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Developing evidence-based behavioural strategies to overcome physiological resistance to weight loss in the general population

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Abstract

Physiological and behavioural systems are tolerant of excess EI and responsive to energy deficits. Weight loss (WL) changes body structure, physiological function and energy balance (EB) behaviours, which resist further WL and promote subsequent weight regain. Measuring and understanding the response of EB systems to energy deficits is important for developing evidence-based behaviour change interventions for longer-term weight management.

Currently, behaviour change approaches for longer term WL show limited effect sizes. Self-regulation of EB behaviours (e.g. goal setting, action plans, self-monitoring, relapse prevention plans) and aspects of motivation are important for weight loss maintenance. Stress management, emotion regulation and food hedonics may also be important for relapse prevention, but evidence is less concrete.

Although much is known about the effects of WL on physiological and psychological function, little is known about the way these dynamic changes affect human EB behaviours. Key areas of future importance include (i) improved methods for detailed tracking of energy expenditure, balance and by subtraction intake, using digital technologies, (ii) how WL impacts body structure, function and subsequent EB behaviours, (ii) how behaviour change approaches can overcome physiological resistance to WL and (iii) who is likely to maintain WL or relapse. Modelling physiological and psychological moderators and mediators of EB-related behaviours is central to understanding and improving longer-term weight and health outcomes in the general population.

Introduction

Getting energy balance right

Forty percent of the world's population of 7.7 billion people are chronically over or undernourished in roughly equal proportions [1]. This suggests that at global, national, community and individual level energy balance (EB) remains a key societal challenge. It is important to consider EB from a multi-disciplinary perspective. The causes and consequences of energy imbalance operate at the societal, policy, public health and individual level [2]. Addressing this challenge necessarily requires consideration of the physiological systems believed to regulate EB, their impact on human behaviour and their interaction with the environment in which such putative regulatory systems operate. The current paper focuses on physiological and behavioural responses to negative EBs and the potential role for longer-term weight management interventions.

Energy balance and obesity

Obesity is a chronic relapsing condition with multiple co-morbidities. Such complex conditions have a large behavioural component to their development and maintenance. Management requires concerted action through multi-component interventions aimed at both prevention and treatment [3]. To date no one organisation, approach or sector has made a significant impact on long-term obesity prevalence trends. Evidence-based interventions and commercial programmes for weight loss (WL) are widely available [4; 5] . In developed countries approximately 42% of adults report trying to lose weight and 23% report trying to maintain weight annually [6]. Eighty percent of those who achieve clinically significant WL fail to sustain that WL over a period of 12 months or more [7]. Factors responsible for weight regain include physiological resistance to WL [8] (see below), the obesogenic environment [9], individual experience of stress and life events and emotional eating [10], and a general lack of knowledge on the part of the general public on how to effectively manage EB behaviours (dietary intake and physical activity) - perhaps exacerbated by the extensive use of popular rather evidence-based weight management practices. Thus, the development of obesity and resistance to WL is due to an interaction between physiology and behaviour in a food, lifestyle and marketing environment that facilitates over-consumption of energy and low levels of physical activity energy expenditure (EE) [9]. Many marketed solutions for WL tend not to comprehensively implement evidence-based components of behaviour change interventions for weight management [4; 11]. The actual evidence for effective components of weight management (i.e. WL and WL maintenance (WLM)) programmes is limited [12]. Obesity research and practice tends to focus on separate domains of physiology and health on the one hand and behaviour change solutions on the other. This segmented approach may limit the effectiveness of longer-term WL interventions.

This paper considers (i) how energy deficits influence physiology and behaviour, (ii) how those responses may shape our ability to develop evidence-based practices to help people manage long-term EB and (iii) the types of evidence needed to inform more effective and personalised interventions for longer-term weight management.

Physiological and behavioural responses to energy deficits

Human responses to WL are dynamic and complex. WL follows exponential decay curves in three phases - a relatively short phase 1, a slower, more-steady rate of WL in phase 2, which (if WL unfortunately continues) is followed by phase 3, a shorter, pre-mortal phase [13; 14]. Phase 1 is accompanied by rapid decrease in weight, depletion and change in the composition of fat-free mass (FFM), which stabilises to a slower rate of loss after 4-6 weeks (maximally 12) depending on factors such as initial body composition, extent of energy deficit, degree of exercise and sex of subjects[13; 14]. Phase 2 is characterized by a decrease in the rate of FFM loss and an increase in the rate of mobilisation of body fat [13]. The majority of voluntary WL interventions operate across phase 1 and into phase 2 of WL suggesting that dynamic changes in multiple physiological systems operate to oppose initial WL by reducing EE and defending loss of FFM from further rapid loss [13]. These physiological changes may also be associated with compensatory changes in eating and physical activity behaviours[8]. The effectiveness of behaviour change interventions for weight management could potentially be improved by considering those interventions in the quantitative context of EB physiology (**FIGURE 1**).

Physiological models of EB regulation and weight management interventions should account for a number of salient features of the way human EB behaves, namely (i) the inherent asymmetry of EB regulation, which underlies the tendency for most humans to gain weight under modern environmental conditions, (ii) to regain weight in response to weight management attempts and (iii) the dynamic physiological responses to energy deficits and their potential impact on behaviour. Some integrative functional body composition models of EB regulation are beginning to unravel the dynamic relationships between body structure, physiological function and the way these interactions influence human behaviour and health [8].

It has been argued that the asymmetry of EB regulation in many mammalian species is due to an evolutionary history characterised by alternations between periods of feast with those of famine. It has been argued that environmental uncertainty in food supply would result in physiological and

behavioural programmes that favoured the deposition of reserves in adipose tissue when good quality food was readily available[15; 16]. In other words, the capacity for overconsumption and a tendency to gain weight in the face of nutritional abundance appears to be a strategy for survival and reproduction that evolved in resource-limiting environments [16]. Such design characteristics of human eating behaviour would only become maladaptive in environments where the nutritional supply is superabundant, energy-dense and hyperpalatable. Humans have manufactured and currently live under such environmental conditions.

Physiological resistance to weight loss

Body composition

The composition of WL is not constant as WL proceeds [13; 14; 17; 18; 19; 20; 21; 22]. The rapid depletion of FFM in phase 1 of WL is associated with rapid glycogen losses, initial (relatively large) losses of nitrogen (i.e. protein) and associated body water [13]. The rate of these dynamic changes in FFM tends to stabilise beyond 4-6 weeks such that glycogen is depleted, protein and water losses decelerate dramatically and the proportion of fat mass (FM) contributing to WL increases as WL progresses [13]. Hence, both the proportion of body WL as FFM decelerates and the contribution of glycogen and water to FFM loss decrease throughout phase 1[13]. Furthermore, the source of protein losses changes from phase 1 to phase 2, largely coming from peripheral organs in phase 1 and shifting to skeletal mass in phase 2 [13]. These changes are associated with reductions in energy requirements and increases in the energy density of tissues lost that collectively tend to reduce the overall rate of WL, for a given energy deficit, beyond 4-6 weeks. During phase 2 of WL the proportionate contribution of FFM to WL decreases and the contribution of fat mass (FM) to WL increases along exponential decay curves that are heavily influenced by initial body fatness at the start of WL, the severity of the energy deficit, physical exercise, macronutrient composition of the diet, sex and some hormones and drugs[14]. It appears that visceral adipose tissue may be preferentially mobilized in the earlier stages of FM loss [23; 24]. In essence, a greater FM operates as a buffer that defends loss of FFM during WL [25]. The dynamic changes in body composition within phase 1 and the shift in tissues mobilized across phase 2 of WL account for the exponential decay curve of body weight during a prolonged energy deficit [13]. These changes affect both EE (metabolic and behavioural changes) and EI (behaviour) and have been mathematically modelled [13; 14; 17; 18; 19; 20; 21; 22]. However, more is currently known about some components of EE than EI and more is known about physiology than behaviour.

Energy expenditure

As WL proceeds energy requirements decrease in line with a decrease in metabolically active tissues and to some extent beyond that predicted by changes in metabolically active tissue, indicating some degree of metabolic adaptation [26; 27]. Such changes are most evident in extreme WL. There is limited data on the effect of extreme energy deficits on change in body weight, composition and EE (and its components). The seminal Minnesota semi-starvation study examined the effect of 24-weeks semi-starvation on total EE and (by calculation) its components. The effects of a 40% WL in initially lean men (comprised of 70% fat loss; 18-20% FFM loss) on both EE and subsequent EI were amongst the most dramatic compensatory changes in EB components ever recorded[28].

