MRC DTP iCASE studentship: Using Behavioural Insights to Improve the Effectiveness of Digital Weight Loss Interventions

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ABSTRACT

Excess weight is one of the leading preventable causes of morbidity and mortality in high income countries. Behavioural weight loss programmes are effective for weight loss but often resource-intensive and costly, limiting their scalability. Digitally delivered interventions offer a promising alternative, yet their effectiveness is limited by challenges in maintaining engagement and retention. Therefore, this thesis investigated possible strategies to optimise the effectiveness of digital weight loss programmes, in part through enhancing engagement. The work was conducted in partnership with Second Nature, a digital weight management service provider to the NHS.

I initially conducted a prospective observational study using existing Second Nature data to explore the association of goal setting with weight loss and programme dropout. I found that individuals who set higher weight loss goals or reported health- or fitness-related motivations achieved greater weight loss and were less likely to drop out.

Alongside this I helped to develop a fully automated, self-management app, grounded in self-regulation theory (ARTEMIS: Adults Regulating Their weight Everyday with Mobile Internet Support). The app was evaluated in a large-scale randomised controlled trial (n = 1,607), compared to simple advice to lose weight. At six months, the app led to 1.85 kg greater weight loss, doubled the odds of losing ≥ 5% body weight, halved the odds of symptoms of disordered eating, and improved body image.

The modest engagement levels and effect sizes from a self-managed intervention like ARTEMIS prompted me to explore whether adding support components could improve

outcomes. I applied the Multiphase Optimisation Strategy (MOST) framework to develop and test four candidate components: an introductory video call with a health coach, coaching drop-in webchat sessions, goal-setting statements, and food diary reviews plus feedback. A 2^4 factorial optimisation trial was conducted to evaluate their individual and combined effects. I found that the health coach intro call led to 1kg greater weight loss at 24 weeks, while the food diary was associated with poorer outcomes and engagement.

Engagement and retention were a recurring issue throughout the thesis. Thus, the final study explored 'planned pauses' in dieting as a novel strategy to sustain adherence. A systematic review and meta-analysis compared planned pauses with continuous energy restriction. Planned pauses produced weight loss outcomes comparable to continuous energy restriction, but with no clear evidence that they improved retention.

Overall, this thesis illustrates how behavioural theory can inform multiple stages of intervention development, from observational studies to optimisation trials, to enhance engagement and outcomes. Both fully automated and supported interventions were effective, though not universally so, and sustaining engagement remained a consistent challenge. Further work is needed to identify what works best for whom and when, while enabling more responsive collaboration between academia and industry. This highlights the need for more flexible, adaptive evaluation frameworks, and in the discussion, I proposed a set of design principles to support a more fit-for-purpose framework for digital health interventions.

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STATEMENT OF CONTRIBUTION

I declare that this thesis is entirely my own work, completed under the supervision of Professor Susan Jebb, Dr Dimitrios Koutoukidis, and Dr Jadine Scragg, at the Nuffield Department of Primary Care Health Sciences, University of Oxford, and Michael Whitman at Second Nature Ltd. Each project presented in this thesis was conceptualised in discussion with my supervisory team. I led the writing of all chapters and associated journal manuscripts presented herein. Contributions from co-authors and collaborators are acknowledged below. I hereby declare that no part of this thesis has been submitted for any other degree at this or any other University.

For ***Chapter 2***, Michael Whitman extracted the data from the Second Nature database and cleaned the data. I performed the analysis and interpreted the data with support from two Statisticians, Richard Stevens and Paul Bateman.

For ***Chapter 3***, the concept, protocol, and ethical approval were developed by other team members (Dr Paul Doody, Professor Paul Aveyard, and Cristian Stewart), based on pilot work by a previous DPhil student (Dr Kerstin Frie). The app development was carried out by me, Dr Paul Doody, and Dr Simona Haasova, with input from Professor Paul Aveyard. The app was programmed by Mr Nick Goodall. I co-led the trial set-up and overall trial management with Dr Paul Doody, supported by Sarah Mounsey. I was the lead statistician for the trial, responsible for drafting the statistical analysis plan, monitoring data during the trial, data cleaning, and conducting all statistical analyses. I led the qualitative analysis with support from Dr Paul Doody and Stella Haffner. I co-wrote the initial manuscript with Dr Paul Doody, which was reviewed by all co-authors,

and I subsequently adapted the manuscript into Chapter 3 of this thesis, reflecting my contributions.

For ***Chapter 4***, the interviews with current programme participants were supported by Second Nature's product team (Victoria Lim, Dóra Melher, and Robbie Puddick). I led the development of four candidate intervention components in consultation with my supervisory team and three Second Nature health coaches (Grace Preston, Marianne Hennessy, and Daisy Estephane). I created all intervention content with support from the health coaches. I prepared the ethics application with input from my supervisory team.

For ***Chapter 5***, I led all trial set-up activities and the trial delivery, with input from my supervisory team. The intervention was delivered by Second Nature health coaches (Grace Preston, Marianne Hennessy, Kirstie Lawton, and Jemma Joel), with whom I met weekly to review trial conduct, monitor progress, and address any issues. I also trained and supervised two Research Assistants (Lia Willis and Danni Wang), who supported trial management and with whom I held weekly meetings. Michael Whitman extracted and cleaned the trial data. I conducted the analysis and interpreted the findings with support from Jillian Strayhorn, a Statistician with expertise in factorial experiments.

For ***Chapter 6***, I developed the search strategy with support from Nia Roberts, a specialist librarian. I conducted the search, screened all articles, and extracted data with second reviewers (Elena Tsompanaki and Alice Hobson). Disagreements were resolved through discussion with Dr Dimitrios Koutoukidis and, where necessary, the wider supervisory team. I undertook all data synthesis and analysis and wrote a manuscript for publication.

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Gina Wren, July 2025

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AI	Artificial Intelligence
ARTEMIS	Adults Regulating Their weight Everyday with Mobile Internet Support
BCT	Behaviour Change Technique
BMI	Body Mass Index
BOCF	Baseline Observation Carried Forward
CER	Continuous Energy Restriction
CI	Confidence Interval
CS	Coaching Drop-in Webchat Sessions
DAIVE	Decision Analysis for Intervention Value Efficiency
DPP	Diabetes Prevention Programme
EDE-QS	Eating Disorder Examination Questionnaire – Short Form
EPIS	Exploration, Preparation, Implementation, Sustainment
FD	Food Diary Review Plus Feedback
GLP-1	Glucagon-Like Peptide-1
GS	Goal Setting Statements
HC	Health Coach Introductory Video Call
IER	Intermittent Energy Restriction
IMD	Index of Multiple Deprivation
JITAI	Just-In-Time Adaptive Intervention
LOCF	Last Observation Carried Forward
MOST	Multiphase Optimisation Strategy
MRC	Medical Research Council
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OR	Odds Ratio
PP	Planned Pause

PPI	Patient and Public Involvement
PREVAIL	People REgulating themselVes to Achieve weIght Loss
RCT	Randomised Controlled Trial
RE-AIM	Reach, Effectiveness, Adoption, Implementation, Maintenance
RR	Risk Ratio
SD	Standard Deviation
SMART	Sequential Multiple Assignment Randomised Trial
UK	United Kingdom

Chapter 1 : Introduction

1.1 Summary

This chapter provides the background to the work presented in the rest of this thesis. I start by giving an overview of the prevalence, health and economic consequences, and aetiology of overweight and obesity, as well as the benefits of losing excess weight. I then consider different treatment approaches to weight loss, with a focus on behavioural interventions, and highlight that the high costs and labour-intensive nature of these programmes can make them difficult to implement at scale. I introduce digitally delivered programmes as a promising solution, offering convenient, cost-effective, and scalable alternatives to traditional approaches. However, their effectiveness is often limited by challenges in maintaining user engagement and preventing attrition. Addressing these issues is essential to realising the full potential of digital interventions. In the final sections, I identify gaps in the literature, which inform the aims and objectives of this thesis.

1.2 Overweight and Obesity: A Global Health Challenge

1.2.1 Prevalence

Excess weight is one of the leading preventable causes of death in high income countries, and their prevalence has steadily increased in recent decades (1, 2). Obesity is most commonly classified as having a body mass index (BMI) of 30 kg/m^2 or above,

whilst a BMI between 25 and 30 kg/m^2 is classified as 'overweight'. In 2021, 64% of adults in England were considered overweight and 26% were living with obesity (3), a large increase from 1993 where 53% of adults were overweight and 15% were living with obesity. Following this trend, it is anticipated that by 2050 over half of the United Kingdom (UK) adult population could be living with obesity (4). Similarly, 22% of children aged 4-5 were overweight or obese in 2021/22, and 38% at age 10-11 (5). Evidence also shows that being overweight in childhood is likely to track into adulthood. Children with obesity at 10-14 years old, and who have at least one parent with obesity, have a 79% chance of obesity in adulthood (6).

In middle- and high-income countries, there is a strong relationship between deprivation and obesity. In England, for instance, the prevalence of obesity was found to be 20% among adults living in the least deprived areas, compared with 34% in the most deprived areas (3). This difference is even more pronounced in children, with obesity prevalence double amongst those living in the most deprived areas compared to the least deprived areas (5). In recent years, there has been a concerning rise in obesity levels in more deprived areas in England, widening the gap between the most and least deprived areas, and contributing to growing health inequalities. There are also ethnic disparities in obesity prevalence, with women from Black Caribbean (74%), Pakistani (74%), and Black African (73%) backgrounds most likely to be overweight or obese, while the proportions of men who were overweight or obese varies little across ethnic groups (7).

1.2.2 HEALTH & ECONOMIC CONSEQUENCES

Excess weight is associated with reduced life expectancy and is a risk factor for a range of chronic diseases, including cardiovascular disease, type 2 diabetes, and certain types of cancer (e.g. postmenopausal breast, endometrial, prostate, kidney, and colon) (8). Roughly 80–90% of type 2 diabetes patients are living with overweight or obesity (9); 78% of the hypertension cases in men and 65% in women can be directly attributed to obesity (10); and over two-thirds of deaths related to high BMI are due to cardiovascular disease (11). On average, severe obesity is associated with a reduction in life expectancy of around 10 years, and it is estimated that obesity is responsible for more than 30,000 deaths (6% of all deaths) in the UK each year, now surpassing smoking at the biggest contributor to preventable death (12, 13).

