by strategies that promote emotion regulation and that may thereby increase coping with stress.

Digital weight loss maintenance interventions

Evidence of the effectiveness of long-term digital interventions and strategies to support WLM is limited [42]. Digital solutions, such as smartphone applications and wearables, have potential to be effective in supporting WLM if they are evidence-based and offer a choice of behavior change techniques to encourage the use of self-regulatory techniques (e.g., self-monitoring). Interventions with human contact are more effective that those that are fully automated [43]. Digital solutions are potentially cost-effective and scalable to large populations, which could engage citizens in healthcare innovations that are convenient and effective for weight management in the face of limited public budgets [44]. Recent systematic reviews indicate that weight management apps may have positive effects on weight-related outcomes, although methodological quality of many studies is low and effect sizes modest [45-47]. While there is a need for sustainable and cost-effective solutions that are easy and convenient to use for the consumer and manageable for the health care provider, it is important to conduct randomised trials of digital technologies for WLM and to try to understand the mechanisms by which they may influence weight and health outcomes.

Study objectives and hypotheses

The study's primary objectives were to evaluate whether using a new digital toolkit was effective for WLM by improving: (i) self-regulation and motivation (M), (ii) contextual behavioural aspects of emotion regulation (E), or (iii) these factors in combination (M+E), compared to an active control (generic toolkit content, regular self-weighing and wearable tracking device (Fitbit®) use)) in 1627 participants total at three European research centers. We hypothesized that the combined intervention would be more effective for WLM compared to the self-regulatory or emotion regulatory interventions alone, which individually would also be more effective than the active control group.

Secondary objectives were to determine how the intervention affected health markers (e.g., levels of glycated haemoglobin [HbA1c]), cholesterol and cortisol levels and body composition. The study also examined: (i) the intervention impact on physical activity, sleep, self-reported dietary intake, depression, anxiety, stress, quality of life and wellbeing; (ii) potential mediators of WLM, such as self-regulation (e.g., planning capacity), motivation (e.g., autonomous motivation) and emotion regulation processes (e.g., self-compassion) (iii) quantitative and qualitative assessment of user-experience, acceptability, engagement and drop-out; (iv) intervention cost-effectiveness. Secondary outcome analyses (ii-iv) are being reported in separate publications e.g. [48,49].

Materials & Methods

Study population

The trial examined WLM in those who had lost ≥5% of their weight during the previous 12 months. Prior to randomisation, potential participants were asked to provide documented verification (by a health professional, WL counsellor/friend, WL programme record booklet, diary or smartphone app or before/after photographs) that they had achieved a clinically significant WL of >5% during the previous 12 months. The complete inclusion/exclusion criteria for the trial, recruitment, interventions, assessment and study procedures are described in a previously published protocol paper [50].

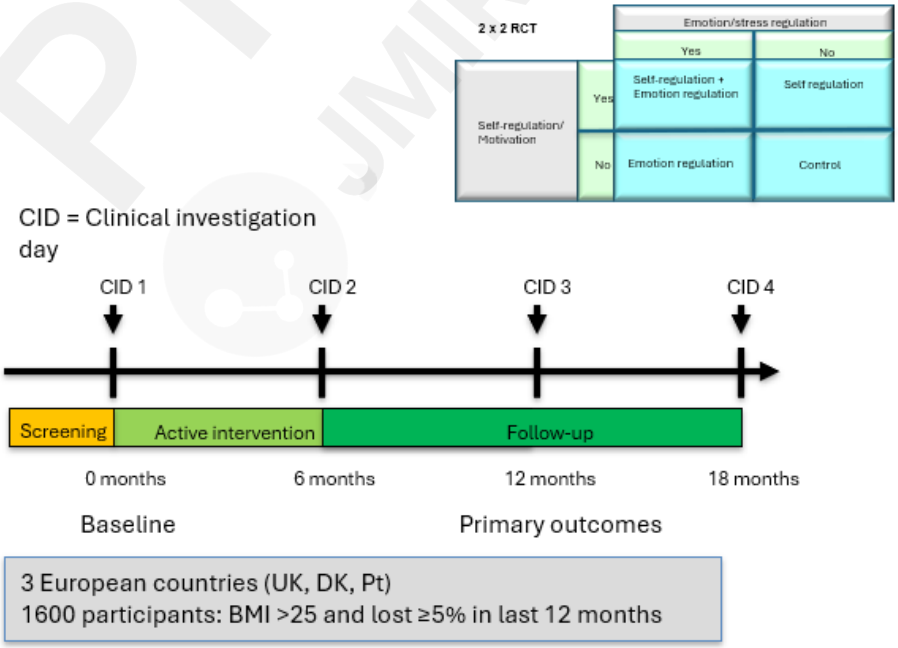
Study Design

The NoHoW trial was a three-centre (University of Leeds (UK), Frederiksberg and Bispebjerg University Hospital (Denmark) and University of Lisbon (Portugal)) 2×2 factorial, randomised, single blind, controlled trial testing the proof-of-concept of a digital toolkit for WLM. The toolkit included a mobile-enabled website and tracking technologies: activity and sleep tracker (Fitbit Charge 2) and smart wireless body weight scale (Fitbit Aria). The toolkit development followed the MRC guidance for complex interventions [51], with specific intervention logic models and theory-driven behaviour change techniques [52]. The study was conducted between March 2017 and September 2019 in the three academic research institutions. The study duration was 18 months with a follow-up at 6, 12 (primary endpoint, reported in the current study), and 18 months post-baseline [50]. Changes in the primary outcome (weight in kg) and secondary outcomes (health biomarkers, physical activity, sleep and dietary intake, self-reported psychological processes) are reported at 12

months from baseline.

In total, 1627 participants (536-555 per centre) were enrolled and randomised into one of the four intervention arms in a factorial structure. All arms included self-weighing and activity trackers: 1) active control arm (consisting of generic toolkit content); 2) self-regulation and motivation (M) arm; 3) emotion regulation E arm; and 4) combined self-regulation/motivation and emotion regulation (M+E) arm (figure 1). Participants were allocated to one of the four treatment arms by adaptive stratified sampling using minimization, where differences in age, weight lost and current BMI were minimized between treatment arms, which were also balanced for gender. The protocol was harmonised across trial centres using Good Clinical Practice guidance, research-grade translation/backtranslation of trial materials, two training workshops and weekly trial management meetings. The final protocol (V2.1 20/09/2017) was approved by the Trial Steering Committee and adhered to the Standard Protocol Items: Recommendations for Interventional Trials guidelines [53]. Ethical approval was granted by Institutional Ethics Committees at the Universities of Leeds (17-0082; 27February 2017), Lisbon (17/2016; 20 February 2017) and Capital Region of Denmark (H-16030495, 8 March 2017). A complete description of the trial design can be found elsewhere [50] . The trial registration number is ISRCTN88405328.

Figure 1. The 2 x 2 factorial design of the NoHoW trial.



Measurements

A full description of trial measures and associated references (including mediators and moderators of any trial effects) are described in a previous publication [50]. The primary and secondary outcomes related to health markers, well-being and quality of life, energy expenditure and physical activity, energy and nutrient intake and eating behaviour traits are described here.

Primary outcome

Change in weight (kg) at 12 months from baseline.

Body weight (±0.1kg) was measured using a Seca 704s instrument (SECA, Germany) in participants wearing light clothing. Participants were asked to self-weigh themselves at least twice weekly, in the morning after voiding and before eating using the provided Fitbit Aria™ scales for 18 months.

Secondary outcomes

Body composition and height

Multi-frequency whole Bioimpedance spectroscopy (BIS) was measured by ImpediMed™ SFB7, Queensland, Australia), which measures impedance over a spectrum of frequencies for the estimation of body composition. Hanai mixture theory equations and standard resistivity constants [54] were used to calculate fluid volumes to estimate total body water and hence fat and fat-free mass. Height (±0.1cm) was measured with participants barefoot, using a Seca 704s instrument (SECA, Germany).

Waist and Hip measurements

Waist and hip measurements were taken according to the World Health Organization's (WHO) guidance. A tape measure was used to record the hip and waist circumference to the nearest 0.1 cm [55].