During prolonged energy deficits (i.e. phase 2 of WL) most weight that is lost is in the form of reduced FM but FFM also decreases with WL, depending on initial body composition and the rate of WL [25]. Decreases in weight and FFM also reduce spontaneous (volitional) physical activity EE [28; 29], resting metabolic rate (RMR) and total daily EE [29; 30; 31; 32], potentially increase muscular efficiency [33] and decrease the energy cost of weight bearing activities [29]. The adaptations may persist for 12 months or longer after WL [34; 35]. These effects have been found in obese [34; 35] and slightly overweight subjects losing 10-13% of their weight [29; 31]. The estimated maximum change of RMR/kg FFM under such conditions is ~5-10% [36]. Extreme energy deficits in the Minnesota study led to a 45% drop in estimated total daily EE (**Table 1**) and in the Biggest Loser study reductions of total daily EE of 21% were estimated by the end of the 30 week competition[34]. In the latter study 37.9% loss of an initial mean body weight of 149.2 kg, induced by caloric restriction and very large increases in physical activity, led to a reduction of RMR independent of changes in body composition of 504 kcal/d [37]. Interestingly, a near doubling of physical activity (kcal/kg/d) was insufficient to offset the substantial decrease in total daily EE due to changes in body size and metabolic adaptation[34; 37; 38]. The estimated change in whole body EE under conditions of 10-20% therapeutic WL appears to be in the region of ~15% or ~30kcal/kg weight lost/day [21; 30]. Thus, both physiological and behavioural components of EE significantly change in response to moderate or extreme, prolonged energy deficits in a way that tends to oppose further WL.

Appetite and energy intake

While EE and its components change in response to energy imbalances in a quantitatively important manner, it is likely that compensatory changes in EI have a greater capacity to produce relatively large alterations in EB and body composition. Indeed, much of weight regain subsequent to WL is due to increases in EI rather than decreases in EE[19; 21].

In order to understand responses to therapeutic WL, extreme examples of semi-starvation provide exaggerated responses in which physiological mechanisms and behaviour changes can be more clearly observed. During the Minnesota study 32 lean men (mean percent body fat 22%) were underfed by ~40% relative to their normal EI for 24 weeks. For the next 12 weeks they were incrementally refed, but by the end of this period they were still in a deficit of ~25% for FM and 12-15% for FFM. During the final 8 weeks, 12 subjects had ad libitum access to a range of foods, with EI initially increasing to 160% of requirements and gradually subsiding to pre-WL levels. The cessation of post-WL hyperphagia coincided with a massive overshoot of FM, and repletion of FFM to baseline levels [28]. These (limited) data suggest that there is an integrated response from FM and FFM that is associated with hyperphagia, subsequent to semi-starvation.

Very high levels of ad libitum EI in response to prior semi-starvation have been reported by Widdowson in 12 German men in Wuppertal immediately after the Second World War. These subjects (mean weight 59.3 kg) consumed ~6000 kcal/day over an observation period of 8 weeks, in which they had unlimited access to food, gaining 10.3 kg in weight [39]. Similar levels of hyperphagia have been reported in a study of concentration camp (Sandbostel) prisoners, who consumed ~8000 kcal/day [40] and increased their weight from 56 to 61 kg over 22 days. In both studies the rate of weight gain decelerated as the observation period proceeded.

It is important to question whether such compensatory physiological and behavioural changes are relevant to therapeutic WL in initially overweight or obese people. The work by Leibel et al., Redman et al. and Muller et al. suggest that for EE this is the case [27; 29; 30; 31; 32; 34; 35; 41]. Energy deficits under conditions relevant to therapeutic WL also affect appetite control. Doucet and Cameron document how 25% energy restriction typical of WL programmes leads to a substantial elevation of appetite over 15 weeks[42]. Sumithran et al have shown that a 13.5 kg (14%) WL in 50 obese subjects through very low-calorie diet led to an elevation in subjective appetite during a standardised test-meal protocol, immediately after WL and after 12 months where WL was maintained at 8.2%. Thus, WL leads to increased hunger under standardised test-meal conditions 12 months later [43]. Nymo et al also showed an increase in hunger over 12 months after 15% WL induced by a very low-calorie diet. Interestingly, this was accompanied by an increase in fullness, which may be due to gastric contraction [44]. Anton et al. found an increase in subjective sensations of hunger or appetite in the fasted state in the first 2 months of energy restriction, which then stabilised between 3-6 months in the CALERIE study [45]. Increases in motivation to eat in response to WL are not always apparent e.g. [46]. A review by Hintze et al. 2017 argues that on balance, the literature (primarily in women) suggests that WL (i) tends to elevate fasting and post-prandial subjective/self-reported appetite, (ii)

alters appetite-related peptides in a manner that can be interpreted as broadly consistent with a WL-induced elevation of appetite and (iii) shows some evidence of increased food cravings and hedonic responsivity (liking and wanting) [47]. Recently Polidori et al. used a previously validated mathematical model [48] to estimate long-term changes in EI from body weight (assuming no change in physical activity EE) during a year-long placebo-controlled trial in 153 people treated with Canagliflozin, a sodium glucose transport inhibitor that operates peripherally to increase urinary glucose production. Canagliflozin increases urinary glucose output by ~90g/day (producing an energy deficit equivalent to ~360 kcal/d), that was independent of EE, central appetite control mechanisms or cognition and therefore represented a truly covert energy deficit [21]. The study found that EI compensation (~100kcal/kg/day per kg of WL) was proportionate to WL and appears to be ~ 3 times greater than estimated compensation of estimated EE in response to 10-20% WL (~30kcal/kg/d) [30]. This study and the modelling of responses to WL pharmacotherapy [22] suggests that prolonged WL attempts lead to a prolonged and exponential increase in appetite (using estimated EI as a proxy) in proportion to the weight that is lost [21]. Reports of changes in peripheral appetite peptides in response to 10-20% WL produce results that can be interpreted as being consistent with WL increasing homeostatic increases in appetite [43; 44; 47; 49; 50].

Weight loss influences body structure, which in turn affects EB physiology (the composition of tissues mobilised and EE) and behaviours (physical activity and EI), in a way that attempts to restore body weight to pre-WL levels. Extreme WL leads to pronounced decreases in components of EE and increases in appetite and EI that tend to ameliorate as body weight and composition are restored. Similar responses occur in relation to therapeutic WL, but they are more muted. Appetitive responses to therapeutic WL are not always easy to detect using psychometric or physiological measures at fixed timepoints, probably because participants already have an excess FM (which acts as an energy buffer) and because the rate and extent of WL is less pronounced. Nevertheless, mathematical modelling of changes in EI tracked over weeks and months suggest that there are compensatory increases in EI contribute substantially to weight regain.

Physiological and behavioural responses to weight loss: implications for weight management

WL invokes physiological changes on the intake and expenditure side of the EB equation that predispose those engaged in WL attempts to weight regain. The NIH working group on maintenance of WL has produced a conceptual framework to articulate how such changes undermine longer-term WLM through changes in (i) appetite and eating behaviour, (ii) components of EE and (iii) the

motivational cost of adherence to weight management programmes versus the rewards of continued WL attempts [51]. These changes tend to oppose or undermine sustained behavioural attempts at reducing EI and increasing EE. This is the physiological challenge for behavioural interventions aimed at achieving WLM, subsequent to WL attempts. As weight is progressively lost evidence suggests that physiological signalling systems actively oppose further WL through compensatory decreases in activity behaviours and increases in appetite and EI [21; 28; 30; 32; 35; 47; 51; 52; 53]. It appears that the strength of such signalling systems increases on going from the modest amounts typically seen during voluntary WL to the large amounts characteristic of semi-starvation [8; 28; 39; 40]. Thus, while WL is achievable in the short-to-medium term, there is a need to measure and understand the physiological resistance to WL and its impact on compensatory EB behaviours. This may inform behavioural strategies to prevent weight regain in the longer-term. However, EB behaviours are notoriously difficult to measure and the use of self-report dietary intake and physical activity estimates have been heavily criticised as methodologically flawed [54]. Almost all dietary intake and many physical activity measures have a large subjective component - they are self-reported by the subjects. A consensus statement of the Energy Balance Assessment Working Group highlights the flawed nature of self-report dietary intake methods and that the potential inaccuracies of self-report data make findings in many studies questionable, incorrect or misleading [54]. One answer to this problem will be to develop tracking technologies for estimation of EE from physical activity and energy storage from tracking of body weight over time, so that mathematical models can be refined to resolve the EB equation, enabling errors and uncertainty associated with self-report measures of EB behaviours to be appreciated.

While relatively few plausible physiological systems have been identified that may protect individuals from overconsumption, the asymmetry of EB regulation is a major factor that should be considered when designing behavioural interventions for longer-term weight management (i.e. WL and prevention of weight regain). This might seem like an obvious notion, but it is apparent that the majority of longer-term WL interventions decrease in intensity as the intervention progresses (i.e. greater intervention intensity is focused on the WL rather than the WLM phase). However, progression of a weight control intervention is associated with decreased adherence, lapse in the control of EB behaviours, increased dropout and hence weight regain, and as such it is more logical for intervention dose to be maintained or increase, rather than decrease, over time. Evidence supports an extended care approach, in which obesity is treated as a chronic disease requiring continuous therapist contact to prevent weight regain [55]. It is perhaps useful to consider the challenges that the physiology of EB regulation presents for behaviour change interventions for WL and WLM.