People living with obesity are more likely to experience musculoskeletal problems due to increased demand on joints, leading to conditions such as knee osteoarthritis and chronic back pain (9, 14, 15). Individuals with obesity are at a higher risk of additional complications, such as sepsis and infections, while receiving medical treatment in the hospital (16, 17). Aside from physical health, obesity has also been associated with a range of mental health issues such as anxiety, depression, dementia and severe mental illness (18-21).

The health consequences associated with obesity have significant demands on the economy and our health services. In 2019/2020, there were more than one million hospital admissions related to obesity in England (22). Treating obesity-related ill health currently costs the National Health Service (NHS) over £6 billion annually, a figure that is

expected to rise to over £9.7 billion by 2050 (12, 22). More broadly, obesity has a serious economic impact on the wider society due to factors such as increased unemployment, increased sick leave, and overall reduced productivity. The total cost of overweight and obesity to the wider society is estimated to be at least £27 billion each year (12). Therefore, addressing obesity is not only a public health priority but also an economic imperative.

1.2.3 Aetiology of Obesity

At a basic level, excess weight gain occurs when energy intake consistently exceeds energy expenditure. While this is widely recognised as the fundamental driver of obesity, there is increasing recognition of a range of other factors that influence energy intake or expenditure, which are discussed briefly below.

Certain genes have been convincingly linked to obesity risk, through effects on appetite regulation, energy metabolism, and the distribution and storage of adipose tissue (23-25). Research, especially twin studies, has shown that genetic factors account for approximately 47-80% of BMI heritability (24), but genetic predisposition alone cannot explain the rapid rise in obesity prevalence observed in recent decades.

In fact, the aetiology of obesity is multifactorial, encompassing a complex interplay of genetic, behavioural, and environmental factors. The Government Office for Science Foresight report outlines the complex system of interlinked causes underlying obesity (1). Central to the understanding of obesity is the homeostatic biological system that aims to maintain an appropriate energy balance to maintain body weight. This system, influenced by genetic, epigenetic, neural, and metabolic factors, aims to

maintain a stable body weight through pathways regulating appetite regulation, metabolic rate, and energy expenditure (26). Despite its regulatory function, this system is poorly adapted to the rapid technological and lifestyle changes of recent years. As a result, it is often insufficient to protect individuals from weight gain when exposed to modern environments where energy-dense food is abundant and there is little need to be physically active (1).

Dietary intake and physical activity are both shaped by environmental and psychological factors. The term ‘obesogenic environment’ encompasses a range of social, cultural, and structural factors that create an environment that promotes behaviours leading to obesity. These environments encourage excessive energy intake, sedentary behaviour, and limited physical activity, making it more likely that individuals will gain weight (27). Environmental influences on dietary intake include increased availability and accessibility of energy-dense, nutrient-poor foods, which are often cheaper and more heavily marketed than healthier options. Environments that lack safe and accessible opportunities for physical activity, combined with technological advancements that increase screen time, further exacerbate the problem by promoting more sedentary lifestyles (28). These ‘obesogenic environments’ are more prevalent in deprived areas; for example, there is a clear association between deprivation and density of fast-food outlets (29).

The broader cultural and social context also significantly influences our behaviours. The values, beliefs and practices within organisations, such as workplaces, educational institutions, and community groups, can guide how individuals behave and interact in these settings (30). Social norms - the informal and unwritten rules that guide behaviour

- influence individuals' food choices in social settings (31). Media consumption has been directly associated with body weight, with possible explanations including increased sedentary time, exposure to food advertisements, and more 'mindless' eating (32). Additionally, individual-level psychological factors, including health-related knowledge (33), motivational drivers (34), attitudes toward weight (35), and levels of self-efficacy and self-control (36), can collectively impact an individual's motivation or ability to adopt and maintain healthy behaviours.

In summary, the prevalence of overweight and obesity is higher than ever before and rapidly rising. Obesity has a biological basis but usually only manifests in the presence of a conducive environment. The interplay of these factors highlights the complex, multifaceted nature of obesity, which makes treatment a huge challenge. Given the associated health and economic consequences, there is an urgent need to find effective treatment strategies that can be implemented on a large scale.

1.3 Health Benefits of Weight Loss

The benefits of weight loss are extensive and well documented. A $\geq$ 5% reduction in weight is widely accepted as clinically meaningful, is associated with measurable improvements in health risk factors, and is recommended by current guidelines as a weight loss target for people with overweight or obesity (37-39). However, greater weight losses are associated with greater health benefits, in a monotonic relationship (40).

Research has shown that individuals that lose weight have improvements in cardiovascular disease risk factors, better glycaemic control, improved lipid profiles, and reduced blood pressure (41, 42). Individuals are therefore less likely to develop type

2 diabetes and hypertension and, for those who already have these conditions, weight loss significantly improves their management (41, 43, 44). Moreover, weight loss has been shown to be associated with type 2 diabetes remission, making it an effective treatment strategy also (45, 46). A meta-analysis of 15 randomised clinical trials found that intentional weight loss was associated with approximately a 15% decrease in mortality (47), which was largely due to a reduction in deaths from diabetes, cardiovascular disease, and obesity-related cancers (48).

Weight loss alleviates stress on the joints, which can reduce pain and improve mobility, particularly in individuals with conditions like knee osteoarthritis (49). Additionally, weight loss has been associated with improved mental health, reducing symptoms of depression and anxiety (50). Therefore, supporting people to lose weight has considerable health benefits and is critical for disease prevention, as well as reducing costs associated with obesity-related ill-health.

1.4 Current Treatment Options for Obesity

1.4.1 Obesity Treatment in the UK Health System

In the UK, obesity is managed in a four-tier model of care. Tier 1 is usually delivered by Local Authorities and consists of universal primary prevention interventions that include reinforcement of healthy eating and physical activity messages, including public health campaigns providing brief advice. Public health initiatives are aimed at enhancing knowledge and are largely intended for the prevention of weight gain rather than weight loss. Tier 2 services are intended for people with BMI $\geq$ 25 kg/m^2 and are typically delivered by local teams, such as dietetic services. Tier 2 involves community-based

behavioural weight management services, which provide comprehensive support for diet, physical activity, and behaviour change. Tiers 3 and 4 are specialist weight management services intended for people with BMI $\geq$ 40 kg/m^2, or $\geq$ 35 kg/m^2 in the presence of major comorbidity such as type 2 diabetes. They provide specialist assessment, monitoring, and comprehensive tailored treatment by a clinician-led, multidisciplinary team. More specifically, Tier 3 involves non-surgical intensive medical management, including pharmacotherapy, whilst Tier 4 involves bariatric surgery.

However, national geographical coverage of Tier 2 and 3 services is estimated to be only 63%, with variation in provision at a regional and local level (51). Further, only 3% of people eligible for weight management services in England between 2007 and 2020 were referred, and only 1% of people eligible for bariatric surgery received it (52). This was largely due to the availability of services, but also convenience and personal preferences. Moreover, most Tier 3 and 4 services are only accessible to individuals who have completed a Tier 2 programme without achieving successful results. Given the rising prevalence of obesity, demand for services across all tiers is likely to exceed capacity, highlighting the need for scalable solutions to effectively deliver these services.

1.4.2 Bariatric Surgery

The most effective treatment for severe obesity in recent decades has been bariatric surgery, which covers a range of procedures that achieve weight loss by altering the digestive system to limit food intake and/or reducing nutrient absorption. Bariatric surgery has been shown to achieve substantial weight loss of 25-30% total body weight at 12-18 months (53). In addition to weight loss, bariatric surgery has been associated

with improvements in cardiovascular risk factors and increased rates of type 2 diabetes remission (54), as well as lower all-cause mortality rates and longer life expectancy (55). Similarly, in a large multicentre cohort study, bariatric surgery was found to be associated with a lower long-term risk of cancer, particularly obesity-associated cancers, such as postmenopausal breast cancer, endometrial cancer, and colon cancer (56).

1.4.3 Pharmacotherapy

Recently, there have also been significant advances in obesity pharmacotherapy which offers a promising non-surgical alternative to treating severe obesity. Drugs such as semaglutide and tirzepatide (glucagon-like peptide-1 [GLP-1] agonists) have been approved for treatment by the National Institute for Health and Care Excellence (NICE) for the treatment of obesity (57). In randomised clinical trials, semaglutide has demonstrated significant weight losses of 14-17% at 68 weeks, alongside meaningful improvements in cardiovascular risk factors (58-60). Tirzepatide has shown even greater efficacy than semaglutide (61), with 15–21% weight loss at 72 weeks (62).

1.4.4 Behavioural Weight Loss Programmes

Whilst highly effective, both surgical and pharmacotherapy approaches are reserved for those with severe and complex obesity, due to factors such as workforce capacity, costs, concerns related to safety and risk of complications, and possible side effects (63, 64). Moreover, these approaches alone are unlikely to equip people with the skills necessary for long-term behaviour change and sustained weight. This is evidenced by the fact that weight regain is common after medication cessation, and faster than observed following

behavioural programmes (65, 66). Therefore, integrating dietary and physical activity modifications through behavioural support programmes is essential for sustaining long-term weight management across all tiers of care.

My DPhil research is focused on behavioural weight loss programmes. Behavioural programmes aim to support weight loss by using behavioural strategies to promote behaviour change towards a healthier diet and increased physical activity. Support can be delivered in many ways, and there is a large diversity of programmes on offer ranging from simple advice to meal replacements, to structured counselling, or group-based sessions. These programmes have the potential to deliver significant benefits at the population level, if implemented in a scalable and cost-effective way.

1.4.4.1 Evidence for Effectiveness

The current evidence strongly supports the effectiveness of behavioural programmes for supporting weight loss in adults with overweight or obesity (67-69). A meta-analysis found that multicomponent behavioural weight management programmes produced an additional 2.8 kg of weight loss at 12 months compared with non-behavioural programmes (69).

The findings are complemented by two landmark studies, the Diabetes Prevention Programme (DPP) and the Look AHEAD study. In the DPP, over 3,200 participants were randomised to placebo, metformin, or an intensive lifestyle intervention which consisted of 16 individual counselling sessions, followed by monthly contact until the end of the study; a reduced-energy, low-fat diet; and 150 minutes of weekly physical activity. After 2.8 years, the lifestyle group lost an average of 5.6 kg, compared to 0.1 kg and 2.1 kg in

the placebo and metformin groups, respectively, with a 58% reduction in type 2 diabetes incidence (70). Similarly, the Look AHEAD trial included over 5,000 individuals living with type 2 diabetes and overweight or obesity. The intervention group received intensive behavioural support (three group and one individual session for six months, followed by reduced frequency for the remainder of the year), while the control group received diabetes education (71). The intervention group lost 8.6% of initial body weight at one year and 4.7% at eight years, compared to 0.7% and 2.1% in the control group (72). Both programmes also showed improvements in cardiovascular risk factors (73-75).