Biomarkers

HbA1c and Cholesterol. Fasted capillary blood samples were collected to determine HbA1c (mmol/mol, %), estimated average glucose (eAG, mol/L) and calculate full lipid profiles, including total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides, non-HDL and cholesterol/HDL (mmol/L) assayed using a bench-top analyzer (Alere Afinion™ AS100

Analyzer, Alere, Stockport, UK) [56].[5]

Systolic and diastolic blood Pressure and resting heart rate were measured with the participant at rest in the sitting position (Microlife BP A2 Basic, Gentle Technology, Microlife, Clearwater, FL, USA, Inc.). Values were taken as the average of three measurements.

*Cortisol. Hair c*ortisol was included as a measure of chronic stress using hair samples following a previously described protocol [57]. Hair samples were cut from the posterior vertex as close to the scalp as possible. Between 10-30 mg of the hair from 2 cm closest to the scalp was cut in small pieces and dissolved in 1 mL methanol and incubated at ultrasound sonication for 30 minutes, followed by 18 hours at 52°C in a shaking incubator (300 rpm.). Hair samples were not collected among participants with less than 2 cm of hair. The methanol was transferred to a new tube and evaporated to dryness under a stream of nitrogen at 45°C. Dried samples were stored at -20°C until analysis. Before analysis, samples were re-dissolved in 500µl PBS pH 8 and centrifuged at 2000 rpm for 2 min. Reconstituted samples were analysed with a cortisol ELISA assay (Alpco.com).

Physical activity

Minute-by-minute physical activity data and heart rate were measured by the Fitbit Charge 2™ for the study duration. Data were used from 2 weeks after randomization for baseline and for the 8 weeks prior to the 12-month point for the trial outcome. Physical activity was also self-reported at 0, 6, 12 and 18 months (8-week intervals), using the International Physical Activity Questionnaire, (IPAQ) [58]and the Activity Choice Index (ACI) [59].

Sleep quality and quantity

The Fitbit Charge 2™ estimates sleep quantity (hours/minutes) and quality (stages of sleep) using proprietary algorithms. Data were collected daily throughout the trial.

Dietary intake and eating behavior

Four consecutive 24-hour-web-based dietary recalls, including at least one weekend day, were collected within seven days of each CID visit using INTAKE 24 [60] and average daily intake of energy and macronutrients was calculated. Not all participants completed all four 24-hour recalls [61].

The following measures were collected at the time of each CID at 0, 6, 12 and 18 months.

Three Factor Eating Questionnaire-51 (TFEQ). TFEQ includes 51 items measuring eating disinhibition, susceptibility to hunger, and dietary restraint [62].

Binge Eating Scale (BES) [63]. Includes 16 items and assesses the behavioural, cognitive, and emotional dimensions of binge eating symptomatology.

Intuitive Eating Scale-21 (IES-21). Is a 21-item scale that assesses three susbcales of intuitive eating: eating for physical rather than emotional reasons, unconditional permission to eat and reliance on hunger and satiety cues [64].

Well-being and Quality of Life

EQ5D-5L Is a measure of generic health-related quality of life including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression[65].

Warwick-Edinburgh Well-Being Scale (WEWBS) is a 14-item single factor scale which assesses mental wellbeing [66].

Statistical Analysis

Power calculations were based on the primary outcome (weight change) at 12 months and also conducted for the secondary outcome change in HbA1c. To detect a difference between treatment arms of >1.5 kg body weight with a Cohen's d value of 0.25 for 80% power, comparing more than two groups required a sample size of 250 per trial arm. To detect an effect size of 0.25 SD units for HbA1c, 245 participants in each trial arm gave 80% power, at 5% significance. Assuming 38% dropout, a sample size of 1600 (533 per centre) was needed to achieve a sample of 1002 (334 per centre, ~250 per trial arm) participants at 12 months.

The primary statistical analysis was Intention to Treat (ITT), so that the effectiveness of the interventions could be assessed. For the primary outcome we also reported the results on two other study subsets, the completers (those who had measurements at 12 months), and the per protocol sample, i.e. those who had measurements at 12 months and who also completed at least 80% of the toolkit modules for their assigned trial arm.

Statistical analyses were carried out using linear models where response was the change in outcome value from baseline to 12 months. Explanatory terms were centre, gender, M intervention, E intervention and two-way interactions between these terms M+E. Age group, BMI group and pre-trial weight loss group were included as additional covariates. Significance was assessed using type II sums of squares to maximise power to detect main effects in the absence of significant interactions in an Analysis of Variance of the linear model. Predefined subgroup analyses were carried out for men and women separately. Means presented are marginal means estimating the effects in a population in which other factors are equally balanced between trial arms.

ITT requires imputation of outcome data for those who had dropped out. An assumption of missingness at random did not appear valid, and so standard multiple imputation was unsuitable. Carrying forward the last observation would assume no weight regain in those who dropout, which appeared likely to treat dropouts as having an unreasonably optimistic outcome. We therefore used the most conservative assumption that drop-outs had regained all weight lost before the trial i.e. we carried forward the highest weight in the 12 months before CID 1 (baseline observation carried forward). Weight lost before the trial was available but other outcomes were not. As using CID 1 measures for baseline carried forward would appear optimistic for these outcomes also, we imputed values by predicting them from participant characteristics and a weight change imputed as described above. Multiple imputation, using the R library “mice” was used to account for the uncertainty in this prediction. Data analysis was carried out using R version 3.5 (R Foundation for Statistical Computing, Vienna).

Results

Participants

The sample consisted of 1,117 women (68.7%) and 510 (31.3%) men. In the 12 months prior to randomisation the women lost ~11% (10.8 kg) and the men lost ~ 12% (10.7 kg) of their weight ($p<0.001$). The mean (SD) age was 44.5 years (11.9 years), weight was 84.7 kg (17.2kg) and BMI was 29.7 kg/m^2 (5.5 kg/m^2). At baseline, the majority of participants had a BMI of either 25-29.9 kg/ m^2(42.3%) or 30-34.9 km/m^2 (24.5%). In total 1,594 participants provided data on employment. Most (68.3%) were employed full-time, 8.3% part-time, 8.7% retired, 6.3% were students, 2.4% were unemployed, 0.9% self-employed and 0.5% were carers. Most (89.4%) UK participants

described themselves as White British; 97.2% participants from Denmark described themselves as Danish. 69.78% participants from Portugal described themselves as Portuguese. The majority (85.1%) of the sample were educated beyond secondary level education (e.g., degree level). Forty three percent of participants were married. The median household income for the Danish and UK sample fell into the same category as their national average (range of €22,400 – €53,713). For the Portuguese sample median household income fell below their national average (€12,000 – 18,000). Mean baseline values of the study variables per centre and per gender are reported in Table 1.

Table 1. baseline measurements: historical weight loss, anthropometry (Height, body weight, Waist circumference, fat mass, fat free mass), Health markers (HbA1c, blood pressure, plasma lipids, resting heart rate), stress, depression, anxiety, well-being and QoL, for men and women in the four arms (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined).

		Female			
		Control	M	E	M+E
Pre-trial weight loss (kg)		9.42 ±0.55	10.52 ±0.56	9.89 ±0.54	9.70 ±0.55
	Weight (kg)	92.66 ±0.62	92.97 ±0.63	92.73 ±0.62	92.75 ±0.63
Body composition					
	Fat free mass (kg)	57.05 ±0.46	57.02 ±0.47	56.79 ±0.46	56.9 ±0.47
	Fat mass (kg)	35.46 ±0.45	35.86 ±0.45	35.76 ±0.45	35.73 ±0.45
Waist circumference (cm)		99.29 ±0.54	99.48 ±0.55	99.94 ±0.54	100.15 ±0.55
Biomarkers					
	HbA1c_mmol_mol	33.45 ±0.37	33.6 ±0.38	33.37 ±0.37	33.33 ±0.37
	HbA1c_percent	5.23 ±0.03	5.24 ±0.03	5.23 ±0.03	5.22 ±0.03

	Total Cholesterol mmol/L	4.63 ±0.07	4.75 ±0.07	4.77 ±0.07	4.82 ±0.07
	LDL cholesterol mmol/L	2.54 ±0.06	2.63 ±0.06	2.66 ±0.06	2.72 ±0.06
	HDL cholesterol mmol/L	1.53 ±0.03	1.53 ±0.03	1.52 ±0.03	1.53 ±0.03
	Triglycerides mmol/L	1.31 ±0.06	1.37 ±0.06	1.31 ±0.06	1.35 ±0.06
	Systolic blood pressure	119.99 ±0.84	120.07 ±0.86	121.86 ±0.84	121.41 ±0.85
	Diastolic blood pressure	74.52 ±0.56	74.46 ±0.56	75.35 ±0.55	75.81 ±0.56
	Heart rate (bpm)	68.85 ±0.7	69.08 ±0.71	68.81 ±0.69	69.83 ±0.7
	Hair cortisol (log)	4.03 ±0.09	3.99 ±0.1	4.06 ±0.1	4.05 ±0.1