In simplistic terms the key challenges for longer-term weight management involve (i) engaging a significant proportion of the population in evidence-based behavioural approaches to WL, (ii) adapting behaviour change attempts to navigate around the physiological resistance to WL that undermines maintenance of WL, (iii) providing behavioural solutions to facilitate coping with lapses in the control of EB behaviours and relapses in weight and (v) finding methods to scale evidence-based solutions to longer-term weight management across the general population. These challenges are individually considerable and collectively daunting. The behavioural evidence for longer-term weight management is less robust than one might expect. The quantification of EB behaviours is inexact, making lapses difficult to detect. Several weight management solutions are scaled across the general population, with limited effect and (excluding drugs and surgery) the mechanisms of action remain unclear.

The effectiveness of behaviour change interventions for weight management

Weight loss

There is now considerable evidence documenting the effects of non-commercial and commercial behavioural, pharmacological or surgical interventions on initial WL [4; 5; 11; 45; 56; 57; 58; 59; 60; 61; 62; 63; 64; 65; 66]. Diet and lifestyle interventions produce mean WLs of <5kg after 2-4 years, which is disappointing compared to pharmacological therapies (mean WLs 5-10 kg over 1-2 years) and surgery (mean WLs of 25-75kg after 2-4 years) [67]. All of these approaches are subject to some degree of longer-term weight regain [56; 68].

Behavioural programmes have central elements of dietary restriction, behavioural counselling /support and physical activity advice (see below) [69]. But programmes vary in modes of delivery, settings, and implementation strategies [70]. Macronutrient composition of the diet seems relatively unimportant in terms of its impact on WL [11; 70]. A lower energy dense diet may be more efficacious for appetite control [71; 72], which may improve adherence during WL attempts. Evidence that high fibre or high protein diets may enhance satiety is inconsistent [73; 74]. Whether these are nutrient-specific effects that are completely independent of energy density is less clear [73].

Many evaluations of WL programmes now involve 1-year follow up [4; 11; 56; 59; 67]. Many trials of such programmes are characterised by high attrition, relatively short duration, lack of blinding and tend to report best-case scenarios (e.g. completer analyses or last observation carried forward analyses) [4]. For completers of non-surgical WL clinical trials mean WLs of 5-9% occur, plateau at ~6-12 months and gradually creep upwards between 24-48 months (where data is available) [56]. In

real-life settings a greater number of potential participants will not actually engage with the programme and outcomes may be more variable. Commercial programmes tend to produce slightly but significantly greater WL than non-commercial (e.g. primary care setting) programmes [59]. Performance of commercial weight management programmes is broadly comparable (Johnston 2014, Vakil 2016). In the US few community-based programmes meet the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society guideline for the management of overweight and obesity in adults [66]. Very low-calorie diets induce faster and greater WL but also faster and greater weight regain (Franz 2007; Gudzune 2015). Several analyses suggest that initial WL and programme attendance are important predictors of weight outcomes [75; 76; 77; 78; 79]. However, it seems that in real-life programmes (rather than clinical trials) average attendance is limited to 7-8 weeks and over a 12-month time window the vast majority of participants (>90%) drop out of such programmes [80]. Thus, for many these attempts are short in duration (days to weeks) and result in cessation of the behaviour changes that initiated the WL attempt and/or lead to subsequent weight regain.

Weight loss maintenance

There is debate as to whether WLM represents a separate behavioural phase to WL, requiring a different skills-set or whether it involves a continuation of the skills developed for WL in the first place [81] . There is evidence that some of the behaviours that lead to WL are continued during WLM, and that some additional behaviours are recruited during the period of WLM [82]. For this reason, it is useful to consider longer-term weight control as a dynamic interaction between behavioural strategies to lose weight, maintain that loss and the physiological (and environmental) resistance to WL, which creates a tonic pull on EB behaviours that can undermine the behaviours that achieved initial WL. It is more appropriate to view the transition from WL to WLM as a dynamic process. Those who lose weight are at high risk of weight regain. Given the limited effectiveness of diet and lifestyle programmes for WL most people who have engaged in an initial WL attempt are actually aiming to achieve further WL rather than WLM. Many people attempting to maintain their WL therefore experience periods where they re-visit strategies they originally used to lose weight, in order to cope with weight relapse or lose further weight. In this sense the study of WLM is something of a misnomer and would be better described as the study of weight regain prevention.

Studies aimed specifically at supporting WLM or longer-term weight management after a period of clinically significant WL are relatively few and have been systematically reviewed by Middleton, Ddouketis, Curioni, Neve and Ramage [55; 67; 83; 84; 85] and more recently and extensively by Dombrowski et al [86] and Varkevisser [87]. The majority of such studies usually involve a

continuation of interventions that are used for initial WL i.e. diet/lifestyle interventions (primarily diet) and/or use of pharmacological treatments (e.g. orlistat). While the majority of interventions aimed at producing or maintaining WL are, by design, complex, evidence of their specific behavioural mechanisms of action is limited. Almost all successful WL interventions reviewed by Ramage et al. combined elements of dietary restriction, physical activity advice and behaviour change approaches to support alterations in EB behaviours [85]. These involved standard or cognitive behavioural therapy, education on behavioural strategies delivered by a behavioural practitioner and self-monitoring (including self-weighing, social support, goal setting, stimulus control, relapse prevention strategies, problem solving and promoting intrinsic motivation). Successful WLM appears to involve a continuation of some or all of these strategies but it is unclear what differentiates those who maintain from those who regain.

While those who adhere to evidence-based weight management programmes can achieve significant WL, they appear to be the minority of those who initially engage in such programmes. For many, initial engagement in weight management programmes occurs in the backdrop of an obesogenic environment, which is relatively hostile to sustained WL attempts and presents risks for relapse. Many individuals experience frustrations and lapses, adherence to initial behaviour change becomes sporadic, weight control behaviours discontinue leading to weight relapse and regain. Repeated failed attempts at WL may decrease motivation, physical and emotional well-being (**FIGURE 2**).

Behavioural mechanisms of weight loss maintenance interventions

Behaviour change approaches for WL and WLM should be both theoretically informed and evidence-based in order to understand and target effective intervention components to the needs of specific individuals [88; 89; 90; 91]. There is currently more theory than clear evidence. It is unclear what specific behaviour change approaches, modes of delivery, settings, and implementation strategies are most effective for sustained change in EB behaviours. Behaviour change approaches for WLM might be undermined by compensatory changes in EE and EI as WL proceeds. This field is still poorly developed because the majority of studies examining predictors of longer-term weight outcomes have either used pre-treatment predictors [92; 93] or correlates of WL and maintenance, rather than sequential measures of outcomes throughout intervention and follow-up periods. Few/no studies have directly linked longitudinal changes in compensatory EB physiology and behaviour to mechanisms of action of behaviour change interventions. The current discussion focuses on the process of WLM given that pre-treatment predictors of WL tend to explain relatively little of subsequent weight outcomes [87; 92; 93] and WLM studies appear to focus on self-selected, non-representative samples [94; 95; 96; 97].

The majority of systematic reviews of WLM interventions find considerable heterogeneity between studies [86; 87; 98]. Many determinants of WLM are established by association rather than longitudinal change scores. Studies use different theoretical frameworks, constructs and measures [87]. A significant proportion report completer analyses e.g. [56]. For many specific predictors of long-term weight outcomes, the evidence is insufficient to reach a strong conclusion [87; 88; 98]. In the last few years evidence that self-regulation of weight control and EB behaviours improves longer-term weight outcomes has grown. Dombrowski et al have found in 45 studies that behavioural interventions targeting both diet and physical activity behaviours for WLM are moderately effective (~1.6 kg difference compared to control/placebo interventions) at promoting WLM over 1 year. There is some evidence of effectiveness over 2 years, and limited evidence relating to weight outcomes beyond 2 years[87; 88; 98]. They found no evidence that mode of intervention delivery (number of intervention components or frequency of contact, internet versus control or face-to-face versus remote delivery of the same intervention), for diet, physical activity or nutritional supplements/food replacements have a greater effect when used as interventions alone. Teixeira et al [98] have systematically reviewed 42 putative self-regulatory and psychological mechanisms as mediators of longer-term weight outcomes and EB behaviours across 35 behavioural interventions. They identified mediators of successful weight outcomes as higher autonomous motivation, self-efficacy/barriers, self-regulatory techniques, flexible restraint and positive body image. Mediators of sustained increases in physical activity were autonomous motivation, self-efficacy and use of self-regulatory skills. No mediators of long-term dietary intake were identified. In this analysis, weight change was empirically measured in 26 studies, but physical activity was objectively measured in only 4 of 19 studies and dietary intake was objectively measured in none of the 11 studies examining mediators/ predictors of dietary intake. Varkevisser et al. [87] have recently systematically reviewed 49 studies and evaluated 5 demographic, 59 behavioural, 51 psychological/cognitive and 9 social and environmental determinants of weight outcomes in observational, long-term WL and maintenance interventions. They found that aspects of self-regulation of eating, activity and weight control behaviours are effective for WLM, through their impact on change in behaviour during weight management attempts. This is important because pre-treatment predictors explain very little of the variance in WL [87; 92; 93].