However, systematic reviews have noted considerable heterogeneity in outcomes between different programmes (69, 76). This variation could be due to differences in content and the incorporation of specific behavioural strategies. Many programmes now employ established behaviour change techniques (BCTs), which are the 'active ingredients' of an intervention and are grounded in psychological theories and supported by empirical evidence (77). Diet and/or physical activity interventions that incorporate established behavioural techniques have been shown to be more effective for weight loss (78), and health behaviour change (79), than those without such techniques. Interventions that use BCTs such as goal setting, self-monitoring, feedback, and social comparison have been associated with greater weight loss (69, 80, 81), as well as improved adherence and maintenance of behaviour change (82). However, many programmes use a limited range of strategies and underutilise others, primarily goal setting, action planning, and feedback (69). Despite evidence that behavioural strategies enhance programme effectiveness, in most interventions, theory use is often unreported

or inconsistently applied, limiting our understand of which components are the most effective (83, 84).

Programme intensity is another key factor that could explain the variation in outcomes. A systematic review reported weight losses of 4-7 kg for programmes with 12-26 intervention sessions compared to 1.5-4 kg in programmes offering fewer than 12 sessions (67). Other reviews confirm that higher contact frequency is linked to better outcomes (78, 85). Similarly, one randomised controlled trial found that participants receiving 16 treatment sessions lost 6.7 kg, which was more than those receiving eight sessions (3.5 kg) or the nutrition education control (2.9 kg). However, the 16-session group did not differ significantly from a 24-session group, indicating there could be an upper limit to the added benefit of increasing intensity (86). Given the resource demands of high-intensity programmes (87, 88), low or very low intensity interventions could offer an alternative but there is scepticism surrounding their effectiveness (89, 90).

Research into interventions that reduce resource and costs without decreasing effectiveness is needed. However, traditional randomised controlled trials that evaluate interventions as a whole, prevent us from isolating the effects of individual components, making it difficult to determine which components are most effective for weight loss. Testing small changes to programmes through traditional trials is challenging because the expected effect size is small, requiring a large sample size for adequate power. This limitation underscores the need for alternative methods for testing components, such as drawing on natural experiments or continuous service improvement, driven by routine data collection and analysis.

1.4.4.2 Delivering Programmes at Scale

There is a pressing need to adapt behavioural programmes to reach more people, and primary care presents one opportunity to do this. However, interventions shown to be effective in research settings often prove less effective in routine practice. For example, a weight loss programme adapted from the DPP and delivered by primary care teams, failed to produce significant weight reduction (91). A systematic review of interventions delivered in routine practice concluded that those implemented in primary care were largely ineffective (76), whilst another review found that such programmes produced only modest reductions in weight, which was unlikely to be clinically meaningful (84). A more recent review did find that programmes delivered in primary care had greater weight losses at 12 months of -2.3 kg compared to no treatment or minimal interventions (92). These mixed findings, combined with barriers such as staff resources, training needs, set up time, and costs, highlight the challenges of implementing programmes in primary care settings.

Outside of primary care, commercial providers, such as Slimming World and Weight Watchers, are an effective option to deliver services. Private providers often operate referral schemes for the NHS, allowing commissioners to purchase referral packages at a reduced cost, which are then provided to patients free of charge. Many of these commercial services are not solely available on NHS and are also offered direct to privately paying consumers. On average, commercial programmes have been shown to achieve weight losses of 2.2–5 kg at 12 months, outperforming minimal or low-intensity interventions and offering additional benefits such as reduced blood pressure and improved glycaemic control (93-96). Randomised controlled trials have found that

people living with overweight or obesity who were referred to a commercial programme by their primary care provider for 12 months, lost around twice as much weight compared to standard care (brief advice and self-help materials) (97, 98). Commercial programmes are normally delivered in large groups, meaning these programmes may be more affordable than NHS-led services and are more widely accessible (99, 100). Moreover, modelling of long-term outcomes suggest that these programmes may be cost-saving because of reductions in weight-related disease and associated healthcare costs (101).

Commercial providers have primarily been used to deliver Tier 2 services, but they are now also moving into Tier 3 services. NICE recently announced an early value assessment of digital technologies for delivering multi-disciplinary weight management services, enabling faster access to promising treatments whilst additional evidence is generated for a full evaluation (102). Seven commercial providers were recommended for use in the NHS to prescribe and monitor semaglutide treatment (103). This aims to increase access, allowing more people to use semaglutide outside of a hospital setting, decentralising care and easing the burden on healthcare resources. Commercial partnerships have thus become key to expanding delivery capacity and supporting national scale-up.

Two major national programmes illustrate this approach. The NHS DPP which was first rolled out in 2016 in waves and, alongside commissioning of independent commercial providers, reached national coverage in 2018. It is an intensive behavioural support programme developed to prevent or delay onset of type 2 diabetes in adults identified to be at high risk, through evidence-based behaviour change (104). Early outcomes suggest that the NHS DPP successfully promotes reductions in weight and HbA1c which are

indicative of future reductions in the incidence of type 2 diabetes in participants (105). The programme is also likely to be cost-effective and cost-saving, with the initial investment in the intervention recouped within 12 years through NHS savings (106). NHS DPP was the world's first nationally implemented diabetes prevention programme and established a scalable delivery model that could be applied to other programmes.

Building on this, the NHS Type 2 Diabetes Path to Remission Programme completed national rollout in 2024. This programme provides a low calorie, total diet replacement treatment for people who are living with type 2 diabetes and obesity or overweight and was based on evidence from two large-scale trials. The Diabetes Remission Clinical Trial (DiRECT) demonstrated that total diet replacement was successful for weight loss and type 2 diabetes remission (107). Whilst The Doctor Referral of Overweight People to Low Energy Total Diet Replacement Treatment (DROPLET) trial found that similar weight loss could be achieved via commercial providers (108). The initial pilot phases of the programme have demonstrated encouraging weight losses of 11.4 kg at 12 months, which was comparable to those achieved in the randomised controlled trials (109). Economic modelling based on DiRECT suggests the programme is likely not only cost-effective but cost-saving, with NHS savings of £1,337 per person over a lifetime (110).

A digital service model for delivering behavioural support presents a promising alternative to in-person delivery, offering more affordable and accessible services to a wider audience. This model is already available as an option within both the NHS DPP and the Path to Remission Programme. It has the potential to widen access, reduce waiting times by expanding capacity, and offer greater convenience for patients. Findings from pilot studies of digital delivery of the NHS DPP, suggest that people using a digital

intervention achieved greater weight loss than those using either remote or group-based, in-person interventions (111). Building on findings from the NHS DPP, the NHS launched the Digital Weight Management Programme which is a step towards improved access to weight management services. It offers a 12-week online behavioural programme to people living with obesity with a diagnosis of diabetes and/or hypertension, at differing levels of intensity (112). Early outcomes of referrals made from general practice demonstrate clinically meaningful weight loss of -3.92 kg at 12 weeks for those who completed the programme, which compares favourably to other similar digital interventions (113). Together, these findings support national implementation of digital weight management as a cost-effective and scalable treatment option.

1.4.5 Digitally Delivered Programmes

Digital weight loss programmes typically include those delivered via electronic delivery modalities, such as an application (app) for a smartphone, in formats that can be accessed via a computer, and/or social media networks. Recent technological advances, including widespread internet access and increased smartphone use, have driven the development of numerous digital interventions. A trend further accelerated by the shift to remote service delivery during the COVID-19 pandemic (88, 114).

Several systematic reviews have reported that digital weight loss programmes are more effective compared to control or minimal interventions, with meta-analyses showing mean differences in weight loss ranging from 1.1 kg to 2.7 kg (115-118). Whereas comparisons with in-person programmes show mixed results. A 6-month randomised controlled trial comparing a behavioural weight loss programme delivered either in-

person, via the internet, or in a hybrid format, demonstrated weight losses of 8.0, 5.5, and 6.0 kg respectively, and the proportion losing >5% body weight did not differ between groups (119). Another randomised controlled trial compared a behavioural weight loss programme delivered via a smartphone to a standard group-based programme and found no significant difference in weight loss between the two groups at 18 months (120). Some systematic reviews show digital interventions result in short-term weight loss that is at least 20-35% smaller than in-person programmes (121, 122), whilst others suggest that digitally-delivered programmes produce weight loss comparable to in-person interventions (69, 123, 124). These reviews however reported substantial heterogeneity, largely due to differences in delivery modality, control groups, study design, and the duration, content, and intensity of interventions, making comparisons across studies difficult. The literature also currently lacks sufficient evidence on the long-term outcomes of digital interventions. Trials frequently do not include follow-up beyond the intervention, meaning there is limited data on their long-term effectiveness for sustaining weight loss.

In addition to fully digital interventions, several studies have explored whether incorporating digital components into conventional weight loss programmes can enhance accessibility without compromising effectiveness. One randomised controlled trial found that more participants in a combination group (partially delivered in-person and partially via an app) achieved a 5% or more weight reduction compared to the app-alone group at 12 weeks, with no difference in weight loss between the combination group and the conventional in-person group (125). Similarly, Allen et al. found that participants in an intensive counselling plus app group and a less intensive counselling

plus app group achieved greater weight loss (5.4 kg and 3.3 kg, respectively) compared to those in the counselling-alone (2.5 kg) or app-alone groups (1.8 kg) at 6 months (126). The POWeR+ trial evaluated the effectiveness of a control group receiving dietetic advice plus nurse follow-up, a web-based intervention plus in-person nurse support, and a web-based intervention plus remote nurse support in a primary care setting (127). At 12 months, the in-person group achieved an additional weight reduction of 1.5 kg, and the remote group achieved an additional 1.3 kg, compared to the control group. More participants maintained a clinically significant weight reduction of 5% in the in-person group (29%) and remote group (32%) compared to the control group (21%), although differences were modest. In cost-effectiveness analyses, the POWeR+ interventions achieved weight loss at a cost per kg below the threshold required by NICE to be cost-effective. Together, these findings suggest that supplementing conventional programmes with digital elements can offer an accessible, cost-effective, and scalable strategy for achieving clinically meaningful weight loss.

These findings also draw attention to an important point of variation across digital interventions, the extent of personal interaction or intensity of behavioural support. Some evidence suggests that digital interventions require some degree of remote behavioural support or coaching to achieve significant results (89, 90). Several reviews have found that digital interventions with some human contact (e.g., a coach or counsellor) are more effective than fully automated interventions (117, 128). Although this contact does not necessarily need to be intensive to reap benefits, adding remote support to digital programmes increases their cost and complexity, potentially undermining some of their advantages.