		Male			**Overall p-values**		
		Control	M	E	M+E	p-gender	p-group
Pre-trial weight loss (kg)		10.14 ±0.66	11.23 ±0.66	10.61 ±0.66	10.42 ±0.67	0.208	0.441
	Weight (kg)	106.91 ±0.72	107.22 ±0.73	106.98 ±0.71	106.99 ±0.72	**0.000**	0.967
Body composition							
	Fat free mass (kg)	74.06 ±0.54	74.02 ±0.54	73.8 ±0.54	73.9 ±0.54	**0.000**	0.948
	Fat mass (kg)	32.59 ±0.52	32.99 ±0.52	32.9 ±0.51	32.86 ±0.52	**0.000**	0.848
Waist circumference		109.78 ±0.63	109.97 ±0.63	110.42 ±0.62	110.63 ±0.63	**0.000**	0.407

(cm)							
Biomarkers							
	HbA1c_mmol_mol	33.93 ±0.42	34.09 ±0.43	33.86 ±0.42	33.82 ±0.43	0.119	0.901
	HbA1c_percent	5.28 ±0.04	5.29 ±0.04	5.27 ±0.04	5.27 ±0.04	0.119	0.933
	Total Cholesterol mmol/L	4.5 ±0.08	4.62 ±0.08	4.64 ±0.08	4.69 ±0.08	**0.024**	0.056
	LDL cholesterol mmol/L	2.67 ±0.07	2.76 ±0.07	2.79 ±0.07	2.85 ±0.07	**0.010**	**0.026**
	HDL cholesterol mmol/L	1.26 ±0.03	1.26 ±0.03	1.26 ±0.03	1.26 ±0.03	**0.000**	0.996
	Triglycerides mmol/L	1.26 ±0.07	1.33 ±0.07	1.27 ±0.07	1.31 ±0.07	0.387	0.703
	Systolic blood pressure	131.31 ±0.97	131.38 ±0.99	133.18 ±0.97	132.72 ±0.98	**0.000**	0.071
	Diastolic blood pressure	80.84 ±0.64	80.78 ±0.65	81.67 ±0.64	82.13 ±0.65	**0.000**	0.052
	Heart rate (bpm)	64.23 ±0.8	64.46 ±0.81	64.19 ±0.8	65.21 ±0.81	**0.000**	0.460
	Hair cortisol (log)	4.19 ±0.12	4.14 ±0.12	4.22 ±0.12	4.21 ±0.12	0.092	0.891

M = self-regulation and motivation, E = contextual behavioural aspects of emotion regulation, M+E = these factors in combination.

Primary outcome

In the ITT population, there was an overall tendency for pre-trial weight loss to be regained on average (Table 2). For those who completed measures (i.e. the per protocol sample) at 12 months, men regained 0.14 kg (0.27%) of the weight they lost and women regained 0.54 kg or (0.85)% of the weight they lost. However, there was substantial variation between participants. Participants were

assigned to the following weight change categories: >-3% weight loss (weight loser), between -2.99% and +2.99% (weight maintainer) and >+3% weight gain (weight gainer) [67]. For the per protocol population 24% continued to lose weight, 41% maintained weight and 35% regained weight. For the ITT population 19% continued to lose weight, 32% maintained weight and 49% regained some weight (at ±3% weight change¿. When we investigated weaker assumptions, such as regain of a proportion of this weight loss the main assessment of the intervention effects was similar, although absolute estimates of weight regain were lower in all arms (Table 2).

Table 2. Outcome results for weight (kg) change between CID 1-3 at 12 months using the intention to treat analysis where regain all pre-trial weight loss is assumed for missing data. Values shown are mean of weight change ± SEM.

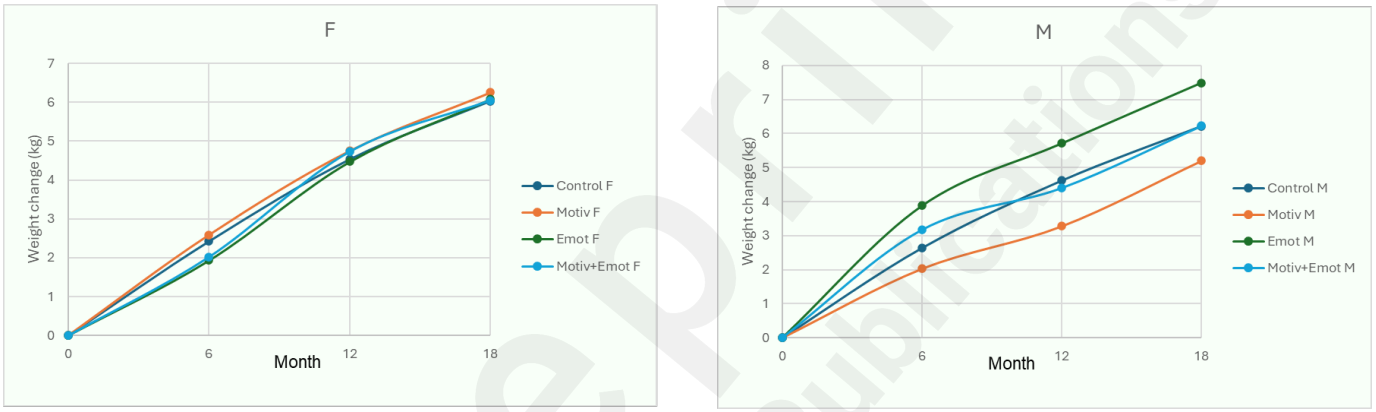
	Female				**Male**			
	Control	M	E	M+E	Control	M	E	M+E
ITT, full regain assumed if missing	4.53 ±0.56	4.75 ±0.58	4.47 ±0.56	4.73 ±0.57	4.62 ±0.84	3.28 ±0.85	5.71 ±0.84	4.41 ±0.86
Per protocol sample	0.13 ±0.62	-0.57 ±0.71	0.11 ±0.73	-0.46 ±0.78	0.8 ±0.92	-0.91 ±1.09	-1.23 ±1.15	-2.79 ±1.3
Completer sample	0.61 ±0.53	0.71 ±0.55	0.56 ±0.53	0.64 ±0.54	1.09 ±0.78	0.08 ±0.78	1.32 ±0.78	0.28 ±0.79

	Overall p-values		**Subgroup p-values female**				**Subgroup p-values male**		
	M	E	M x E	M	E	M x E	M	E	M x E
ITT, full regain assumed if missing	0.49	0.38	0.95	0.57	0.91	0.85	**0.04**	**0.08**	0.73
Per protocol sample	0.05	0.39	0.89	0.36	0.63	0.86	**0.04**	**0.03**	0.93
Completer sample	0.44	0.94	0.97	0.63	0.95	0.85	**0.03**	0.57	0.99

M = self-regulation and motivation, E = contextual behavioural aspects of emotion regulation, M+E = these factors in combination.

Table 2 and Figure 2 show the weight changes for each trial arm for the whole sample, men, and women using the ITT model. For the whole sample in the ITT and the completer populations, the M arm, the E arm and the combined E + M arms did not significantly affect weight outcomes compared to the active control. Gender differences showed that a small effect of the M arm was significant in men only for the ITT, per protocol and completer populations. Analysis was factorial, looking at the effect of M and effect of E and interactions. The effect of M was slightly significant, but we could not conclude the interaction was significant, i.e. we could not conclude we had enough evidence to say M+E was more effective than M.