The limited evidence from these meta-analyses suggests that navigating from initial WL to habitual WLM requires long-term self-management of EB behaviours in the face of physiological resistance to WL. Avoiding slow, gradual and the more pronounced weight regains require behavioural strategies in which relapse coping and WLM become learned skills of self-regulation, action planning, developing self-efficacy, autonomy and motivation [99; 100; 101; 102; 103; 104] as part of a longer-term process. Core features of modestly more effective WLM interventions include behaviour change

techniques that improve self-efficacy in self-monitoring (of weight and behaviour), relapse prevention, goal setting, and action plans for diet and physical activity [81; 86; 87; 90; 98; 99; 105]. Autonomous self-regulation and intrinsic motivation may augment self-regulatory goals and self-efficacy [92; 101; 105; 106]. However, physical activity and dietary interventions based on current behaviour change theories characteristically achieve relatively small effects on weight outcomes, in the region of ~1.5 kg compared to controls. This is disappointing and there is considerable interest in improving the effectiveness of such interventions. This could be achieved by greater standardisation of predictive constructs and outcome measures that are tracked longitudinally to improve cause-effect models, by providing more accurate objective tracking of EB behaviors, to facilitate self-monitoring and improve analyses of the mechanism of action of behavior change interventions for weight management. This in turn may lead to personalised intervention content and delivery to meet individual needs and improve weight outcomes.

Historically, behaviour change models have focused on social cognition (e.g., beliefs, intentions, attitudes and decisions), emphasising pathways of reasoned action in which pre-decisional motivation leads to the formation of intentions and the implementation of intentions as volitional action [107; 108]. It is also believed that automatic processes (emotions, desires, habits resulting from associative learning and physiological states) may also have a large impact on behaviour and behaviour change. These processes tend to be relatively rapid, impulsive (less conscious) and habitual in comparison to the slow, deliberative processes of motivation and self-regulation[109; 110]. Furthermore, in the context EB behaviours, the development of self-regulatory behaviour change is effortful, particularly in the face of physiological resistance to WL, while unconscious or automatic components of EB behaviours are rapid and effortless [111]. Such processes may have considerable capacity to undermine initial self-regulation of EB behaviours (particularly eating behaviours) in the face of a physiological system that resists longer-term WL [111]. Physiological mediators of homeostatic and hedonic appetitive drives, and changes in physical activity that are triggered by WL may feed into such automatic process of behaviour change to undermine self-regulation of EB behaviours. These concepts are depicted in **Figure 3**, which is an adaptation of Witkiewitz and Marlett's (2004) relapse model [112]. Automatic components of self-regulation may also promote longer-term behaviour change if they are engaged and developed.

Another aspect of automaticity potentially affecting EB behaviours is distress tolerance and emotion regulation. Individuals trying to lose weight can experience increased psychosocial stress and weight-related stigma, [113; 114; 115] which may undermine self-regulatory practices and weight loss attempts. Repeated attempts at WL followed by weight regain can have a negative emotional impact, leading

to self-critical thoughts and negative emotions. For some, 'comfort eating' may be a means of coping with these negative experiences, potentially derailing strategies of planned behaviour [116; 117; 118; 119; 120]. Contextual-behavioural approaches to WL and WLM suggest that specific skills could be developed to promote self-regulation and to prevent relapse [121]. These include mindfulness and cognitive awareness of automaticity, behavioural commitment with personally-relevant values, and acceptance of internal negative or aversive states (e.g., negative emotions or cognitions) [121; 122; 123; 124]. Mindfulness and acceptance-based interventions, which are one attempt to address difficulties in emotion regulation, show modest promise in changing obesity-related eating behaviours (e.g., binge eating and emotional eating) and improving weight management [121]. Augmenting current self-regulatory approaches with components that help manage weight-related emotions could potentially lead to more effective WLM.

Developing more effective, personalised interventions for longer-term weight management.

There is some evidence that aspects of self-regulation and motivation may improve the odds of sustaining changes in EB behaviours and if those changes become automatic in the longer-term the chances of preventing weight regain may improve. However, it is likely that automatic processes (emotions, desires, appetitive drives and habits resulting from associative learning and physiological resistance to WL) are powerful forces that can undermine the relatively transient and fragile attempts at changing EB behaviours during phase 1 and 2 of WL. It is perhaps in this dynamic transition where we need to better understand the interplay between physiology and behaviour to improve longer-term weight management and the prevention of weight regain. Key areas where there is a need to develop new evidence to inform behaviour change interventions are detailed below.

There is an urgent need to understand the relationship between WL-induced EB physiology and compensatory changes in EB behaviour that appear to collectively drive weight regain. At present this endeavour is hampered by the fact that EB behaviours are extremely difficult to measure. Measurement of EI and EE in free-living subjects (with the exception of doubly-labelled water) usually relies on self-report measures that are known to be unreliable [54]. Furthermore, it is likely that significant components of EB behaviours are automatic and therefore extremely difficult to measure using self-report methods. Given the apparent unreliability of self-report measures of EI and EE, development of objective tracking technologies would enable better quantification of EI and EE. Numerous tracking devices are available to estimate physical activity but the relationship between such measurements and estimates of EE is uncertain [125]. Such devices have the advantage of being cost-effective, objective, unobtrusive and capable of considerable data storage and aggregation.

However, such devices are limited by their lack of accuracy [125]. It is important to bridge the gap between the tracking of physical activity and estimates of free-living EE. Accurate tracking of EE and body weight would allow approximate estimates of changes in EB and its components. Such developments would provide a major leap forward in longitudinal estimates of EB behaviours and their relative contribution to altered states of EB. Such methodological developments would potentially provide the quantitative framework on which behaviour change interventions for longer-term self-management of body weight could be based. Objective quantification of EI and EE would help us understand and better use self-reported psychological and behavioural factors. Longer-term weight management interventions should be designed around the known compensatory physiological responses to WL and developing approaches to tracking EB behaviours is a critical gap that needs to be addressed in improving future interventions.

There is currently a gap between detailed, small-scale physiological studies of WL and the larger scale interventions that seek to understand mechanisms of action of behaviour change approaches[51]. Such behavioural studies tend to ignore both physiological resistance to WL and compensation of EB behaviours. It is important to improve our understanding of the mechanisms by which WL facilitates subsequent weight regain as a context in which behaviour change interventions attempt to operate. The use of mathematical modelling represents a major advance in estimating the contribution of EI and EE to longer-term weight outcomes [17; 18; 19; 21; 22; 27]. Current models assume a level of physical activity EE and estimate change in body energy stores from changes in body weight or composition. If two of the three components of the EB equation and known (change in EE and energy stores) the third (EI) can be estimated by difference. These models could be refined if mobile tracking technologies can improve estimates of free-living EE.

There is a need to develop longitudinal interventions using logic models based on theoretically informed, evidence-based intervention content, employing repeat measures of components of EB (e.g. physical activity, weight) tracked over the course of WL attempts, so that cause-effect relationship can be established to better understand the mechanisms of action of behaviour change interventions. Such interventions should also, where possible, examine user interactions with intervention content. Given the evidence reviewed above it is likely that such secondary analyses will yield critical information about who responds to certain intervention components and how those components affect EB behaviours, to inform personalised interventions in the future. If the typical effect sizes produced by multi-component interventions is small, personalisation of such interventions, by better matching evidence-based behaviour change content to the specific needs of individuals may improve longer-term weight outcomes.

Greater standardisation of predictive constructs and outcome measures, in clearly defined study populations, tracked longitudinally, would improve cause-effect models that characterise (i) how WL impacts on body structure, function and subsequent EB behaviours, (ii) how behaviour change approaches can overcome physiological resistance to WL and (ii) who is likely to maintain WL or relapse (**Figure 4**). Modelling physiological and psychological moderators and mediators of EB-related behaviours is central to understanding and improving longer-term weight and health outcomes in the general population. Improved measurement of EB and associated behaviours may help us bring together research on physiological and behavioural responses to energy deficits, better understand the factors that lead to weight regain and help people navigate more effectively to sustained changes in their weight and health outcomes.