Conversely, self-guided or unsupported programmes, which require no professional input, are highly scalable and cost-effective. These programmes have been shown to promote modest but significant weight loss of at 6 months compared to minimal interventions (129, 130). However, results in terms of effectiveness for unsupported interventions are variable, and behavioural support is widely acknowledged to increase weight loss over unsupported efforts. Therefore, finding a balance between personal interaction and programme scalability is important for optimising the effectiveness of digital weight loss interventions.

Like in-person programmes, digital weight loss programmes vary greatly in content and the incorporation of different behavioural strategies, which contributes to the variability in observed outcomes and makes comparisons across studies difficult. Common behavioural techniques used in such programmes include self-monitoring of behaviour and/or outcome, goal setting, feedback, and social support (121). Research aiming to identify features of effective programmes has found that tailored feedback, personalised content, and self-monitoring differentiate more effective interventions (117, 121). However, many findings are based on observational or comparative studies and further experimental evidence is needed to determine which specific components are associated with effectiveness.

1.4.5.1 Engagement and Retention

Engagement is a key determinant of effectiveness in behavioural weight loss programmes but is a particular challenge for digital programmes. Although there is no single definition of engagement, it is typically measured by the overall frequency or

duration of use, or the depth of usage in terms of use of individual features (131, 132). Numerous studies have found a positive association between engagement and weight loss, despite variability in how engagement is defined (89, 133-136). Greater engagement with specific components, such as monitoring food intake and self-weighing, also predicts weight loss (89, 133, 137, 138).

Early engagement, particularly within the first 4-6 weeks, has been shown to predict long-term outcomes. Individuals who engage more in the initial stages achieved greater weight loss from anywhere between 3 months and 2 years (135, 139, 140). For example, those engaging in all four initial weeks lost 3.8% of their body weight by 3 months, compared to 1.3% in those who did not (139), meaning that the early stage of treatment is a critical window for engagement. These findings suggest that enhancing engagement is key to maximising the effectiveness of behavioural weight loss programmes, especially in digital formats.

One of the critical methodological challenges in the evaluation of digital interventions is high attrition rate, which is due to a combination of participants being lost to follow-up and/or discontinuing use of the intervention (141). High attrition rates are typical of digital interventions, and attrition rates range from 9-86% for digital interventions (142), and from 9-89% in digital weight loss interventions specifically (115). It has also been consistently reported that engagement declines over time and maintaining engagement in the long-term is difficult, with eventual disengagement from the intervention entirely (133-135). Overall intervention engagement has been shown to decline by 33.6% in the first six months (134), and log-in percentage dropped from 82% to 47% at 6 months (143). Further, a meta-analysis found that web-based digital interventions led to greater short-

term but not long-term weight loss when compared to offline interventions in individuals with overweight and obesity (116). The finding that digital interventions were not superior in the long term suggests that engagement and adherence over time are key issues, particularly as most studies in the reviews reported low engagement and high attrition in digital programmes (114).

Several factors have been found to influence engagement, including the intervention itself (content and delivery); contextual factors (setting and population), and psychological characteristics (motivation and self-efficacy) (131, 144). Additionally, studies have shown that factors related to weight loss outcomes, such as weight loss expectations or previously achieved weight losses, also affect engagement (133, 145). There is also some evidence to suggest that demographic characteristics such as age, gender, education, employment, and ethnicity are associated with engagement (131, 144). Engagement and attrition are likely to be closely related, but some factors appear to influence attrition more specifically. These include ease of enrolment and drop-out, usability issues, the degree of personal contact, push reminders, and participant burden (141, 146). Researchers are increasingly exploring new strategies such as user-centred design, personalisation, social support, tailored feedback, and gamification as a means to reduce attrition and increase engagement rates (147). However, there is little experimental evidence on their effectiveness, meaning strategies to maintain user engagement over time remain poorly understood.

Overall, engagement is consistently linked to weight loss in digital programmes, but engagement declines over time. While various factors have been proposed to influence both engagement and attrition, research focused on designing and optimising

interventions to sustain participant engagement and increase retention, is crucial for maximising the effectiveness of digital programmes.

1.5 Limitations in the Evidence Base and Unanswered Questions

Digital interventions for weight loss offer promise as a convenient, potentially lower cost, and scalable treatment option for obesity. However, there remains unanswered questions that hinder us harnessing their full potential. Addressing these gaps in the evidence base will allow us to develop more effective interventions and, when paired with the scalability of digital interventions, this has the potential to provide considerable public health impact. This thesis aims to address some, but not all, of these gaps as outlined below:

Which approaches can be used to enhance engagement and retention in digital weight loss interventions?

As outlined above, high attrition rates are a common issue in digital interventions, significantly impacting their overall effectiveness. Sustained engagement is also critical to the success of any intervention but is a particular challenge for digital programmes. Yet, strategies to maintain user engagement over time are not well understood, and many studies still report low engagement and high attrition in digital programmes. Throughout this thesis, I will explore engagement and drop-out rates within an existing programme (***Chapter 2***) and investigate new strategies for enhancing engagement and retention (***Chapter 5*** & ***Chapter 6***), with a focus on optimising the intervention content and delivery.

What is the effectiveness of a digital weight loss intervention in a real-world setting?

Many studies on digital weight loss interventions are conducted in controlled research settings, making it difficult to scale these interventions to meet need, and potentially failing to reflect their performance in real-world environments. To address this, the thesis will have an overarching emphasis on real-world data collection through mobile health technologies and trials conducted under real-world settings (Chapters 2-5).

How can we optimise the effectiveness of current programmes?

Understanding the behavioural components that are associated with the effectiveness of digital interventions is critical for improving current services and developing more effective programmes in the future. Much of the current evidence base is centred on observational or comparative studies and further experimental evidence is needed. However, traditional randomised controlled trials evaluate interventions as a whole, making it difficult to understand which components are the most effective in supporting weight loss. More recently, approaches such as the Multiphase Optimisation Strategy (MOST) are being applied to digital interventions to explore which intervention components are associated with effectiveness (148, 149).

Here, I will use a variety of approaches to identify and test intervention components aimed at enhancing the overall effectiveness of digital programmes, including quantitative data analysis of an existing programme (***Chapter 2***), the use of the MOST framework to identify new intervention components (***Chapter 4***), and to screen these intervention components in a factorial optimisation experiment (***Chapter 5***).

Are there entirely new approaches to support weight loss in digital programmes beyond current offerings?

Despite the large number of mobile applications supporting weight loss, most focus on delivering diet and/or physical activity advice in various formats and often lack a clear theoretical underpinning. Some emerging interventions are more theory-based, e.g. Acceptance and Commitment Therapy interventions (150). This may enhance their effectiveness and improve understanding of underlying mechanisms of action. This thesis will explore two new approaches, a new intervention grounded in self-regulation theory (***Chapter 3***), and a novel strategy to enhance retention (***Chapter 6***).

1.6 Collaboration with Second Nature

My DPhil is an Oxford-MRC Enterprise (iCASE) studentship in collaboration with Second Nature. Second Nature is commissioned by NHS England and local commissioning groups as a service provider of the NHS DPP and the NHS Digital Weight Management programme. They were also one of commercial digital technologies recommended by NICE for use in the NHS to prescribe and monitor semaglutide treatment as part of their early value assessment (103).

Second Nature is a digitally delivered behavioural intervention, designed to support people to increase their physical activity and create sustainable healthy eating habits, to thus achieve weight loss. The programme consists of educational articles covering topics such as nutrition, exercise, stress management, and sleep; mentoring from a registered dietitian or nutritionist (health coach); tracking technology; and peer group support. Further details of the programme are provided in the relevant chapters.

The Second Nature programme has been developed based on several BCTs (77), shown to be effective in diet and physical activity interventions (79), such as: self-monitoring (behaviour and outcome), goal setting (behaviour and outcome), feedback (behaviour and outcome), social support (practical), instruction on how to perform the behaviour. The Second Nature programme has been previously shown to achieve clinically significant weight loss averaging 7.12 kg in those who weighed themselves at 6 months (151, 152), and averaging 6.2 kg after 12 months (153). Findings also suggest a potential positive association between programme engagement and weight loss (136).

It has been argued that mobile health development would benefit from collaboration between commercial app developers and behaviour change experts (154). This close academic and industrial partnership has allowed me to test more effective weight loss approaches that can be immediately incorporated into NHS care, thus creating impact on a national scale if successful.

1.7 Thesis Aims and Overview

The overarching aim of this thesis is to investigate possible strategies to optimise the effectiveness of digital weight loss programmes, in part through enhancing engagement. I aim to identify and test intervention components that foster sustained participant engagement and enhanced weight loss. Throughout the DPhil, I collaborated with Second Nature to provide commercial insights into the design and delivery of digital interventions, and my projects have evolved organically as follows:

Chapter 2: The association between goal setting and weight loss: prospective analysis of a community weight loss programme

I began by familiarising myself with the existing Second Nature programme and data by conducting a prospective longitudinal analysis to investigate the association of goal setting with weight change and programme drop-out.

Chapter 3: The effectiveness and safety of a mobile application based self-regulation intervention to support weight loss among adults living with obesity: a randomised controlled trial

Following the exploration of a supported digital intervention in ***Chapter 2***, I had the unexpected opportunity to design and evaluate a fully automated alternative, which provided a useful point of comparison with the Second Nature programme which includes human-based coaching. This project involved developing a novel self-managed mobile app based on self-regulation theory, which was tested in a randomised controlled trial (ARTEMIS: Adults Regulating Their weight Everyday with Mobile Internet Support).

Chapter 4: Intervention development of four candidate components aimed to enhance weight loss and engagement in a commercial digital weight loss programme

The modest engagement levels and effect sizes from a self-managed intervention like ARTEMIS prompted me to explore whether adding further support components could improve outcomes. As part of my iCASE studentship, I conducted an internship with Second Nature. I observed health coaches and interviewed current programme participants to understand key barriers to programme success**. *Chapter 4,*** outlines the work I conducted to identify and develop four candidate intervention components,

hypothesised to increase weight loss and programme engagement when added to the Second Nature programme.

Chapter 5: Optimising a digitally delivered behavioural weight loss programme: a factorial cluster randomised controlled trial

Building on the work in ***Chapter 4,*** I designed and conducted a factorial cluster randomised controlled trial to systematically test these candidate intervention components. The aim was to optimise the Second Nature programme for clinical effectiveness, guided by the Multiphase Optimisation Strategy (MOST) framework.