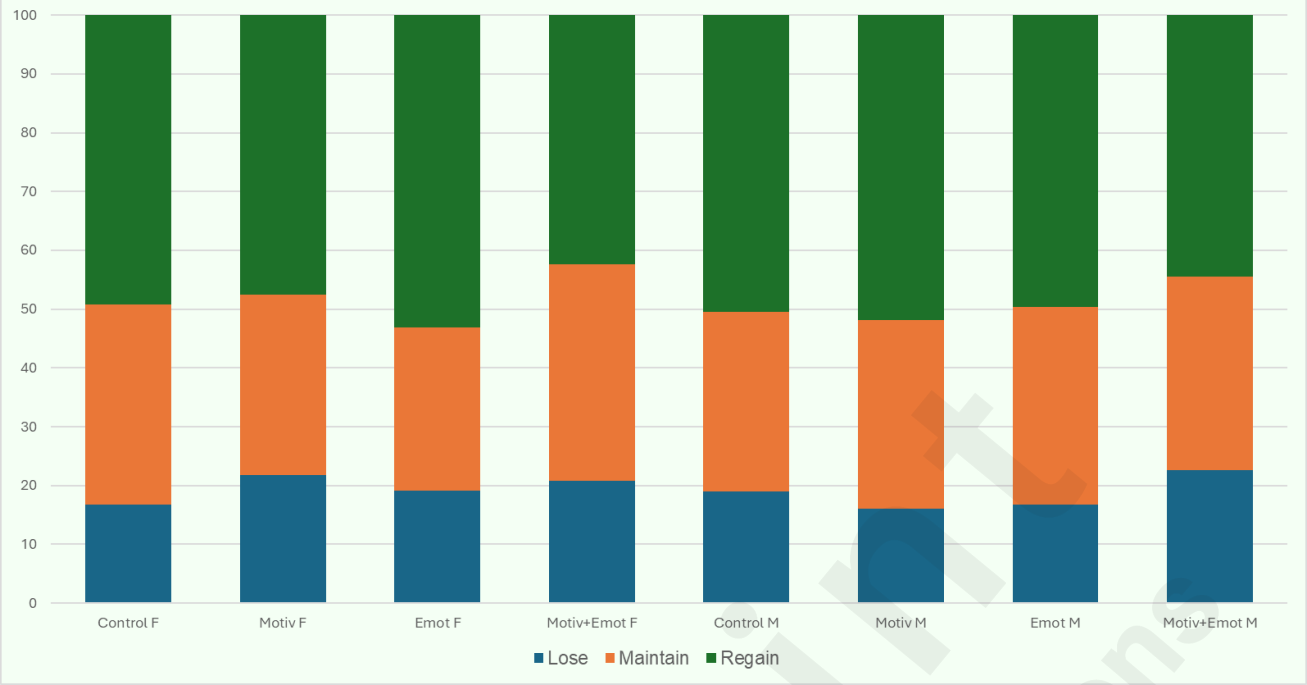
Figure 2. longitudinal changes in body weight by trial arm (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined) for men and women in the ITT population.



F = Female, M = Male.

Figure 3 shows longitudinal changes in body weight by trial arm (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined) for men and women. Figure 3 shows the percentage of the ITT population gaining, losing or maintaining pre-trail weight loss, by trial arm (control, M, M+E and E). Percentage weight change was calculated as (CID3 kg – CID1 kg) / CID1 kg x 100. Weight category was then calculated from percentage weight change.

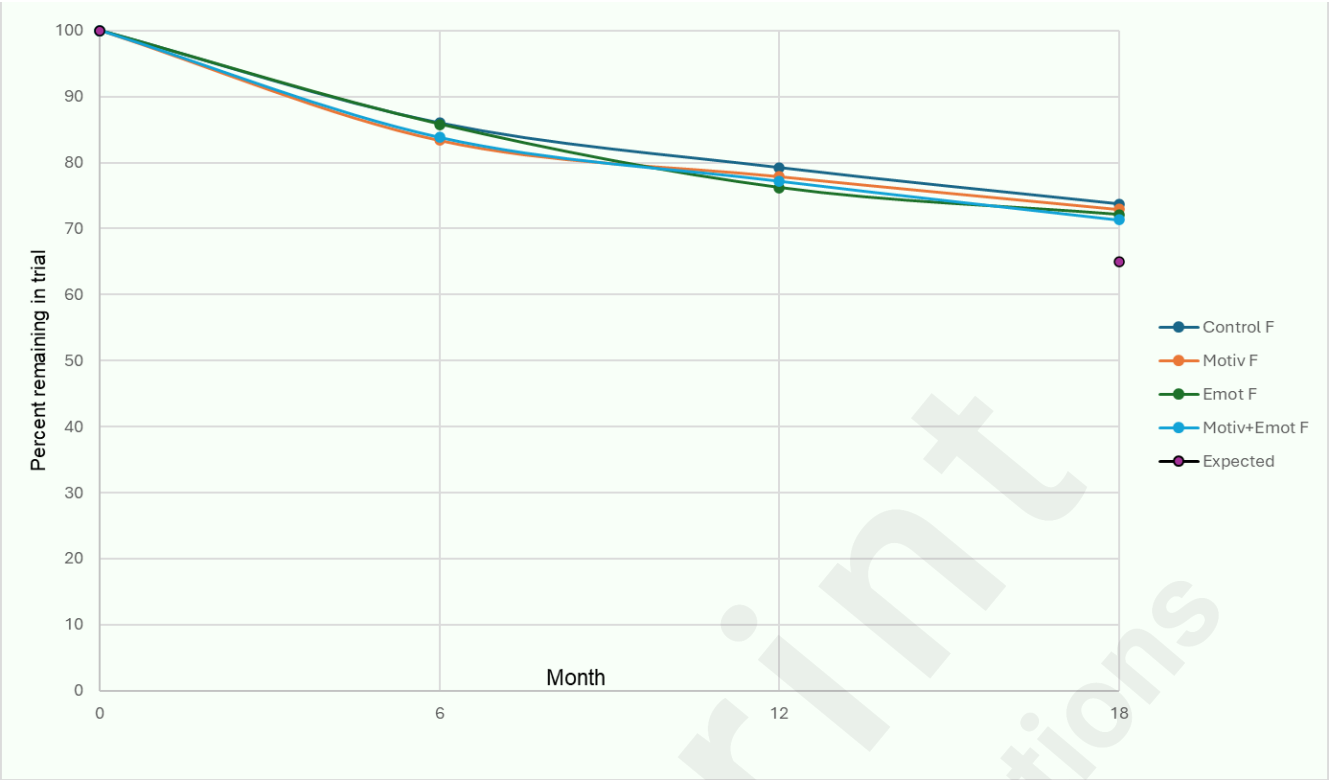
Figure 3. Percentage of the ITT population gaining, losing or maintaining pre-trail weight loss, by trial arm (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined). Percentage weight change was calculated as (CID 3 kg – CID 1 kg) / CID 1 kg x 100. Weight category was then calculated from percentage weight change. Participants were assigned to the following weight category: >-3% weight loss (weight loser), between -2.99% and +2.99% (weight maintainer) and >+3% weight gain (weight gainer).



F = Female, M = Male.

Figure 4 shows that retention of participants in the trial was high and greater than assumed for the power calculations. By the 12-month primary outcome, over 76% of the ITT sample was still engaged in the intervention and by 18 months over 71% of the ITT sample was still engaged in the intervention for all trial arms.

Figure 4. Cumulative drop-out from the trial between months 0-12 by trial arm (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined). The black dot at month 18 indicates assumed drop-out of 38% estimated from previous RCTs.



F = Female, M = Male.

Secondary outcomes

Biomarkers, body composition and health outcomes

Overall, there were no significant effects of the interventions on biomarkers, body composition or health outcomes (Table 3).

Table 3. Change in anthropometry (WC, FM, FFM) and health markers (HbA1c, blood pressure, plasma lipids, resting heart rate).