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Conflict of Interest

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Table 1: Estimated changes in TEE and its components in response to prolonged semi-starvation in the Minnesota study. The decrease in basal metabolic rate was 65% due to change in metabolically active tissues and 35% due to metabolic adaptation. The decrease in physical activity was 36% due to the energy cost of physical activity and 64% due to a change in physical activity behaviour. The total estimated decrease in daily energy expenditure after 6 months semi-starvation was 45% of baseline daily energy expenditure.

Energy expenditure (MJ/d)	Baseline (MJ/d)	Decrease at 24 weeks semi-starvation (MJ/d)
Diet-induced thermogenesis	1.4	0.8
Basal metabolic rate	6.7	2.6
Physical Activity	6.5	4.6
Total	14.6	8.0

566 **Figures**

567

568 **Figure 1**: Schematic diagram illustrating how initial body composition, rate and extent of weight loss
569 can affect the proportion of fat (green curve) and fat free mass (red curve) lost (percent fat free mass
570 loss is greater at higher rate, extent and lower initial fat mass), the impact of these changes in body
571 structure on physiological functions (fat mass, green lines; fat free mass, red lines) and their likely
572 impact on energy balance behaviours. Behaviour change interventions attempt to override the
573 compensatory EB behaviours that resist weight loss. Physiological and behavioural responses occur
574 throughout the process of weight loss and are likely to escalate on going from stages one through two
575 of weight loss.
576 Note: Proportionate body composition changes are given for overweight subjects assigned to caloric
577 restriction and very low-calorie diets, achieving 10-14% weight loss from Heymsfield et al. [13]. The
578 proportion of fat and fat free mass lost would vary with initial body composition, rate and extent of
579 weight loss.

580

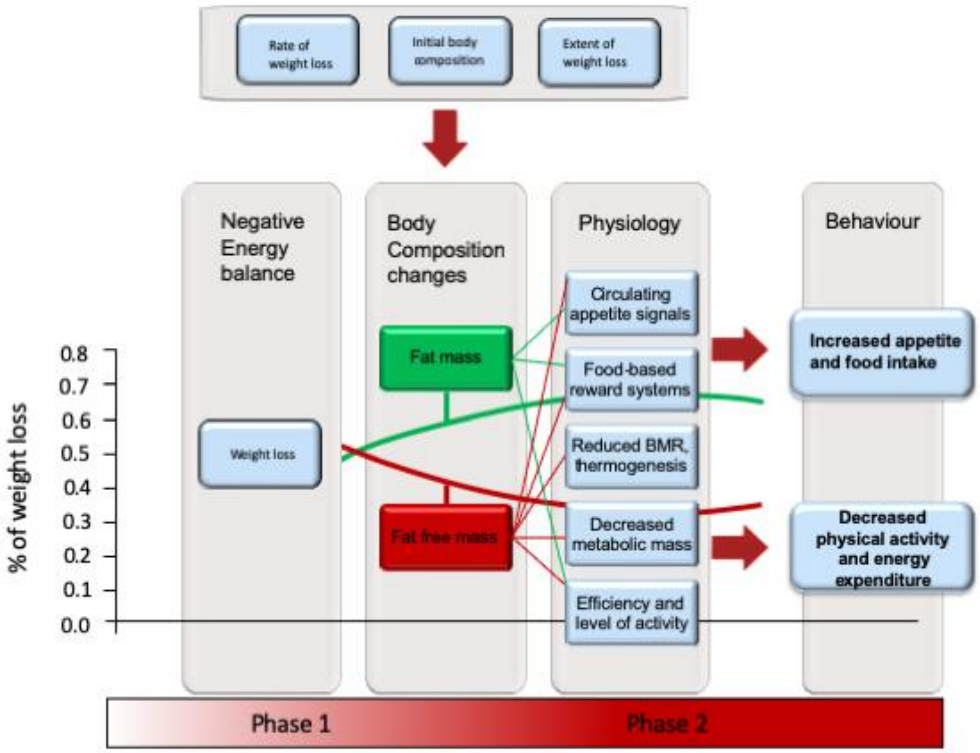
581 **Figure 2**: The cycle of weight loss and weight relapse. The left side indicating the pathways by which
582 weight loss attempts are opposed by both an obesogenic environment and physiological resistance to
583 weight loss. The right side illustrating how better matching behaviour change approaches to tracking
584 of EB behaviours may facilitate rapid monitoring and adjustments of energy intake to help avoid
585 weight regain.

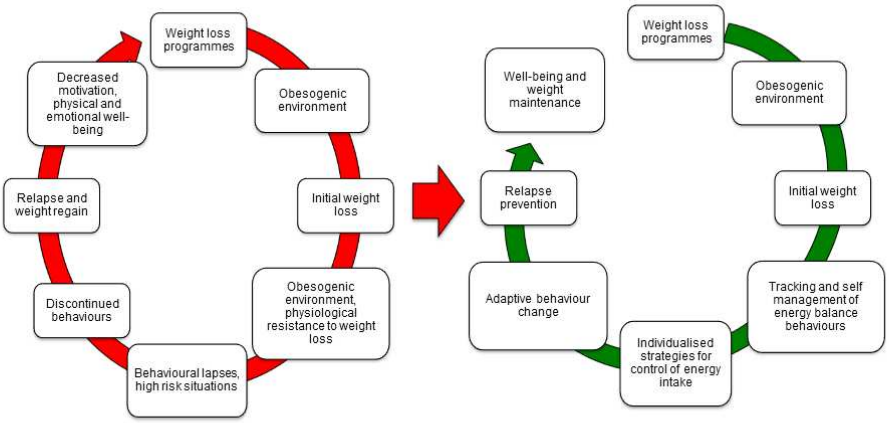
586

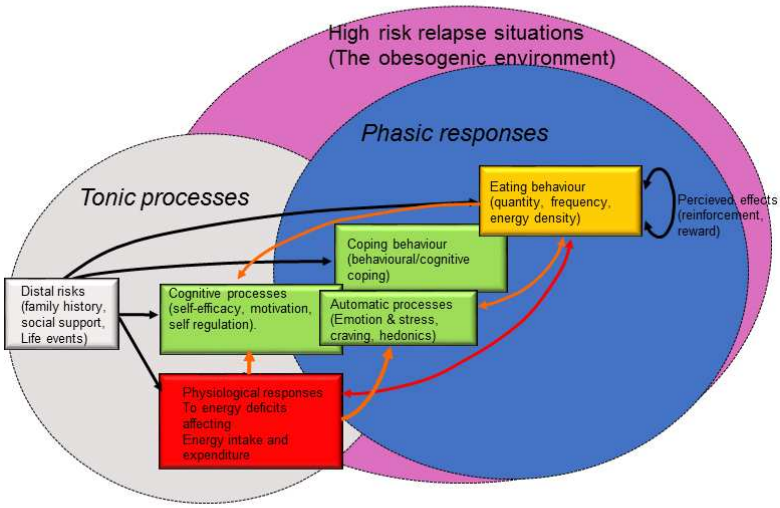
587 **Figure 3**: An adaptation of Witkiewitz and Marlett's relapse prevention model [112] focusing on the
588 factors that influence relaxation of controlled eating behavior during a weight loss attempt. Energy
589 intake appears to be a quantitatively more important route for weight regain and is likely to be the
590 most promising target for prevention of weight relapse during weight loss attempts, in the context of
591 tracking EB and its components.

592

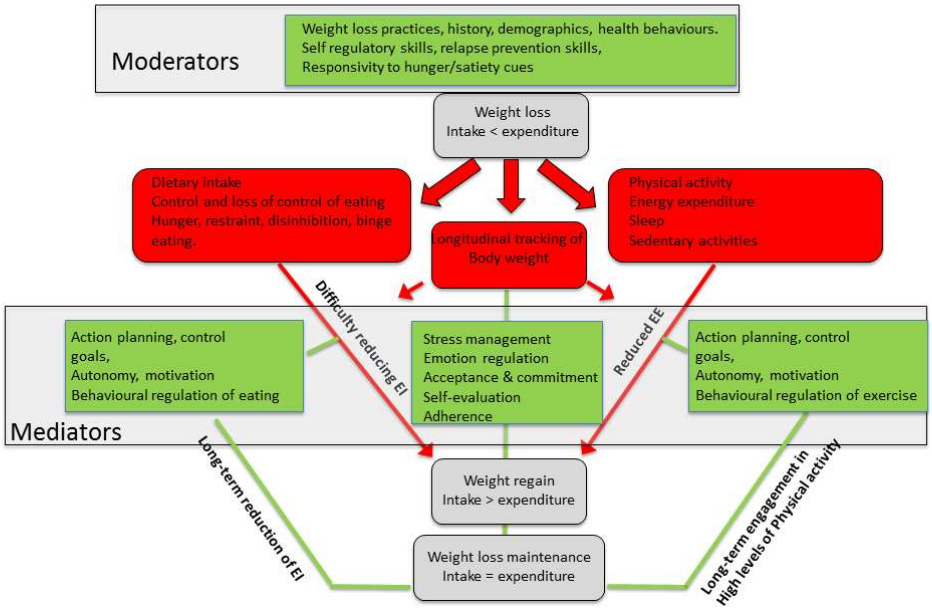
593 **Figure 4**: Illustration of how the NIH conceptual framework [51] for weight loss maintenance can be
594 adapted to develop cause-effect models that characterise how WL impacts on body structure, function
595 and EB behaviours, how behaviour change approaches can mediate physiological resistance to WL
596 and who is likely to maintain or regain weight lost.