Chapter 6: Effect of planned pauses versus continuous energy restriction on weight loss and attrition: a systematic review & meta-analysis

Engagement and retention were a recurring issue in Chapters 2-5. Therefore, in my final project, I explored a new approach, 'planned pauses', as a potential strategy to enhance retention. This chapter outlines a systematic review comparing the effectiveness and attrition rate between continuous energy restriction and a 'planned pause' in a weight loss programme.

Chapter 7: Discussion

My final chapter summarises the findings and learnings from my doctoral research as well as discussing opportunities for future research in the context of the wider landscape of public policy and academic research.

Chapter 2 : The association between goal setting and weight loss: a prospective analysis of a community weight loss programme

2.1 SUMMARY

Goal setting supports health-related behaviour change, but the impact of different types of goals on weight loss outcomes remains unclear. This chapter presents a prospective longitudinal analysis of participants in Second Nature's 12-week digital behavioural weight loss programme, examining the association between three aspects of goal setting and both weight change and programme dropout over a 24-week period.

Weight and engagement data were extracted for eligible participants (N = 36,794). Participants were UK adults with a BMI ≥25 kg/m^2 and a recorded weight reading at baseline. At enrolment, participants self-reported three aspects of goal setting: motivation for weight loss (appearance, health, fitness, or self-efficacy), overall goal preference (low, medium, or high), and percentage weight loss goal (<5%, 5%–10%, or >10%). Weight was measured at 4, 12, and 24 weeks. Mixed models for repeated measures were used to examine the association of goals with weight at 24 weeks as the

primary endpoint. Dropout was analysed using logistic regression, and engagement was tested as a potential mediator.

Of the total sample, 13.1% (n = 4,818) reported weight at 24 weeks. I found that, most people set weight loss goals of 5%–10% (64.3%), but greater weight loss was observed among those who set goals of >10% (mean: 5.21 kg; 95% CI: 5.01, 5.41; P < 0.001). There was no significant difference between 5%–10% and <5% goals. Appearance was the most reported weight loss motivation (40.1%), but health and fitness motivations were associated with greater weight loss (health vs appearance: 1.40 kg; 95% CI: 1.15, 1.65; P < 0.001; fitness vs appearance: 0.38 kg; 95% CI: 0.05, 0.70; P = 0.03). Overall goal preference was not clearly associated with weight loss.

Engagement independently predicted weight loss but did not mediate the relationship between goal setting and weight loss. Participants who set goals of >10% were less likely to drop out compared to those with 5%–10% goals (OR: 0.40; 95% CI: 0.38, 0.42; P < 0.001). Those who preferred setting high overall goals were more likely to drop out than those preferring medium goals (OR: 1.20; 95% CI: 1.11, 1.29; P < 0.001). Health and fitness motivations were also associated with reduced dropout compared to appearance (health: OR 0.84; 95% CI: 0.78, 0.89; P < 0.001; fitness: OR 0.92; 95% CI: 0.85, 0.995; P = 0.04).

In summary, setting higher weight loss goals and being motivated by health or fitness were associated with greater weight loss and lower dropout. However, due to the observational nature of this analysis, randomised controlled trials testing the effect of setting these types of goals are needed to confirm causality.

Note: this chapter has been published in a peer-reviewed journal article.

- **Wren GM** et al. The Association Between Goal Setting and Weight Loss: Prospective Analysis of a Community Weight Loss Program. Journal of Medical Internet Research. 2023. 25:e43869. https://doi.org/10.2196/43869

2.2 INTRODUCTION

In ***Chapter 1***, I introduced digital behavioural weight loss programmes as a promising and scalable treatment option for overweight and obesity and discussed how commercial providers can play a role in delivering these services at scale. I began my DPhil with a project aiming to explore engagement and attrition within one such programme, Second Nature. This allowed me to familiarise myself with the programme and dataset, while also examining how behavioural science was being implemented in practice. In this chapter, I focus on one specific BCT used in the programme, goal setting.

Goal setting is an important motivational factor underlying health behaviour change (155). Goal setting theory is based on the principle that consciously set goals direct attention and action, and that behaviour is regulated by the individual's goals (156, 157). Setting a weight loss goal has been shown to lead to greater weight loss than not setting a goal (158), prescribing a higher physical activity goal has been shown to lead to greater weight loss (159), and interventions that incorporate both goal setting and self-monitoring have been found to be more effective at promoting health behaviours than interventions without these techniques (80).

The study of goal setting in the context of weight loss is particularly relevant, given the disparity between what physicians and patients with overweight and obesity consider a 'realistic' goal. A 5-10% reduction in weight is widely accepted as clinically meaningful, due to associated improvements in cardiometabolic risk factors, and is recommended by current guidelines as a weight loss target for people with overweight or obesity (37-

39). However, individuals with overweight and obesity regularly set weight loss goals 3 to 4 times (22-34% weight reduction) greater than what is recommended (160-163).

There is some uncertainty regarding the best strategy for incorporating goals into behavioural programmes for weight loss. Based on findings from the broader goal setting literature, when goals are too ambitious, individuals experience impaired performance which often leads to abandonment of the goal (164, 165). In the context of obesity research, retrospective studies have found that setting larger weight loss goals may result in poor weight loss maintenance (166, 167). Likewise, setting a larger weight loss goal was associated with higher rates of attrition from therapy and smaller reductions in BMI after 12 months of treatment for obesity (162, 168, 169). Meanwhile other research found either no relationship or a modest positive relationship between setting larger weight loss goals and achieved weight losses (161, 170-173), and no relationship between failure to meet weight loss goals and attrition (172, 174). Previous studies of weight loss goals had small sample sizes, and it is possible that the importance of goal setting differs across different behavioural programmes.

It may also be important to consider how the perceived magnitude of an individual's goal relates to weight outcomes. Failure to meet weight loss goals that are perceived as realistic may have a greater impact on long-term success than failure to meet ambitious goals, which individuals may recognise are less attainable. However, studies have shown variability in the perceived magnitudes of goals (***Table 2.1***) and mixed results in relation to outcomes. Women with overweight and obesity have been reported to lose more weight when their pre-treatment weight loss expectations are higher (175).

Similarly, participants instructed to set 'realistic' lower goals, lost less weight than those instructed to set 'unrealistic' higher goals, which were 1.5 times higher (176). No association was found between 'goal' weights and outcomes, but 'dream' weights (which participants perceived as less likely to achieve than 'goal' weights) were associated with greater weight loss at 18 months (161). Conversely, the observation that 'dream' BMI, but not 'acceptable' or 'expected' BMI, was negatively associated with BMI change at one year shows that goals that are perceived as high may have a negative impact on the weight loss achieved (168). This observation may however be driven by the greater attrition rate amongst participants with higher weight loss expectations (168). Thus, it could be that setting goals that are perceived as more ambitious may sustain patients in their long-term weight loss efforts.

Table 2.1: Variability of weight loss goals in existing literature

Goal Type	Percent Weight Reduction Goal	References
'Disappointed' Weight	9.9 – 15.7%	(174, 177, 178)
'Acceptable' Weight	11.1 – 24.9%	(174, 175, 177, 178)
Goal Weight	14.8 – 32.0%	(161, 162, 174, 175, 177, 178)
'Dream' Weight	28.3 – 38.4%	(161, 162, 174, 177, 178)

Motivation is a key psychosocial factor that influences weight loss success (179, 180). Frequently reported motivational factors for losing weight include improving physical appearance and health (168, 174, 181, 182) and wanting to feel better about oneself (182, 183). Intrinsic motivations, such as an interest in exercise, predicts long-term weight maintenance (184), whereas extrinsic motivations, such as appearance, have been

associated with smaller weight losses (179, 181, 185). Behavioural weight loss programmes typically focus on increasing an individual's level of motivation, however there is little evidence on how the type of the initial motivation affects subsequent weight change. A better understanding of the initial motivations for considering weight loss programmes is important as lack of participant motivation is commonly used as an explanation for intervention failure or poor intervention outcomes (186). Examining a participant's initial reasons for weight loss could help to predict intervention outcomes.

Given the discrepancies in the existing literature, the primary aim of this study was to investigate the association of three different aspects of goal setting (weight loss motivation, overall goal preference, and percentage weight loss goal) with weight change over a 24-week period. The secondary aims were to investigate whether engagement mediated the association between goals and weight loss, and to explore the association between goals and drop-out.

2.3 METHODS

2.3.1 STUDY DESIGN AND PARTICIPANTS

This prospective longitudinal study used data collected by Second Nature. Second Nature provides a digitally delivered behavioural programme, aiming to support people to increase their physical activity and create sustainable healthy eating behaviours.

Data for eligible participants were retrieved from Second Nature's database in March 2022. I received a deidentified dataset from Second Nature. All participants were UK adults, aged 18 years and over, with a BMI of $\geq$25 kg/m^2 at programme entry. To be eligible for inclusion in the analysis, participants must have paid to participate in the 12-week behavioural programme seeking support for weight loss; recorded a baseline weight reading; and completed the bespoke health questionnaire during the enrolment process. All participants consented to use of their anonymised data for medical research purposes by accepting the privacy policy as part of the sign-up process (***Appendix 2.1***).

2.3.2 PROGRAMME DESCRIPTION

Note: The Second Nature programme and its contents evolved over the course of my DPhil. It is described here as it was at the time of this study.

The 12-week behavioural change programme consists of mentoring from a health coach (registered dietitian or nutritionist), peer group support, educational articles, and activity tracking technology. The programme is accessed via a smartphone or web-based application (***Figure 2.1***). Before the start of the programme, each participant receives an

instructional handbook, recipe book, and can optionally pay extra to also receive wireless weighing scales.