		Female				**Male**			
		Control	M	E	M+E	Control	M	E	M+E
Body composition									
	Fat free mass (kg)	2.44 ±0.53	2.56 ±0.51	2.72 ±0.55	2.77 ±0.58	6.33 ±0.65	6.14 ±0.68	6.37 ±0.73	6.11 ±0.68
	Fat mass (kg)	3.69 ±0.5	3.49 ±0.5	3.4 ±0.5	3.25	2.29 ±0.6	1.67	3.23 ±0.61	2.66

				6	±0.49	1	±0.67		±0.64
	Waist circumference (cm)	3.38 ±0.59	3.07 ±0.53	3.16 ±0.59	3.31 ±0.54	4.66 ±0.79	3.52 ±0.81	5.14 ±0.8	4.46 ±0.81
Biomarkers									
	HbA1c_mmol_mol	1.29 ±0.26	1.16 ±0.23	1.57 ±0.24	1.55 ±0.21	1.67 ±0.29	1.42 ±0.26	1.63 ±0.28	1.49 ±0.26
	HbA1c_percent	0.14 ±0.02	0.12 ±0.02	0.15 ±0.02	0.14 ±0.02	0.16 ±0.02	0.14 ±0.02	0.14 ±0.02	0.12 ±0.02
	Total Cholesterol mmol/L	0.16 ±0.06	0.19 ±0.06	0.22 ±0.07	0.27 ±0.07	0.2 ±0.08	0.23 ±0.08	0.27 ±0.07	0.32 ±0.07
	LDL cholesterol mmol/L	-0.12 ±0.06	-0.1 ±0.06	-0.06 ±0.05	-0.03 ±0.05	0.01 ±0.06	0.06 ±0.07	0.06 ±0.06	0.11 ±0.08
	HDL cholesterol mmol/L	0.16 ±0.02	0.16 ±0.03	0.16 ±0.02	0.18 ±0.03	0.05 ±0.03	0.07 ±0.03	0.02 ±0.03	0.06 ±0.03
	Triglycerides mmol/L	0.3 ±0.09	0.32 ±0.09	0.27 ±0.08	0.28 ±0.08	0.34 ±0.13	0.28 ±0.12	0.41 ±0.12	0.33 ±0.11
	Systolic blood pressure mm/Hg	0 ±0.91	-0.48 ±0.78	0.27 ±0.81	1.27 ±0.83	3.78 ±1.18	3.31 ±1.21	3.08 ±1.02	4.09 ±1.21
	Diastolic blood pressure mm/Hg	0.38 ±0.48	0.15 ±0.46	0.11 ±0.51	0.82 ±0.51	2.4 ±0.66	1 ±0.62	2.06 ±0.69	1.6 ±0.64
	Heart rate (bpm)	2.16 ±0.68	2.47 ±0.86	3.14 ±0.65	2.68 ±0.85	1.35 ±0.88	1.12 ±1.03	2.7 ±0.94	1.7 ±1.03
	Hair cortisol (log)	0.2 ±0.12	0.29 ±0.12	0.28 ±0.12	0.3 ±0.14	0.08 ±0.17	0.13 ±0.	0.06 ±0.15	0.04 ±0.

							19			18
		Overall p-values			**Subgroup p-values female**			**Subgroup p-values male**		
		M	E	M x E	M	E	M x E	M	E	M x E
Body composition										
	Fat free mass (kg)	1.00	0.71	0.69	0.86	0.93	0.75	0.83	0.70	0.65
	Fat mass (kg)	0.36	0.77	0.76	0.68	0.56	0.81	0.13	0.22	0.71
	Waist circumference (cm)	0.35	0.55	0.54	0.83	1.00	0.49	0.14	0.25	0.79
Biomarkers										
	HbA1c_mmol_mol	0.65	0.10	0.73	0.70	0.13	0.65	0.26	0.83	0.92
	HbA1c_percent	0.26	0.78	0.92	0.52	0.30	0.94	0.21	0.88	0.71
	Total Cholesterol mmol/L	0.37	**0.06**	0.78	0.74	0.57	0.86	0.95	0.12	0.78
	LDL cholesterol mmol/L	0.37	0.11	0.86	0.31	0.24	0.79	0.85	0.19	0.58
	HDL cholesterol mmol/L	0.18	0.79	0.68	0.37	0.62	0.69	0.62	0.61	0.85
	Triglycerides mmol/L	0.84	0.80	0.69	0.74	0.74	1.00	0.28	1.00	1.00
	Systolic blood pressure mm/Hg	0.58	0.17	0.21	0.87	**0.06**	0.11	0.91	0.89	0.54
	Diastolic blood pressure mm/Hg	0.82	0.64	0.17	1.00	0.51	0.21	0.23	0.84	1.00
	Heart rate (bpm)	0.78	0.13	0.36	1.00	0.82	0.64	0.52	0.25	0.23

	Hair cortisol (log)	0.74	0.80	0.60	0.66	0.58	0.80	0.66	0.63	0.39

M = self-regulation and motivation, E = contextual behavioural aspects of emotion regulation, M+E = these factors in combination

Physical activity and sleep

Results regarding physical activity and sleep are presented in Supplementary Table 2. There was no significant effects of the intervention on these variables.

Dietary intake and eating behavior

Overall the interventions showed no effect on self-reported dietary energy and macronutrient intakes and eating behaviour (Supplementary Table 2).

Well-being and Quality of Life

There were no significant effects of the interventions on wellbeing and quality of life (Supplementary Table 2)

Self-regulation, motivation and self-efficacy

The interventions showed no significant effects on any of the variables related to self-regulation, motivation and self-efficacy (data not shown).

Emotion regulation and stress management

There were no significant effects of the intervention on the emotion regulation and stress management variables. Small decreases in mindfulness were found for participants in the self-regulation/motivation intervention (data not shown).

Change in energy balance behaviours in relation to weight loss or weight regain.

The lack of intervention effect in this trial raises a further question of whether those whose weight changed, showed a corresponding change in energy balance behaviours. In the ITT population, total daily steps changed by +808, -421 and -667 ($p < 0.001$) in those who lost, maintained or regained

weight; i.e. those who lost weight increased their steps while those who gained decreased their steps. Twenty four hour energy expenditure, estimated by Fitbit proprietary algorithms, changed by -47 kcal/d (losers), +3 kcal/d (maintainers) and +54 kcal/d (gainers)(P = 0.0001). It should be noted these estimates tend to be more precise than accurate and may therefore be less appropriate for between-individual comparisons [68]. Total self-reported daily energy intake estimated by 24hr recall changed by -195 kcal/d (losers), -204 kcal/d (maintainers) and -92 kcal/d (gainers) (P = 0.2233). Self-report dietary intakes have both low precision and accuracy and likely only give approximate between-individual comparisons [69]. Nevertheless, these data indicate that indices of energy balance behaviours did change in the direction expected to achieve measured weight change.

Table 4 shows univariate and multivariate regression analysis using toolkit compliance, Fitbit compliance and self- weighting as predicors of weight outcomes. n univariate models TK usage, Fitbit compliance and self weighing all showed small predictive effects on weight loss but in multivariate models only self weighing remains as a significant predictor, but the proportion of variance explained remains small.

Table 4: Univariate and multivariate regression analysis using toolkit compliance, Fitbit compliance and self- weighting as predictors of weight outcomes.

	Univariate models			Multivariate models		
Predictor	Coefficient	SE	p-value	Coefficient	SE	p-value
Toolkit use compliance (percentage)	-0.0259	0.0076	**0.001**	-0.0113	0.0080	0.159
Fitbit use compliance (no. days >20 hours use)	-0.0048	0.0014	**0.001**	-0.0004	0.0017	0.801
Self-weighing compliance (no. weeks with ≥2 weighings)	-0.0905	0.0109	<**0.0001**	-0.0860	0.0135	<**0.0001**

Discussion

NoHoW was the first project to develop and formally evaluate (via RCT) a digital toolkit combining continuous tracking of EB behaviours and body weight with theoretically informed, evidence-based digital interventions targeting self-regulation and motivation, and emotion regulation in a 2 x 2 factorial design, to target long-term weight management.

The present study was designed to test three hypotheses, that (i) motivation and self-regulation of energy balance behaviours improve longer-term weight outcomes, (ii) emotion regulation strategies help prevent weight relapse and (iii) there is an additive effect between emotion regulation and self-regulation/motivation. Overall, the trial results showed only very weak support for the hypothesis (i) that motivation and self-regulation of energy balance behaviours can improve longer-term weight outcomes and in the men only, who represented 31.4% of the study population, with a small effect not exceeding 1.5 kg. This intervention arm was also the arm in which intervention completion (but not necessarily the number of visits to the toolkit) had the highest correlation with weight loss [48]. The 2 x 2 factorial design was well powered to detect intervention effects, which were not effective in altering primary and all secondary outcomes.