Rate of weight loss
Initial body composition
Extent of weight loss
Negative Energy balance
Body Composition changes
Physiology
Behaviour
Weight loss
Fat mass
Fat free mass
Circulating appetite signals
Food-based reward systems
Reduced BMR, thermogenesis
Decreased metabolic mass
Efficiency and level of activity
Increased appetite and food intake
Decreased physical activity and energy expenditure
% of weight loss
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Phase 1
Phase 2


Weight loss programmes
Obesogenic environment
Initial weight loss
Obesogenic environment, physiological resistance to weight loss
Behavioural lapses, high risk situations
Discontinued behaviours
Relapse and weight regain
Decreased motivation, physical and emotional well-being
Well-being and weight maintenance
Relapse prevention
Adaptive behaviour change
Individualised strategies for control of energy intake
Tracking and self management of energy balance behaviours



Adapted from Witkiewitz K, Marlett GA. American Psychologist 2004; 59:224-235



References

1. World Health Organisation (2017) *The double burden of malnutrition policy brief*. Geneva: World Health Organisation.

2. Shrimpton R, Rokx C (2012) *The double burden of malnutrition : a review of global evidence Health, Nutrition and Population (HNP) discussion paper*. Washington DC: World Bank.

3. Craig P, Dieppe P, Macintyre S *et al.* (2008) Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* **337**, a1655.

4. Gudzune KA, Doshi RS, Mehta AK *et al.* (2015) Efficacy of commercial weight-loss programs: an updated systematic review. *Annals of internal medicine* **162**, 501-512.

5. Vakil RM, Chaudhry ZW, Doshi RS *et al.* (2017) Commercial Programs' Online Weight-Loss Claims Compared to Results from Randomized Controlled Trials. *Obesity (Silver Spring)* **25**, 1885-1893.

6. Santos I, Sniehotta FF, Marques MM *et al.* (2017) Prevalence of personal weight control attempts in adults: a systematic review and meta-analysis. *Obes Rev* **18**, 32-50.

7. Wing RR, Phelan S (2005) Long-term weight loss maintenance. *Am J Clin Nutr* **82(suppl)**, 222S–225S.

8. Stubbs RJ, Hopkins M, Finlayson GS *et al.* (2018) Potential effects of fat mass and fat-free mass on energy intake in different states of energy balance. *Eur J Clin Nutr* **72**, 698-709.

9. Swinburn BA, Sacks G, Hall KD *et al.* (2011) The global obesity pandemic: shaped by global drivers and local environments. *Lancet* **378**, 804-814.

10. Sainsbury K, Evans EH, Pedersen S *et al.* (2018) Attribution of weight regain to emotional reasons amongst European adults with overweight and obesity who regained weight following a weight loss attempt. *Eat Weight Disord*.
11. Johnston BC, Kanters S, Bandayrel K *et al.* (2014) Comparison of weight loss among named diet programs in overweight and obese adults: a meta-analysis. *Jama* **312**, 923-933.
12. Sniehotta FF, Simpson SA, Greaves CJ (2014) Weight loss maintenance: An agenda for health psychology. *British journal of health psychology* **19**, 459-464.
13. Heymsfield S, Thomas D, Nguyen A *et al.* (2011) Voluntary weight loss: systematic review of early phase body composition changes. *obesity reviews* **12**, e348-e361.
14. Heymsfield SB, Gonzalez MC, Shen W *et al.* (2014) Weight loss composition is one-fourth fat-free mass: a critical review and critique of this widely cited rule. *Obesity Reviews* **15**, 310-321.
15. Mela DJ, Rogers PJ (2013) *Food, eating and obesity: The psychobiological basis of appetite and weight control*: Springer.
16. Stubbs R, Tolkamp B (2006) Control of energy balance in relation to energy intake and energy expenditure in animals and man: an ecological perspective. *British Journal of Nutrition* **95**, 657-676.
17. Thomas DM, Schoeller DA, Redman LA *et al.* (2010) A computational model to determine energy intake during weight loss. *The American journal of clinical nutrition* **92**, 1326-1331.
18. Hall KD, Sacks G, Chandramohan D *et al.* (2011) Quantification of the effect of energy imbalance on bodyweight. *The Lancet* **378**, 826-837.
19. Thomas DM, Martin CK, Redman LM *et al.* (2014) Effect of dietary adherence on the body weight plateau: a mathematical model incorporating intermittent compliance with energy intake prescription. *The American journal of clinical nutrition* **100**, 787-795.
20. Ferrannini G, Hach T, Crowe S *et al.* (2015) Energy balance after sodium–glucose cotransporter 2 inhibition. *Diabetes Care* **38**, 1730-1735.
21. Polidori D, Sanghvi A, Seeley RJ *et al.* (2016) How strongly does appetite counter weight loss? Quantification of the feedback control of human energy intake. *Obesity* **24**, 2289-2295.
22. Hall KD, Sanghvi A, Göbel B (2017) Proportional feedback control of energy intake during obesity pharmacotherapy. *Obesity* **25**, 2088-2091.
23. Chaston T, Dixon J (2008) Factors associated with percent change in visceral versus subcutaneous abdominal fat during weight loss: findings from a systematic review. *International journal of obesity* **32**, 619.
24. Hall KD, Hallgreen CE (2008) Increasing weight loss attenuates the preferential loss of visceral compared with subcutaneous fat: a predicted result of an allometric model. *International Journal of Obesity* **32**, 722.

663 25. Hall KD (2007) Body fat and fat-free mass inter-relationships: Forbes's theory revisited. *Br J Nutr*
664 **97**, 1059-1063.
665 26. Hall KD (2010) Mechanisms of metabolic fuel selection: modeling human metabolism and body-
666 weight change. *IEEE Eng Med Biol Mag* **29**, 36-41.
667 27. Hall KD (2010) Predicting metabolic adaptation, body weight change, and energy intake in
668 humans. *Am J Physiol Endocrinol Metab* **298**, E449-466.
669 28. Keys A, Brožek J, Henschel A *et al.* (1951) *The Biology of Human Starvation*. vol. 1.
670 Minneapolis: The University of Minnesota Press.
671 29. Redman LM, Heilbronn LK, Martin CK *et al.* (2009) Metabolic and behavioral compensations in
672 response to caloric restriction: implications for the maintenance of weight loss. *PLoS One* **4**, e4377.
673 30. Leibel RL, Rosenbaum M, Hirsch J (1995) Changes in energy expenditure resulting from altered
674 body weight. *N Engl J Med* **332**, 621-628.
675 31. Martin CK, Heilbronn LK, de Jonge L *et al.* (2007) Effect of calorie restriction on resting
676 metabolic rate and spontaneous physical activity. *Obesity (Silver Spring)* **15**, 2964-2973.
677 32. Schwartz A, Kuk JL, Lamothe G *et al.* (2012) Greater than predicted decrease in resting energy
678 expenditure and weight loss: results from a systematic review. *Obesity (Silver Spring)* **20**, 2307-2310.
679 33. Goldsmith R, Joanisse DR, Gallagher D *et al.* (2010) Effects of experimental weight perturbation
680 on skeletal muscle work efficiency, fuel utilization, and biochemistry in human subjects. *Am J Physiol*
681 *Regul Integr Comp Physiol* **298**, R79-88.
682 34. Fothergill E, Guo J, Howard L *et al.* (2016) Persistent metabolic adaptation 6 years after "The
683 Biggest Loser" competition. *Obesity* **24**, 1612-1619.
684 35. Rosenbaum M, Hirsch J, Gallagher DA *et al.* (2008) Long-term persistence of adaptive
685 thermogenesis in subjects who have maintained a reduced body weight. *Am J Clin Nutr* **88**, 906-912.
686 36. Westerterp K.R. (2013) Metabolic adaptations to over—and underfeeding—still a matter of
687 debate? *European Journal of Clinical Nutrition* **67**, 443–445.
688 37. Johannsen DL, Knuth ND, Huizenga R *et al.* (2012) Metabolic slowing with massive weight loss
689 despite preservation of fat-free mass. *The Journal of Clinical Endocrinology & Metabolism* **97**, 2489-
690 2496.
691 38. Hall KD (2013) Diet versus exercise in "the biggest loser" weight loss competition. *Obesity* **21**,
692 957-959.
693 39. Widdowson E (1951) Studies of undernutrition, Wuppertal 1946-9. XXVII. The response to
694 unlimited food. *Special report series (Medical Research Council (Great Britain))* **275**, 313.
695 40. Murray R (1947) Recovery from starvation. *Lancet* **252**, 507-511.