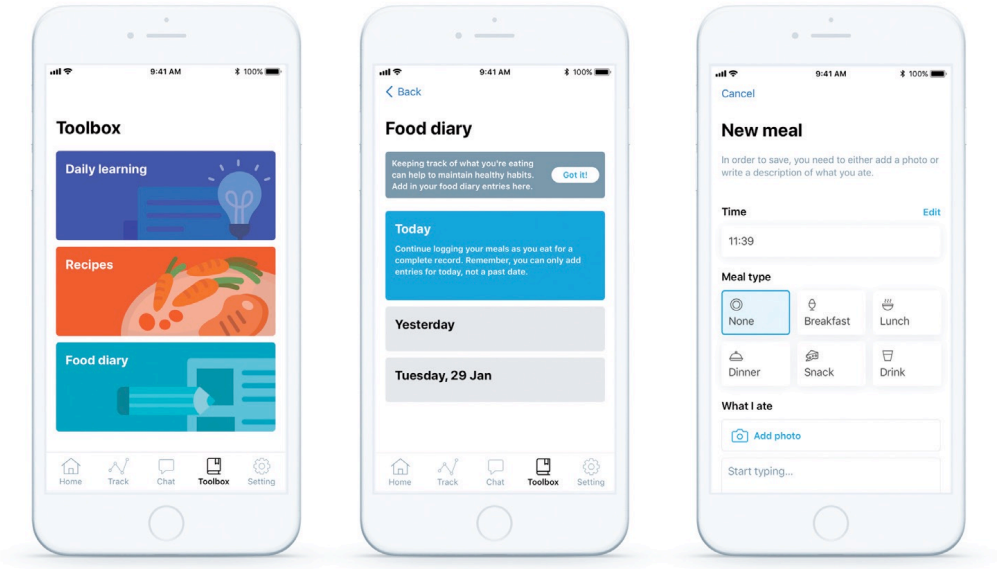

Figure 2.1 : Example Second Nature programme content.

The behavioural component of the intervention has been informed by behavioural frameworks aiming to promote successful behaviour change, including those outlined in the behaviour change wheel (187). A number of BCTs were used within the various functions of the app and incorporated into the health coaching support, including: self-monitoring (behaviour and outcome), goal setting (behaviour and outcome), feedback (behaviour and outcome), social support (practical), and instruction on how to perform the behaviour (77).

Participants were allocated a health coach who delivered personalised support via a text-based messaging service within the app. The messaging support was provided both privately and within a group chat of up to 14 other participants, to provide social accountability and motivation. Educational information, delivered by plain text and

videos, could be accessed by participants through the app. The educational information covered topics which focus on healthy eating, physical activity, stress management, and sleep. Participants could record and view weight and step readings within the app. These could also be viewed by the health coach who encouraged participants to engage with the app and monitor their progress against their goals. The frequency of recording weight readings varied between participants and was informed by individual choice. Health coaches were notified when participants had low engagement (defined as <10 interactions with the app in the last week) to contact them and encourage participation.

The core programme lasted for 12 weeks, after which the participants still retained access to the app and its content, but active support from the health coach was discontinued. Participants could continue to self-monitor their weight, access educational materials, and engage with the peer group if they chose to do so.

2.3.3 Data Collection

At baseline, each participant answered a series of questions in a bespoke health questionnaire including their goals for the programme. Participants also self-reported their gender, height, age, presence of type 2 or pre-diabetes, and home postcode (which was used to calculate socioeconomic deprivation using the Index of Multiple Deprivation [IMD] (188)).

Weight data were either automatically collected using the Bluetooth weighing scales provided at the start of the programme or could be manually inputted into the app. Having a weight reading at baseline was part of the criteria for inclusion in the analysis

so the dataset included complete weight data at baseline. However, for validation purposes, baseline weight readings were only retrieved from the database if they ranged between 40 - 200kg. Weight data were collected at three further follow-up time points: 4 weeks, 12 weeks, and 24 weeks. A single weight reading was extracted for each time point by searching within a specified time period (3-5 weeks for 4 weeks, 10-14 weeks for 12 weeks, and 20-28 weeks for 24 weeks) and the reading closest to the mid-point of each time period was extracted. A validation algorithm, which considered the previous reading and time since this reading was registered, was used for readings at each collection time point to only accept readings within an expected range. These validation processes were put in place to exclude anomalous readings and ensure that consistent and objective readings were extracted for analysis.

For this study, I decided to define engagement in terms of meaningful interactions with app features that could promote behaviour change. Engagement data captured participants' interaction with the three main components of the smartphone application: learn, track, and support. Learn interactions were defined as the total of number of articles read. Track interactions were defined as the number of times a participant viewed or had a recorded weight or steps reading. Support interactions were defined as the number of messages sent or received in either the private or group chat. Engagement was measured as the cumulative total number of interactions with these three components of the app at three time periods: 0-4 weeks, 0-12 weeks, and 0-24 weeks. The exact cut-off time point for each period were defined based on the date of the extracted single weight reading.

2.3.4 MEASURES

2.3.4.1 Exposures

The following three aspects of goal setting were self-reported in the bespoke health questionnaire which was completed as part of the enrolment process and prior to commencement of the programme: (a) **weight loss motivation**: participants selected their primary reason for weight loss, categorised as appearance, health, fitness, or self-efficacy, (b) **goal preference:** participants selected whether they normally like to set low, medium, or high goals, and (c) **percentage weight loss goal**: percentage of initial body weight that participants were aiming to lose, categorised as <5%, 5-10%, or >10%. The questionnaire was completed independently by the participant with no additional instruction.

2.3.4.2 Mediators

I explored whether engagement acts as a mediator in the association between the three aspects of goal setting and weight over the 24-week period. Total engagement, defined as the cumulative number of interactions with the three main components of the app, was considered as a mediating variable.

2.3.4.3 Outcomes

To measure sustained weight change, the primary outcome was weight at 24 weeks. The secondary outcome was drop-out, defined as programme cancellation up to and including each of the time points (4, 12, and 24 weeks).

2.3.5 Statistical Analysis

A pre-specified analysis plan was published on OSF (189). All analyses were conducted using R (version 4.1.3) with the integrated development environment R Studio. All reported *P* values are for two-sided tests, with effects considered statistically significant at $P<.05$.

Descriptive statistics were used to examine baseline characteristics of the study population, and t-tests or chi-squared tests were used to compare differences in characteristics. A cross-tabulation analysis was used to explore the relationship between the different aspects of goal setting. I also explored the association between baseline characteristics and each aspect of goal setting.

2.3.5.1 Primary Analysis

Three independent mixed-model repeated-measures analyses were used to explore the association between the three aspects of goal setting and the dependent outcome variable, weight, over a 24-week period. A between-subjects factor of goal, a within-subjects factor of week, and the interaction between week and goal were included as fixed effects. Participant was included as a random effect to account for the repeated weight measures on the same participant at 4, 12, and 24 weeks. Further models adjusted for pre-specified covariates (gender, age, IMD decile, and type 2 or pre-diabetes) as fixed effects. I decided to include diabetes as a covariate alongside demographic characteristics as it is a weight-related condition that often affects weight

loss and can also influence motivation to complete and submit weight readings in weight loss programmes (151).

In a mixed effects model, missing data can be accommodated through maximum likelihood estimation, which allows for the inclusion of all available data from participants. For this analysis, a sequential testing approach was used, as follows:

Model 1 – random effect: participant ID, fixed effects: goal and week

Model 2 – random effect: participant ID, fixed effect: goal and week, interaction term: goal x week

Model 3 - random effect: participant ID, fixed effect: goal and week, interaction term: goal x week, adjusted for gender (M or F), age (years, continuous), IMD decile (factor), and type 2 or pre-diabetes (yes or no).

The random effects term in the mixed effects model indirectly considered differences in baseline weight. Model fit was compared using the R^2 statistic and a *P* value calculated using a likelihood ratio. The final model, adjusting for all covariates (model 3), produced the best fitting model, and so this is the only model presented hereafter.

A multivariable logistic regression was used to explore the association between goals and the likelihood of drop-out of the programme at each time point. All models were adjusted for gender, age, IMD decile, type 2 or pre-diabetes, and baseline weight.

2.3.5.2 Sensitivity Analyses

A sensitivity analysis was conducted by repeating the analysis of the primary outcome using completers only (i.e., participants with complete data at all time points), to confirm the validity of the findings and to illustrate the pattern of weight change in the same individuals over time. As there were 8,403 missing IMD values and 3,054 missing goal preference values, I also conducted a sensitivity analysis using the missing-indicator method, where a 'missing' category was created and added to the model for each missing value. The random effects term in the mixed effects model will indirectly consider differences in baseline weight, but as I found differences in baseline weight between exposure groups, I conducted a further sensitivity analysis with adjustment for baseline weight to confirm the results were similar.

2.3.5.3 Mediation Analysis

Mediation analysis explored whether total engagement mediated the association between goals and weight (190). Step 1 of the mediation analysis was the primary analysis. Step 2 of the mediation analysis was a mixed effects model on the same sample, testing whether there was a significant association between goals and engagement, whilst adjusting for all covariates. For step 3, the mixed effects model of step 1 was repeated with additional adjustment for engagement as a predictor. An engagement variable was considered as a mediator if engagement significantly predicted weight, and the effect of goals was attenuated with adjustment for the engagement variable. The indirect effect and proportion of total effect mediated were calculated.

2.3.5.4 Secondary Analysis

A multivariable logistic regression was used to explore the association between goals and the likelihood of drop-out of the programme at each time point. All models were adjusted for gender, age, IMD decile, type 2 and/or pre-diabetes, and baseline weight.

2.3.6 Ethics Approval

This study was reviewed by the University of Oxford Medical Sciences Interdivisional Research Ethics Committee (Ref: R84327/RE001). Since the study only involved use of previously collected, anonymised, non-NHS data that cannot be traced back to identifiable individuals, it was confirmed as exempt from ethical review.

2.4 RESULTS

2.4.1 BASELINE CHARACTERISTICS

The mean (SD) age of the sample was 46.7 (11.1) years; baseline BMI was 34.0 (6.46) kg/m^2; and 92.1% of the sample were female (***Table 2.2***).

Table 2.2 : Baseline characteristics of total sample (N = 36,794), participants with complete (n = 3,193), and participants with incomplete weight data (n = 33,601).

	Total (N = 36,794)	Complete data (n = 3,193)	Incomplete data (n = 33,601)	P-value
Age (years), mean (SD)	46.7 (11.1)	48.7 (10.5)	46.5 (11.1)	***<0.001***
Gender, n (%)				
Male	2892 (7.9)	272 (8.5)	2620 (7.8)	0.16
Female	33902 (92.1)	2921 (91.5)	30981 (92.2)	
BMI (kg/m^2), mean (SD)	34.0 (6.46)	33.5 (6.39)	34.1 (6.46)	***<0.001***
IMD Decile, n (%)				
1-3	4379 (11.9)	357 (11.2)	4022 (12.0)	0.07
4-7	12091 (32.9)	1054 (33.0)	11037 (32.8)	
8-10	11921 (32.4)	1103 (34.5)	10818 (32.2)	
Missing	8403 (22.8)	679 (21.3)	7724 (23.0)	

P values were calculated using t-tests for continuous variables or chi-squared tests for categorical variables, to compare differences between participants with complete weight data and participants with incomplete weight data. Complete data is defined as having weight readings recorded at all time points (i.e., at 4, 12, and 24 weeks). Abbreviations: BMI: body mass index; IMD: index of multiple deprivation.