It is interesting to consider how and why the men may have been more responsive to the self-regulation intervention than the women. They were more engaged with the process-based intervention content, but user metrics for the digital intervention does not support this notion. Indeed, focusing on Toolkit engagement (compliance) alone, there was a negative correlation between usage metrics and weight change (all $p<0.05$). However multiple comparison adjustment would weaken these statistics. Measured usage of the toolkit components suggested that men tended to use the toolkit less than women and that usage was lower in the M arm (in which weight loss was greatest in men only), which does not support the hypothesis that compliance or engagement with the M arm of the toolkit explains the slightly greater weight loss in men.

Explaining the negligible effect of the digital intervention for weight loss maintenance.

Possible explanations for the lack of intervention effect may relate to the fact that the intervention was digital, that the toolkit content and dose per se (i.e. the logic models) were not as effective as hypothesised (i.e., those mechanisms are just not very effective, the dose was not sufficient), or that participants did not engage with the intervention (i.e. that the design of the toolkit was not optimal and that had the putative mechanisms of action by which the intervention was supposed to work been delivered more effectively, they may have worked). Evidence based behaviour change interventions tend to show small effect sizes anyway [19,20,25,70-72]. In fact, the evidence tends to point in the direction that the most salient component of this trial associated with weight change was self-weighing.

The participant user engagement and experience evaluation of the content of the toolkit itself was revealing [48]. In the current study actual use of the toolkit during the 18 weeks of the active intervention was relatively high and comparable to other digital health interventions, and as with similar interventions tended to decay with time [48]. Use declined rapidly during the period of discretionary use. Weight outcomes were influenced by degree of engagement with the study as has been shown previously [73]. Weight outcomes were also weakly correlated with use of the digital intervention content, but correlations between weight change from baseline to 12 months and use metrics were small and not consistent with the small differences in weight outcomes across trial arms. While participants had some reservations about the content and ease of use of the toolkit, it does not appear that degree of engagement, as measured by actual use of the toolkit is a viable explanation for the general lack of between-arm effects of the intervention (see above).

Usability was deemed satisfactory, acceptability modest (between 3-4 on a 5-point scale), both of which declined for all trial arms through the trial. Qualitative data showed that these perceptions of the toolkit were similar across centres and intervention arms [48]. Participants appreciated support for self-monitoring of weight, sleep and activity, all of which were derived from the Fitbit devices. Participants also appreciated content of the toolkit based on self-regulation of behaviour and emotion regulation. They associated their decreased toolkit use with frustrations in design that hindered its use, e.g., the log-in process as well as time commitment and frustrations using the toolkit on mobile phones[48]. Participants also tended to compare unfavourably, the design aspects of the toolkit to the Fitbit app and other commercial offerings [48]. Such offerings are also regularly updated, while the NoHoW TK was static for 18 months to ensure that the trial was testing the same intervention in all participants. Thus, the user acceptability and experience data offer important insights into the limited impact of the digital intervention on weight outcomes. The intervention appear to have been less

preferred than the Fitbit app and intervention effects were very small. It does not matter how evidence-based or research-informed an intervention is if it is deemed to be difficult or even mediocre to use compared to other offerings available.

Thus, while it is important that digital behaviour change interventions need to be developed with an interdisciplinary team and that the content, delivery and structure are informed by theory and evidence [52], there are other important design aspects that could be addressed to improve the effect sizes of interventions such as the NoHoW tookit. The NoHoW toolkit was meticulously developed with respect to (1) state-of-art theories (Self-regulation Theory, Self-Determination Theory, and aspects of emotional regulation theory); (2) integration of consumer physical activity and weight tracking devices; (3) web-design expertise; 3) some user-testing; 4) preliminary mixed methods research. However, the delivery of the digital intervention may have benefitted from greater involvement from human computer interactions experts and co-design with prospective users together with commercial partners. Such partners may have offered resource and infrastructure to produce an offering that motivates engagement and re-enforces the practice of behaviour change techniques using refreshed content, that may have improved outcomes. Due to resource constraints, these design aspects were limited in the current trial. Involvement of health care professionals and engagement with social networks as a part of the intervention may improve some outcomes [74,75]. Using optimization designs for iterative development and testing of smaller components (e.g., clusters or individual behaviour change techniques BCTs) could also be beneficial to identify the combination of components that could work better together [76]. The NoHoW trial deliberately excluded interactions with health care professionals and social networks in order to test the effect of a digital-only intervention. A constraint of a randomized controlled trial design is the fixed nature of the intervention during the trial. This approach precludes iterative development, testing and ongoing content and design updates, the lack of which disappointed participants who are used to such features of commercial apps [48]. These factors should be taken into account in developing future digital interventions for weight management.

Is there evidence that Fitbit use predicted weight loss maintenance?

A possible factor (point 2 in the design specifications listed above) that may have limited the effect sizes observed in the current study is the use of an active control in which participants each received and used a Fitbit Charge 2 activity tracker (Fitbit LLC and a set of Fitbit Aria wireless scales (Fitbit

LLC). All participants also had access to the Fitbit smartphone app (Fitbit LLC). Use of trackers and scales was high [77,78] and therefore it is likely that these represented an 'intervention within an intervention'. Ideally it would have been better to conduct a 2 x 2 plus 1 trial in which there was a genuine 'no intervention' control, but resources did not permit this option. In regression models weight change was significantly predicted by all of TK compliance, self-weighing compliance, and Fitbit use compliance. But when all three were included in a model, only self-weighing compliance was significant, i.e., there was little evidence the TK had any effect over and above using the Fitbit devices alone.

Comparison to other trials using behaviour change approaches for longer-term weight management

At present, systematic reviews and meta-analyses show the extent to which behaviour change interventions for weight loss maintenance (WLM) in adult populations are effective (e.g., [18]). Generally, per protocol results show greater WL than intention to treat (ITT) analyses. A number of large trials focusing on evidence-based approaches to WLM have demonstrated effects on weight-related outcomes, generally not exceeding 2kg by trail end, over time periods ranging between 6-12 months (Stubbs et al: obesity facts 2021). These include the Weight Loss Maintenance (WLM) randomized controlled trial [25], DiOGenes [79], PREVIEW [80], NuLevel [81] and NoHoW [50] trials. The Look AHEAD trial produced clinically significant WL (≥5%) after 8 years' intensive lifestyle intervention in 50% of 2,570 adults with type 2 diabetes, a patient population with a strong clinical reason for trying to achieve WLM [82].

In the current study imputing the missing data differently tended to have an effect on absolute but not relative weight outcomes between trial arms. The more pessimistic we were about assumptions relating to drop out the better the weight outcomes, however trial arm comparisons remained the same. When the ITT model was used with a baseline observation carried forward imputation participants regained 40-50% of the weight they had lost prior to the intervention. This is consistent with similar studies in the magnitude and direction of weight regain over 12 months in response to dietary or behaviour change interventions for weight management[25,79,81,82].

Strengths and Limitations of the current study

Key strengths of the current study were the 2 x 2 factorial design of the trial, the sample size at 3

European centres across Northern, Western and Southern Europe, standardisation and harmonisation of standard operating procedures across centres, the use of minimization in randomizing participants, the duration of follow up, the relatively low drop-out rate and the fact that weight losses prior to the intervention were verified. Limitations included the lack of a genuine baseline due to the expediency of recruiting participants who had already lost weight in the previous 12 months, the lack of balance in content type and duration between trial arms, limitations to the design of the toolkit itself that were apparent in the user acceptability and experience data, the absence of a genuine 'no intervention' control, and likely contamination of the intervention itself with the content of the Fitbit app. Several of these limitations may well have impacted weight outcomes and are discussed above.