41. Müller MJ, Enderle J, Pourhassan M *et al.* (2015) Metabolic adaptation to caloric restriction and subsequent refeeding: the Minnesota Starvation Experiment revisited. *The American journal of clinical nutrition* **102**, 807-819.
42. Doucet E, Cameron J (2007) Appetite control after weight loss: what is the role of bloodborne peptides? *Appl Physiol Nutr Metab* **32**, 523-532.
43. Sumithran P, Prendergast LA, Delbridge E *et al.* (2011) Long-term persistence of hormonal adaptations to weight loss. *New England Journal of Medicine* **365**, 1597-1604.
44. Nymo S, Coutinho S, Eknes P *et al.* (2018) Investigation of the long-term sustainability of changes in appetite after weight loss. *International Journal of Obesity* **42**, 1489.
45. Anton S, Han H, York E *et al.* (2009) Effect of calorie restriction on subjective ratings of appetite. *Journal of human nutrition and dietetics* **22**, 141-147.
46. Andriessen C, Christensen P, Nielsen LV *et al.* (2018) Weight loss decreases self-reported appetite and alters food preferences in overweight and obese adults: Observational data from the DiOGenes study. *Appetite* **125**, 314-322.
47. Hintze LJ, Mahmoodianfard S, Auguste CB *et al.* (2017) Weight loss and appetite control in women. *Current obesity reports* **6**, 334-351.
48. Sanghvi A, Redman LM, Martin CK *et al.* (2015) Validation of an inexpensive and accurate mathematical method to measure long-term changes in free-living energy intake. *The American journal of clinical nutrition* **102**, 353-358.
49. Iepsen EW, Lundgren J, Holst JJ *et al.* (2016) Successful weight loss maintenance includes long-term increased meal responses of GLP-1 and PYY3–36. *European journal of endocrinology* **174**, 775-784.
50. Sainsbury A, Wood R, Seimon R *et al.* (2018) Rationale for novel intermittent dieting strategies to attenuate adaptive responses to energy restriction. *Obesity Reviews* **19**, 47-60.
51. MacLean PS, Wing RR, Davidson T *et al.* (2015) NIH working group report: innovative research to improve maintenance of weight loss. *Obesity* **23**, 7-15.
52. Dulloo AG, Jacquet J, Miles-Chan JL *et al.* (2017) Passive and active roles of fat-free mass in the control of energy intake and body composition regulation. *Eur J Clin Nutr* **71**, 353-357.
53. Greenway F (2015) Physiological adaptations to weight loss and factors favouring weight regain. *International journal of obesity* **39**, 1188.
54. Dhurandhar NV, Schoeller D, Brown AW *et al.* (2015) Energy balance measurement: when something is not better than nothing. *International journal of obesity* **39**, 1109.
55. Ross Middleton K, Patidar S, Perri M (2012) The impact of extended care on the long-term maintenance of weight loss: a systematic review and meta-analysis. *Obesity reviews* **13**, 509-517.

730 56. Franz MJ, VanWormer JJ, Crain AL *et al.* (2007) Weight-loss outcomes: a systematic review and
731 meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *Journal of the*
732 *American Dietetic Association* **107**, 1755-1767.
733 57. Gloy VL, Briel M, Bhatt DL *et al.* (2013) Bariatric surgery versus non-surgical treatment for
734 obesity: a systematic review and meta-analysis of randomised controlled trials. *Bmj* **347**, f5934.
735 58. Greaves CJ, Sheppard KE, Abraham C *et al.* (2011) Systematic review of reviews of intervention
736 components associated with increased effectiveness in dietary and physical activity interventions.
737 *BMC public health* **11**, 119.
738 59. Jolly K, Lewis A, Beach J *et al.* (2011) Comparison of range of commercial or primary care led
739 weight reduction programmes with minimal intervention control for weight loss in obesity: Lighten
740 Up randomised controlled trial. *Bmj* **343**, d6500.
741 60. Khera R, Murad MH, Chandar AK *et al.* (2016) Association of pharmacological treatments for
742 obesity with weight loss and adverse events: a systematic review and meta-analysis. *Jama* **315**, 2424-
743 2434.
744 61. Kirk S, Penney T, McHugh T-L *et al.* (2012) Effective weight management practice: a review of
745 the lifestyle intervention evidence. *International journal of obesity* **36**, 178.
746 62. LeBlanc ES, O'connor E, Whitlock EP *et al.* (2011) Effectiveness of primary care–relevant
747 treatments for obesity in adults: a systematic evidence review for the US Preventive Services Task
748 Force. *Annals of internal medicine* **155**, 434-447.
749 63. Madigan CD, Daley AJ, Lewis AL *et al.* (2014) Which weight-loss programmes are as effective
750 as Weight Watchers®?: non-inferiority analysis. *Br J Gen Pract* **64**, e128-e136.
751 64. Norris SL, Zhang X, Avenell A *et al.* (2005) Long-term non-pharmacological weight loss
752 interventions for adults with prediabetes. *Cochrane database of systematic reviews*.
753 65. O'Brien PE, Hindle A, Brennan L *et al.* (2019) Long-Term Outcomes After Bariatric Surgery: a
754 Systematic Review and Meta-analysis of Weight Loss at 10 or More Years for All Bariatric
755 Procedures and a Single-Centre Review of 20-Year Outcomes After Adjustable Gastric Banding.
756 *Obesity surgery* **29**, 3-14.
757 66. Vakil RM, Doshi RS, Mehta AK *et al.* (2016) Direct comparisons of commercial weight-loss
758 programs on weight, waist circumference, and blood pressure: a systematic review. *BMC public*
759 *health* **16**, 460.
760 67. Douketis J, Macie C, Thabane L *et al.* (2005) Systematic review of long-term weight loss studies
761 in obese adults: clinical significance and applicability to clinical practice. *International journal of*
762 *obesity* **29**, 1153.
763 68. Magro DO, Geloneze B, Delfini R *et al.* (2008) Long-term weight regain after gastric bypass: a
764 5-year prospective study. *Obesity surgery* **18**, 648-651.

765 69. Loveman E, Frampton G, Shepherd J *et al.* (2011) The clinical effectiveness and cost-
766 effectiveness of long-term weight management schemes for adults: a systematic review. In *NIHR*
767 *Health Technology Assessment programme: Executive Summaries*: NIHR Journals Library.
768 70. Jensen MD, Ryan DH, Apovian CM *et al.* (2014) 2013 AHA/ACC/TOS guideline for the
769 management of overweight and obesity in adults: a report of the American College of
770 Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society.
771 *Journal of the American college of cardiology* **63**, 2985-3023.
772 71. Buckland NJ, Camidge D, Croden F *et al.* (2018) A Low Energy–Dense Diet in the Context of a
773 Weight-Management Program Affects Appetite Control in Overweight and Obese Women. *The*
774 *Journal of nutrition* **148**, 798-806.
775 72. Ello-Martin JA, Roe LS, Ledikwe JH *et al.* (2007) Dietary energy density in the treatment of
776 obesity: a year-long trial comparing 2 weight-loss diets. *Am J Clin Nutr* **85**, 1465-1477.
777 73. Benelam B (2009) Satiation, satiety and their effects on eating behaviour. *Nutrition bulletin* **34**,
778 126-173.
779 74. Slavin J, Green H (2007) Dietary fibre and satiety. *Nutrition Bulletin* **32**, 32-42.
780 75. Astrup A, Rössner S (2000) Lessons from obesity management programmes: greater initial weight
781 loss improves long-term maintenance. *obesity reviews* **1**, 17-19.
782 76. Ortner Hadžiabdić M, Mucalo I, Hrabač P *et al.* (2015) Factors predictive of drop-out and weight
783 loss success in weight management of obese patients. *Journal of human nutrition and dietetics* **28**,
784 24-32.
785 77. Rissanen A, Lean M, Rössner S *et al.* (2003) Predictive value of early weight loss in obesity
786 management with orlistat: an evidence-based assessment of prescribing guidelines. *International*
787 *journal of obesity* **27**, 103.
788 78. Smith SR, O'Neil PM, Astrup A *et al.* (2014) Early weight loss while on lorcaserin, diet and
789 exercise as a predictor of week 52 weight-loss outcomes. *Obesity* **22**, 2137-2146.
790 79. Stotland S, Larocque M (2005) Early treatment response as a predictor of ongoing weight loss in
791 obesity treatment. *British journal of health psychology* **10**, 601-614.
792 80. Martin CK, Talamini L, Johnson A *et al.* (2010) Weight loss and retention in a commercial
793 weight-loss program and the effect of corporate partnership. *International Journal of Obesity* **34**, 742.
794 81. Stubbs R, Lavin J (2013) The challenges of implementing behaviour changes that lead to
795 sustained weight management. *Nutrition Bulletin* **38**, 5-22.
796 82. Sciamanna CN, Kiernan M, Rolls BJ *et al.* (2011) Practices associated with weight loss versus
797 weight-loss maintenance: results of a national survey. *American journal of preventive medicine* **41**,
798 159-166.