Most participants were motivated to lose weight for appearance reasons (40.1%), said they preferred to set medium goals (59.7%), and set a weight loss goal of 5-10% initial body weight (64.3%), (***Table 2.3***). More participants who said they preferred low goals,

set percentage weight loss goals of <5%. There was no clear relationship between the other aspects of goal setting.

Table 2.3: Cross-tabulation analysis to explore the relationship between A) Goal preference and percent weight loss goal, B) Percent weight loss goal and motivations, and C) Motivations and goal preference. Numbers are the percentage in each category.

A		Goal Preference				Row Total
		Low	Medium	High	Undefined	
Percent goal	<5	27.0	60.2	10.5	2.2	6.4
	5-10	12.5	57.6	20.4	9.5	64.3
	>10	15.3	60.6	15.8	8.3	29.3
Column Total		15.3	59.7	16.7	8.3	100

B		Percent Goal			Row Total
		<5	5-10	>10	
Motivations	Appearance	6.9	62.7	30.4	40.1
	Fitness	8.4	62.9	28.7	13.8
	Health	5.2	66.7	28.1	27.6
	Self-efficacy	5.9	64.8	29.3	18.5
Column Total		6.4	64.3	29.3	100

C		Motivations				Row Total
		Appearance	Fitness	Health	Self-efficacy	
Goal preference	Low	34.6	15.4	30.6	19.3	15.3
	Medium	39.8	14.4	28.4	17.4	59.7
	High	43.6	11.5	23.3	21.6	16.7
	Undefined	44.2	11.4	25.8	18.5	8.3
Column Total		40.1	13.8	27.6	18.5	100

Older participants tended to be motivated by health and fitness, men tended to be motivated less by appearance and self-efficacy than women, those who had a higher baseline BMI were motivated more by health reasons (***Table 2.4***). Those motivated by fitness set the lowest percentage weight loss goals, and those motivated by health set the highest. The distribution of IMD deciles was different between the motivation groups; in general, more people from higher IMD deciles selected appearance as their reason for weight loss and more people from lower IMD deciles selected fitness or self-efficacy.

Table 2.4: Baseline characteristics and weight change categorised by weight loss motivation.

	Appearance (n=14,736)	Fitness (n=5,092)	Health (n=10,177)	Self-efficacy (n=6,789)	P-value
Age (years), mean (SD)	44.8 (10.8)	49.2 (11.2)	49.4 (10.9)	45.1 (10.7)	***<0.001***
Gender, n (%)					
Male	1051 (7.1)	484 (9.5)	1046 (10.3)	311 (4.6)	***<0.001***
Female	13685 (92.9)	4608 (90.5)	9131 (89.7)	6478 (95.4)	
BMI (kg/m^2), mean (SD)	31.7 (4.91)	33.7 (6.26)	36.8 (7.08)	35.1 (6.63)	***<0.001***
IMD Decile, n (%)					
1-3	1659 (11.3)	659 (12.9)	1209 (11.9)	852 (12.5)	***<0.001***
4-7	4819 (32.7)	1638 (32.2)	3434 (33.7)	2200 (32.4)	
8-10	4928 (33.4)	1525 (29.9)	3266 (32.1)	2202 (32.4)	
Missing	3330 (22.6)	1270 (24.9)	2268 (22.3)	1535 (22.6)	
Percentage weight loss goal, mean (SD)	9.22 (3.98)	8.97 (10.9)	9.41 (3.95)	9.35 (3.88)	***<0.001***
Weight change at 4 weeks (kg)					
Mean (SD)	-3.88 (2.58)	-4.13 (2.83)	-4.57(3.37)	-4.15 (2.98)	***<0.001***
Missing, n (%)	8431 (57.2)	2957 (58.1)	5805 (57.0)	4146 (61.1)	
Weight change at 12 weeks (kg)					
Mean (SD)	-5.53 (3.87)	-5.98 (4.26)	-6.66 (4.72)	-5.59 (4.48)	***<0.001***
Missing, n (%)	11632 (78.9)	4062 (79.8)	7925 (77.9)	5548 (81.7)	
Weight change at 24 weeks (kg)					
Mean (SD)	-5.91 (5.38)	-6.24 (5.65)	-7.40 (6.53)	-5.90 (6.37)	***<0.001***
Missing, n (%)	12768 (86.6)	4446 (87.3)	8746 (85.9)	6016 (88.6)	

P values were calculated using t-tests for continuous variables or chi-squared tests for categorical variables. Abbreviations: BMI: body mass index; IMD: index of multiple deprivation.

Participants who preferred to set higher goals were younger, a greater proportion were male, had lower baseline BMI (compared to low), and set higher percentage weight loss goals (***Table 2.5***).

Table 2.5: Baseline characteristics and weight change categorised by goal preference.

	Low (n=5,597)	Medium n=21,963)	High (n=6,180)	Undefined (n=3,054)	P-value
Age (years), mean (SD)	47.9 (11.2)	47.7 (11.0)	43.8 (10.5)	43.9 (11.2)	***<0.001***
Gender, n (%)					
Male	184 (3.3)	1502 (6.8)	816 (13.2)	390 (12.8)	***<0.001***
Female	5413(96.7)	20461(93.2)	5364 (86.8)	2664 (87.2)	
BMI (kg/m^2), mean (SD)	35.5 (6.90)	33.8 (6.34)	33.6 (6.34)	33.6 (6.39)	***<0.001***
IMD Decile, n (%)					
1-3	710 (12.7)	2614 (11.9)	721 (11.7)	334 (10.9)	0.27
4-7	1822 (32.6)	7251 (33.0)	2042 (33.0)	976 (32.0)	
8-10	1750 (31.3)	7199 (32.8)	2049 (33.2)	923 (30.2)	
Missing	1315 (23.5)	4899 (22.3)	1368 (22.1)	821 (26.9)	
Percentage weight loss goal, mean (SD)	8.76 (4.18)	9.18 (6.17)	9.74 (4.38)	9.75 (3.79)	***<0.001***
Weight change at 4 weeks (kg)					
Mean (SD)	-4.08 (3.29)	-4.10 (2.80)	-4.45 (3.10)	-4.18 (2.91)	***<0.001***
Missing, n (%)	3337 (59.6)	12405 (56.5)	3845 (62.2)	1752 (57.4)	
Weight change at 12 weeks (kg)					
Mean (SD)	-5.77 (4.18)	-5.95 (4.17)	-5.85 (4.74)	-6.22 (4.78)	0.17
Missing, n (%)	4468 (79.8)	17238 (78.5)	5101 (82.5)	2360 (77.3)	
Weight change at 24 weeks (kg)					
Mean (SD)	-6.34(6.04)	-6.40 (5.76)	-6.08 (6.37)	-6.97 (6.58)	0.11
Missing, n (%)	4872 (87.0)	19035 (86.7)	5440 (88.0)	2629 (86.1)	

P values were calculated using t-tests for continuous variables or chi-squared tests for categorical variables. N= 3,054 did not select a goal preference in the health questionnaire. Abbreviations: BMI: body mass index; IMD: index of multiple deprivation.

Participants who set higher percentage weight loss goals were younger; a greater proportion were male and had higher baseline BMI (***Table 2.6***).

Table 2.6: Baseline characteristics and weight change categorised by percentage weight loss goal.

	<5% (N=2,370)	5-10% (N=23,629)	>10% (N=10,795)	P-value
Age (years), mean (SD)	49.0 (12.6)	46.6 (11.1)	46.4 (10.8)	***<0.001***
Gender, n (%)				
Male	169 (7.1)	1810 (7.7)	913 (8.5)	***0.04***
Female	2201 (92.9)	21819 (92.3)	9882 (91.5)	
BMI (kg/m^2), mean (SD)	31.4 (5.51)	34.3 (6.58)	33.9 (6.24)	***<0.001***
IMD Decile, n (%)				
1-3	275 (11.6)	2858 (12.1)	1246 (11.5)	0.43
4-7	730 (30.8)	7697 (32.6)	3664 (33.9)	
8-10	751 (31.7)	7596 (32.1)	3574 (33.1)	
Missing	614 (25.9)	5478 (23.2)	2311 (21.4)	
Weight change at 4 weeks (kg)				
Mean (SD)	-3.12 (3.05)	-3.33 (2.16)	-5.36 (3.39)	***<0.001***
Missing, n (%)	1971 (83.2)	14932 (63.2)	4436 (41.1)	
Weight change at 12 weeks (kg)				
Mean (SD)	-3.86 (4.84)	-3.96 (3.09)	-7.71 (4.41)	***<0.001***
Missing, n (%)	2166 (91.4)	20223 (85.6)	6778 (62.8)	
Weight change at 24 weeks (kg)				
Mean (SD)	-3.06 (4.52)	-3.45 (4.28)	-8.65 (6.08)	***<0.001***
Missing, n (%)	2230 (94.1)	21692 (91.8)	8054 (74.6)	

P values were calculated using t-tests for continuous variables or chi-squared tests for categorical variables. Abbreviations: BMI: body mass index; IMD: index of multiple deprivation.

2.4.2 Data Availability

Amongst those who remained in the programme, weight data was incomplete. Of the 36,794 participants in the cohort, 42.0% (n = 15,455) had weight data available at 4 weeks, 20.7% (n = 7,627) at 12 weeks, and 13.1% (n = 4,818) at 24 weeks, whilst 8.7% (n

= 3,193) had weight readings recorded at all time points. Examination of the participants with complete weight data at all time points, compared to participants with at least one missing weight reading, found no difference between gender or IMD decile (***Table 2.2***). Although there were statistically significant differences for age and baseline BMI, these differences were not clinically meaningful.

Cumulative drop-out of the programme at 4, 12, and 24 weeks was 13.9%, 41.4% and 62.0% respectively. ***Figure 2.2*** shows the drop-out from 0 to 24 weeks. To summarise, there was some drop-out in the first two weeks of the programme, then a steady rate of drop-out week-on-week until the end of the programme at 12 weeks. There is a large amount of drop-out at the end of the core 12-week programme, then up to 24 weeks drop-out occurred monthly.