Future directions

The NoHoW trial has demonstrated the immense benefits of using cloud connected digital trackers to help users track their weight, physical activity and sleep. It is notable that the salient predictor of successful weight management was engagement with the Fitbit digital weighing scales. Multi-component behaviour change interventions are by the nature complex [83], as are physiological and behavioural responses to weight loss. It is well-established that weight loss leads to some compensation of energy expenditure and of energy intake and that some behavioural changes in these components of energy balance are not always under conscious control [42]. The limited evidence from systematic reviews and meta-analyses to identify mediators of longer-term weight loss suggests that navigating from initial WL to WLM requires long-term self-management of EB behaviours in the face of physiological resistance to WL [14,19,20,70]. The COM-B model provides an overarching theoretical framework to understand the barriers and facilitators of behaviour change. Specifically, the model suggests that behaviour change requires capability (physiological of physical ability), motivation (reflective and automatic processes the activate or inhibit behaviour) and opportunity (physical and social environment to enable behaviour) [84]. Kwasnicka et al have systematically reviewed theoretical explanations for the maintenance of behaviour change and identified five overarching theoretical explanations for the maintenance of behaviour change representing motives, self regulation, psychological and physical resources, habits and environmental/social influences on behaviour [16]. A key question is how such frameworks for reflective and automatic mechanisms of behaviour change interface with the physiology of energy balance compensation in response to attempted or imposed energy deficits. Tracking compensatory

changes in energy balance behaviours over time may improve prevention of weight regain through provision of behavioural navigation solutions, personalisation of weight management interventions, and by offering a quantitative behavioural context in which psychological moderators and mediators of energy balance behaviours and body weight can be tracked [42]. Similarly using metadata from digital interventions to track user engagement offers a powerful quantitative tool to understand the behaviour of participants during the course of longer-term interventions [48]. Thus, while the NoHoW trial produced very modest results in terms of the hypothesized mechanisms of action of digital interventions, it provided unique insights into the limitations of digital intervention design and how they can be addressed and incorporated into future weight management provision. Our understanding of factors that promote or undermine self-management of eating and physical activity is still limited, but include physiological adaptation and behavioural compensation in eating and physical activity, reactive processes related to, emotions, stress rewards and desires that meet psychological needs. Optimisation and piloting evidence-based intervention content to the needs of individuals may improve outcomes. Objective longitudinal tracking of weight and physical activity and through mathematical modelling of energy balance components over time would provide a quantitative framework in which to understand the dynamics and mechanisms of action of behaviour change interventions [42]. Such tracking also offers users navigational solutions. These can be combined with tracking of user engagement with intervention components to potentially improve weight management intervention design and evaluation.

Conclusions

The NoHoW trial was a well-designed trial, adequately powered to detect changes in weight and health outcomes. We found no evidence of effectiveness of the interventions alone or in combination. In the trial, a significant but clinically small effect was detected in the men in the self-regulation and motivation intervention arm.

Despite being well designed from a theoretical and evidence-based perspective the NoHoW trial showed some limitations in consumer or user acceptability, and the current study highlights some possible design aspects of the digital behaviour change intervention that could be improved to enhance intervention effectiveness. These include development by an interdisciplinary team including specialists in app design and marketing/delivery; content, delivery and structure informed

by theory and evidence [52]; greater involvement from human computer interactions experts; using optimization designs for interactive development and testing of smaller components (e.g. clusters or individual BCTs) to identify the combination of components that could work better together [76]; greater co-design with prospective users [85,86]; commercial partners to make digital intervention appearance and content comparable to those currently available; involvement of health care professionals; embedding interventions and social networks to provide an ecosystem of support. These aspects of intervention design do not lend themselves well to the design and conduct of randomised controlled trials in a traditional grant-funded environment, which are constrained in time and budgetary allocation. We therefore recommend that future digital interventions for weight management are developed through academic and commercial or healthcare partnerships, extensively tested and refined by users and providers by the time they are evaluated through randomised trials. Novel designs including using optimisation designs and modifiable intervention content during trial designs may also enhance effectiveness in the future.

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RJS, BLH, PJT, FFS, ALP and GH conceived the study. RJS is the principle investigator; BLH is the grant coordinator; and SES and CD are the trial managers. SCL, ALP and SES are site coordinators. GH is the trial statistician and leads data management. MH and EM are responsible for the technological development and management of the NoHoW digital toolkit. ALP, MMM, MM and CD developed the content of the arms of the digital toolkit. PJT, JE, IS, BLH, MLM, SL, RJS, SS, BP and LR conducted the trial activities at each respective trial sites. EHE and FS was involved in the development of some of the trial outcome measures. RJS, CD and CAD drafted the manuscript and all authors revised and approved the final version. CAD submitted the manuscript for publication. All authors made substantial contributions to the conceptualisation of the study design and conduct of the protocol.

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Conflict of interest:

RJS consults for Slimming World through the University of Leeds. MMM and GH also conducted consultancy work with Slimming World.

Table legends

Table 1: baseline measurements: historical weight loss, anthropometry (Height, body weight, Waist circumference, fat mass, fat free mass), Health markers (HbA1c, blood pressure, plasma lipids, resting heart rate), stress, depression, anxiety, well-being and QoL, for men and women in the four arms (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined).

Table 2: Outcome results for weight (kg) at 12 months using the intention to treat analysis where regain all pre-trial weight loss is assumed for missing data. Data for completer and per-protocol analyses are also shown. Values shown are mean of weight change ± SEM.

Table 3: Change in health markers: anthropometry (waist circumference, fat mass, fat free mass), health markers (HbA1c, blood pressure, plasma lipids, resting heart rate), for men and women in the four arms (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined).

Table 4: Univariate and multivariate regression analysis using toolkit compliance, Fitbit compliance and self- weighting as predictors of weight outcomes.

Figure legends

Figure 1: The 2 x 2 factorial design of the NoHoW trial.

Figure 2: longitudinal changes in body weight by trial arm (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined) for men and women in the ITT population.

Figure 3: Percentage of the ITT population gaining, losing or maintaining pre-trail weight loss, by trial arm (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined). Percentage weight change was calculated as (CID 3 kg – CID 1 kg) / CID 1 kg x 100. Weight category was then calculated from percentage weight change. Participants were assigned to the following weight category: >-3% weight loss (weight loser), between -2.99% and +2.99% (weight maintainer) and >+3% weight gain (weight gainer).

Figure 4: Cumulative drop-out from the trial between months 0-12 by trial arm (control, self-regulation and motivation, emotion regulation and self-regulation & motivation plus emotion regulation combined). The black dot at month 18 indicates assumed drop-out of 38% estimated from previous RCTs.

Supplementary materials

Supplementary Table 1: Baseline measurement of the most reliable indices of physical activity and energy expenditure (Fitbit measures), and energy and macronutrient intake (intake 24 measures), key scores on eating behaviour trait measures (Binge eating scale, Three factor eating questionnaire, Intuitive eating scale), well-being and quality of life (Warwick-Edinburgh wellbeing scale, EQ5D-5L).

Supplementary Table 2: Change scores of the most reliable indices of physical activity and energy expenditure (Fitbit measures), and energy and macronutrient intake (intake 24 measures), key scores on eating validated eating behaviour trait measures (Binge eating scale, Three factor eating questionnaire, Intuitive eating scale), well-being and quality of life (Warwick-Edinburgh wellbeing scale, EQ5D-5L).