83. Curioni C, Lourenco P (2005) Long-term weight loss after diet and exercise: a systematic review. *International journal of obesity* **29**, 1168.
84. Neve M, Morgan PJ, Jones P *et al.* (2010) Effectiveness of web-based interventions in achieving weight loss and weight loss maintenance in overweight and obese adults: a systematic review with meta-analysis. *Obesity reviews* **11**, 306-321.
85. Ramage S, Farmer A, Apps Eccles K *et al.* (2013) Healthy strategies for successful weight loss and weight maintenance: a systematic review. *Applied Physiology, Nutrition, and Metabolism* **39**, 1-20.
86. Dombrowski SU, Knittle K, Avenell A *et al.* (2014) Long term maintenance of weight loss with non-surgical interventions in obese adults: systematic review and meta-analyses of randomised controlled trials. *Bmj* **348**, g2646.
87. Varkevisser R, van Stralen M, Kroeze W *et al.* (2019) Determinants of weight loss maintenance: a systematic review. *Obesity Reviews* **20**, 171-211.
88. Dombrowski SU, Sniehotta FF, Avenell A *et al.* (2012) Identifying active ingredients in complex behavioural interventions for obese adults with obesity-related co-morbidities or additional risk factors for co-morbidities: a systematic review. *Health Psychology Review* **6**, 7-32.
89. Hartmann-Boyce J, Johns D, Jebb S *et al.* (2014) Effect of behavioural techniques and delivery mode on effectiveness of weight management: systematic review, meta-analysis and meta-regression. *obesity reviews* **15**, 598-609.
90. Michie S, Abraham C, Whittington C *et al.* (2009) Effective techniques in healthy eating and physical activity interventions: a meta-regression. *Health Psychology* **28**, 690.
91. Michie S, Richardson M, Johnston M *et al.* (2013) The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Annals of behavioral medicine* **46**, 81-95.
92. Carraça EV, Santos I, Mata J *et al.* (2018) Psychosocial Pretreatment Predictors of Weight Control: A Systematic Review Update. *Obesity facts* **11**, 67-82.
93. Teixeira P, Going SB, Houtkooper L *et al.* (2004) Pretreatment predictors of attrition and successful weight management in women. *International journal of obesity* **28**, 1124.
94. Butryn ML, Phelan S, Hill JO *et al.* (2007) Consistent self-monitoring of weight: a key component of successful weight loss maintenance. *Obesity* **15**, 3091-3096.
95. LaRose JG, Leahey TM, Hill JO *et al.* (2013) Differences in motivations and weight loss behaviors in young adults and older adults in the National Weight Control Registry. *Obesity* **21**, 449-453.
96. Ogden LG, Stroebele N, Wyatt HR *et al.* (2012) Cluster analysis of the national weight control registry to identify distinct subgroups maintaining successful weight loss. *Obesity* **20**, 2039-2047.

834 97. Thomas JG, Bond DS, Phelan S *et al.* (2014) Weight-loss maintenance for 10 years in the National
835 Weight Control Registry. *American journal of preventive medicine* **46**, 17-23.
836 98. Teixeira PJ, Carraça EV, Marques MM *et al.* (2015) Successful behavior change in obesity
837 interventions in adults: a systematic review of self-regulation mediators. *BMC medicine* **13**, 84.
838 99. Dombrowski SU, Avenell A, Sniehott FF (2010) Behavioural interventions for obese adults with
839 additional risk factors for morbidity: systematic review of effects on behaviour, weight and disease
840 risk factors. *Obes Facts* **3**, 377-396.
841 100. Teixeira PJ, Carraca EV, Markland D *et al.* (2012) Exercise, physical activity, and self-
842 determination theory: a systematic review. *Int J Behav Nutr Phys Act* **9**, 78.
843 101. Teixeira PJ, Mata J, Williams GC *et al.* (2012) Self-regulation, motivation, and psychosocial
844 factors in weight management. *J Obes* **2012**, 582348.
845 102. Maes S, Karoly P (2005) Self-Regulation Assessment and Intervention in Physical Health and
846 Illness: A Review. *Applied Psychology* **54**, 267-299.
847 103. Sniehotta FF, Schwarzer, R., Scholz, U., Schüz, B., (2005) Action planning and coping
848 planning for long-term lifestyle change: theory and assessment. *Eur J Soc Psychol* **35**, 565-576.
849 104. Larimer ME, Palmer RS, Marlatt GA (1999) Relapse prevention. An overview of Marlatt's
850 cognitive-behavioral model. *Alcohol Res Health* **23**, 151-160.
851 105. Silva MN, Markland D, Carraça EV *et al.* (2011) Using self-determination theory to promote
852 physical activity and weight control: A randomized controlled trial in women. *J Behav Med* **33**, 110-
853 122.
854 106. Verstuyf J, Patrick H, Vansteenkiste M *et al.* (2012) Motivational dynamics of eating regulation:
855 a self-determination theory perspective. *Int J Behav Nutr Phys Act* **9**, 21.
856 107. Armitage CJ, Conner M (2000) Social cognition models and health behaviour: A structured
857 review. *Psychology and health* **15**, 173-189.
858 108. Sniehotta FF (2009) Towards a theory of intentional behaviour change: Plans, planning, and
859 self-regulation. *British journal of health psychology* **14**, 261-273.
860 109. Gibbons FX, Houlihan AE, Gerrard M (2009) Reason and reaction: The utility of a dual-focus,
861 dual-processing perspective on promotion and prevention of adolescent health risk behaviour. *British*
862 *journal of health psychology* **14**, 231-248.
863 110. Hofmann W, Friese M, Strack F (2009) Impulse and self-control from a dual-systems
864 perspective. *Perspectives on psychological science* **4**, 162-176.
865 111. Bargh JA, Chartrand TL (1999) The unbearable automaticity of being. *American psychologist*
866 **54**, 462.
867 112. Witkiewitz K, Marlatt GA (2004) Relapse prevention for alcohol and drug problems: that was
868 Zen, this is Tao. *American Psychologist* **59**, 224.

869 113. Carr D, Friedman MA (2005) Is obesity stigmatizing? Body weight, perceived discrimination,
870 and psychological well-being in the United States. *Journal of health and social behavior* **46**, 244-
871 259.
872 114. O'Brien KS, Latner JD, Puhl RM *et al.* (2016) The relationship between weight stigma and eating
873 behavior is explained by weight bias internalization and psychological distress. *Appetite* **102**, 70-76.
874 115. Puhl RM, Brownell KD (2006) Confronting and coping with weight stigma: an investigation of
875 overweight and obese adults. *Obesity* **14**, 1802-1815.
876 116. Adam TC, Epel ES (2007) Stress, eating and the reward system. *Physiology & behavior* **91**, 449-
877 458.
878 117. Dallman MF, Pecoraro N, Akana SF *et al.* (2003) Chronic stress and obesity: a new view of
879 "comfort food". *Proceedings of the National Academy of Sciences* **100**, 11696-11701.
880 118. Gibson EL (2012) The psychobiology of comfort eating: implications for neuropharmacological
881 interventions. *Behavioural pharmacology* **23**, 442-460.
882 119. Tomiyama AJ (2014) Weight stigma is stressful. A review of evidence for the Cyclic
883 Obesity/Weight-Based Stigma model. *Appetite* **82**, 8-15.
884 120. Vartanian LR, Porter AM (2016) Weight stigma and eating behavior: A review of the literature.
885 *Appetite* **102**, 3-14.
886 121. Carrière K, Khoury B, Günak M *et al.* (2018) Mindfulness-based interventions for weight loss:
887 a systematic review and meta-analysis. *Obesity Reviews* **19**, 164-177.
888 122. Forman EM, Butryn M (2015) A new look at the science of weight control: How acceptance and
889 commitment strategies can address the challange of self-regulation. *Appetite* **84**, 171-180.
890 123. Ruffault A, Czernichow S, Hagger M *et al.* (2017) The effects of mindfulness training on weight-
891 loss and health-related behaviours in adults with overweight and obesity: A systematic review and
892 meta-analysis. *Obesity Research & Clinical Practice* **11**, 90-111.
893 124. Lillis J, Kendra K (2014) Acceptance and Commitment Therapy for weight control: Model,
894 evidence, and future directions. *Journal of Contextual Behavioral Science* **3**, 1-7.
895 125. O'Driscoll R, Turicchi J, Beaulieu K *et al.* (2018) How well do activity monitors estimate energy
896 expenditure? A systematic review and meta-analysis of the validity of current technologies. *Br J*
897 *Sports Med*, bjsports-2018-099643.
898