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Supplementary Files

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Figures

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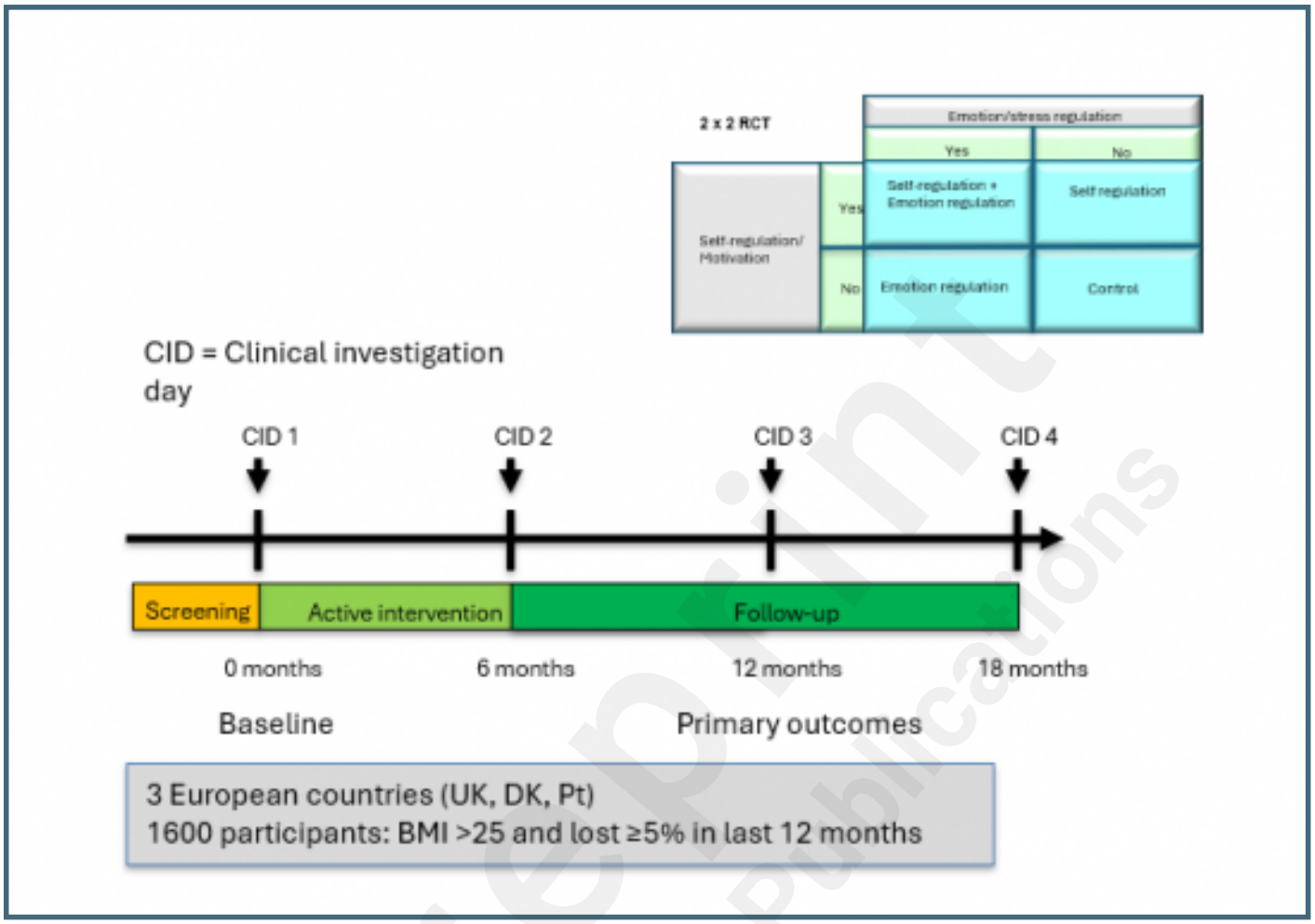
2 x 2 RCT
Emotion/stress regulation
Yes
No
Self-regulation/ Motivation
Yes
Self-regulation + Emotion regulation
Self regulation
No
Emotion regulation
Control
CID = Clinical investigation day
CID 1
CID 2
CID 3
CID 4
Screening
Active intervention
Follow-up
0 months
6 months
12 months
18 months
Baseline
Primary outcomes
3 European countries (UK, DK, Pt)
1600 participants: BMI >25 and lost ≥5% in last 12 months

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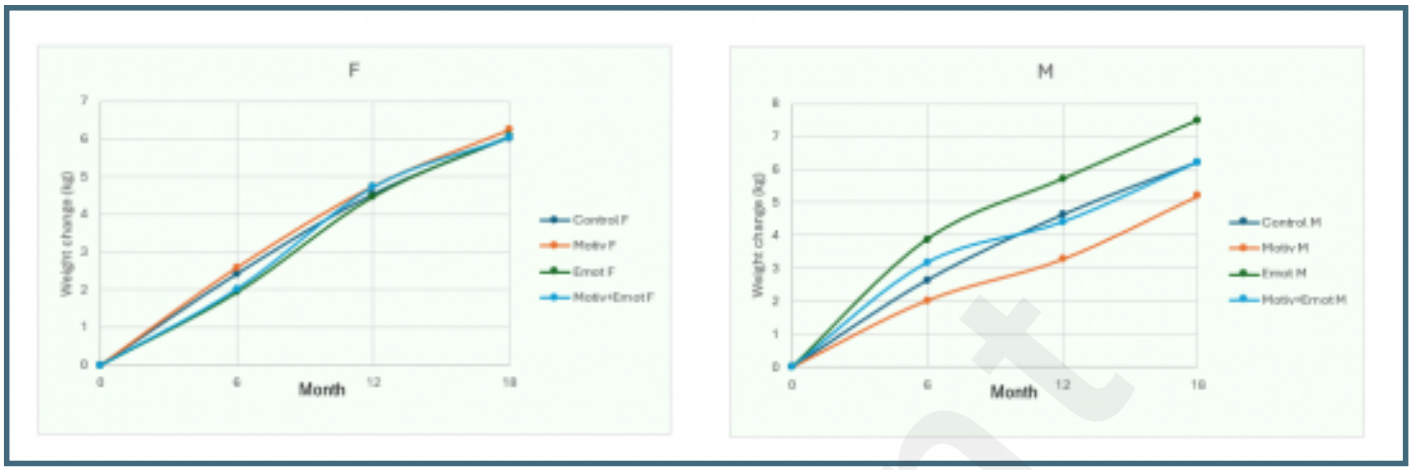

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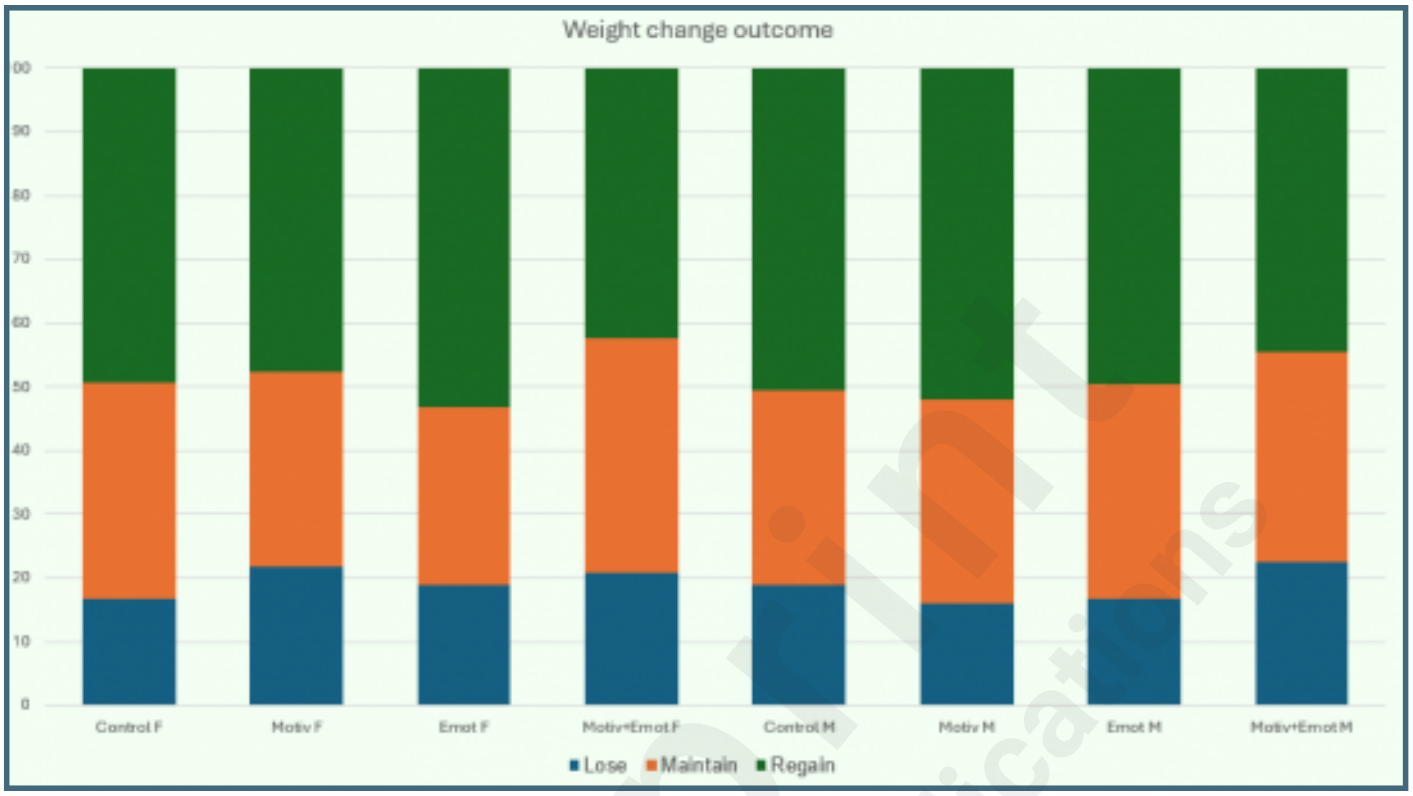

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