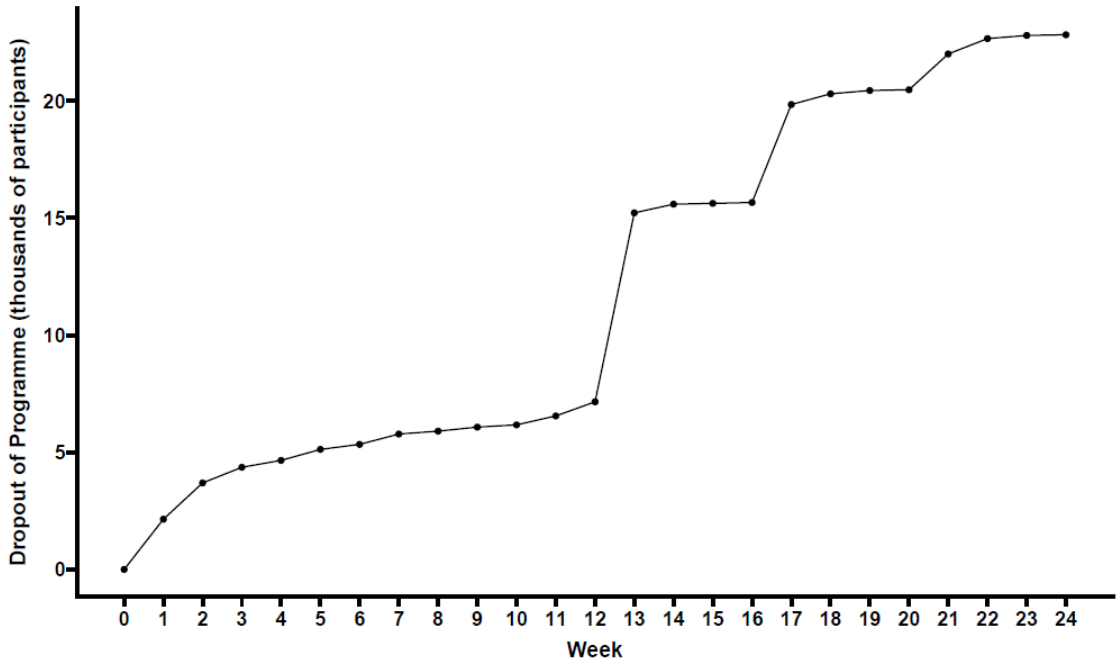

Figure 2.2: Cumulative drop-out of programme at each week

2.4.3 Association Between Goal Setting and Weight Change over a 24-Week Period

Unadjusted weight change at 4, 12, and 24 weeks was found to be -4.16 (2.94) kg, -5.93 (4.31) kg, and -6.40 (5.97) kg, respectively.

2.4.3.1 Weight Loss Motivation

I examined the association between weight loss motivation and weight over a 24-week period and found a between-group difference for baseline weight (***Table 2.7***)**.** At baseline, those motivated for fitness, health, and self-efficacy reasons weighed 6.1 kg, 14.8 kg, and 10.1 kg more than those motivated by appearance, respectively.

On average those motivated by appearance had a weight change of -3.8kg at 4 weeks; -5.24kg at 12 weeks; and -5.57 kg at 24 weeks. At 24 weeks, compared to appearance, those motivated for health reasons lost 1.40 kg more (95% CI: 1.15, 1.65; *P*<.001) and those motivated for fitness reasons lost 0.38 kg more than appearance (95% CI: 0.05, 0.70; *P*=.03). A sensitivity analysis using completers only also found that those motivated by health lost more weight at all time points but there was no difference between appearance and fitness.

Figure 2.3 depicts the results as mean weight change for each type of motivation.

Table 2.7 : Results of mixed effects model for the association between weight loss motivation and weight using all available data (n = 28,391) or completers (n = 2,514).

Variables	All Data (n = 28,391)			Completers (n = 2,514)		
	Coef	95% CI	P-value	Coef	95% CI	P-value
Motivations (ref = Appearance)						
Fitness	6.06	(5.41,6.71)	***<0.001***	6.37	(4.33,8.4)	***<0.001***
Health	14.81	(14.29,15.33)	***<0.001***	14.71	(13.09,16.33)	***<0.001***
Self-efficacy	10.08	(9.51,10.66)	***<0.001***	8.42	(6.43,10.4)	***<0.001***
Week (ref = 0)						
4	-3.80	(-3.91,-3.7)	***<0.001***	-4.59	(-4.84,-4.35)	***<0.001***
12	-5.24	(-5.38,-5.11)	***<0.001***	-6.33	(-6.57,-6.08)	***<0.001***
24	-5.57	(-5.73,-5.4)	***<0.001***	-6.77	(-7.01,-6.52)	***<0.001***
Interaction terms						
Fitness*week4	-0.22	(-0.42,-0.02)	***0.03***	-0.12	(-0.59,0.36)	0.64
Fitness*week12	-0.41	(-0.68,-0.14)	***<0.001***	-0.26	(-0.74,0.22)	0.28
Fitness*week24	-0.38	(-0.7,-0.05)	***0.03***	-0.34	(-0.81,0.14)	0.17
Health*week4	-0.73	(-0.89,-0.58)	***<0.001***	-0.75	(-1.12,-0.38)	***<0.001***
Health*week12	-1.12	(-1.32,-0.91)	***<0.001***	-1.15	(-1.52,-0.79)	***<0.001***
Health*week24	-1.40	(-1.65,-1.15)	***<0.001***	-1.54	(-1.91,-1.17)	***<0.001***
Self-efficacy*week4	-0.25	(-0.44,-0.07)	***0.01***	-0.14	(-0.61,0.32)	0.55
Self-efficacy*week12	-0.06	(-0.31,0.19)	0.63	0.21	(-0.25,0.68)	0.37
Self-efficacy*week24	0.08	(-0.22,0.39)	0.59	0.21	(-0.25,0.68)	0.37

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes. 8,403 participants had missing IMD values.

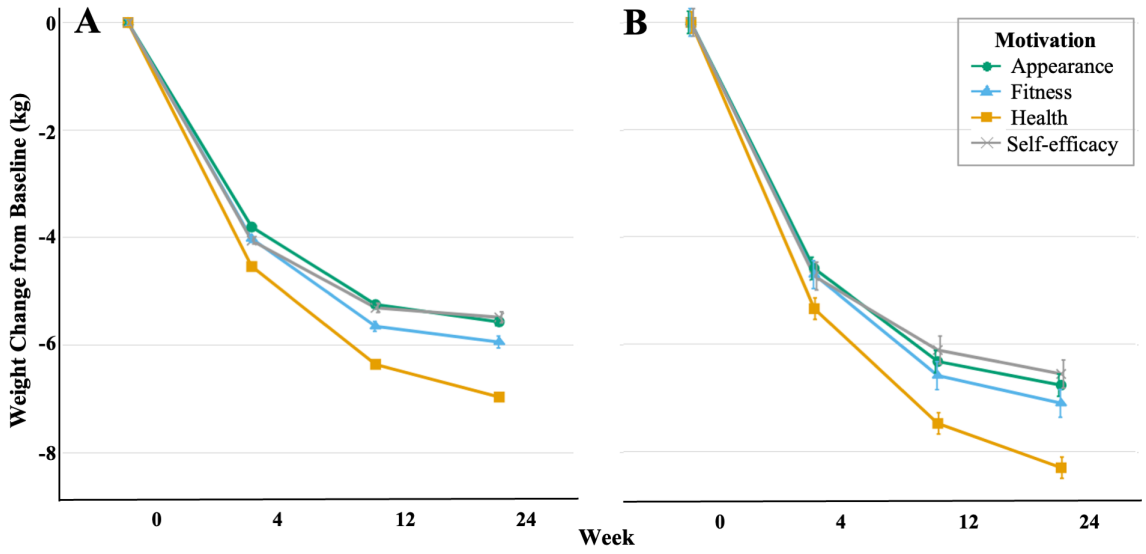

Figure 2.3: Mean adjusted weight change for each type of weight loss motivation using A) all available data (n = 28,391) or B) completers (n = 2,514). Weight change (kg) at 4, 12, and 24 weeks calculated from mixed effects models, adjusted for age, gender, IMD, and Type 2 and/or pre-diabetes. Values represent mean (standard error of mean).

2.4.3.2 Overall Goal Preference

I examined the association between goal preference and weight over a 24-week period and found that at baseline, those who preferred low goals were 3.60kg (95% CI: 2.98, 4.22; *P*<.001) heavier at baseline than those who preferred medium goals (***Table 2.8***). There was no difference between medium and high goals.

On average those who preferred medium goals had a weight change of -4.03kg at 4 weeks; -5.63kg at 12 weeks; and -6.02kg at 24 weeks. There was no difference between medium and high goals. Compared to those who preferred medium goals, high goal preference was associated with greater weight loss at 4 weeks, but less at 24 weeks. At 24 weeks, those who preferred high goals lost 0.34kg less (95% CI: 0.05, 0.64; *P*=.02) than those who preferred medium goals. A sensitivity analysis using completers only did not

replicate these results and found that there was no difference between the different goal preferences at either 4, 12, or 24 weeks. ***Figure 2.4*** depicts the results as mean weight change for each type of goal preference.

Table 2.8 : Results of mixed effects model for the association between goal preference and weight using all available data (n = 26,158) or completers (n = 2,294)

Variables	All Data (n = 26,158)			Completers (n = 2,294)		
	Coef	95% CI	P-value	Coef	95% CI	P-value
Goal Preference (ref = medium)						
High	-0.01	(-0.61, 0.59)	0.98	-0.24	(-2.31,1.83)	0.82
Low	3.60	(2.98,4.22)	***<0.001***	3.32	(1.34,5.3)	***<0.001***
Week (ref = 0)						
4	-4.03	(-4.11,-3.95)	***<0.001***	-4.77	(-4.96,-4.58)	***<0.001***
12	-5.63	(-5.74,-5.53)	***<0.001***	-6.63	(-6.82,-6.43)	***<0.001***
24	-6.02	(-6.16,-5.89)	***<0.001***	-7.23	(-7.42,-7.03)	***<0.001***
Interaction terms						
High*Week4	-0.29	(-0.47,-0.1)	***<0.001***	-0.25	(-0.7,0.21)	0.29
High*Week12	0.06	(-0.19,0.31)	0.63	0.00	(-0.45, 0.46)	0.99
High*Week24	0.34	(0.05,0.64)	***0.02***	0.19	(-0.26, 0.65)	0.41
Low*Week4	-0.02	(-0.21, 0.16)	0.79	-0.10	(-0.53, 0.34)	0.67
Low*Week12	0.11	(-0.14, 0.36)	0.38	-0.01	(-0.44, 0.43)	0.98
Low*Week24	-0.01	(-0.31, 0.29)	0.95	0.02	(-0.41, 0.46)	0.92

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes. 8,403 participants had missing IMD values. 3,054 participants had missing goal preference values.

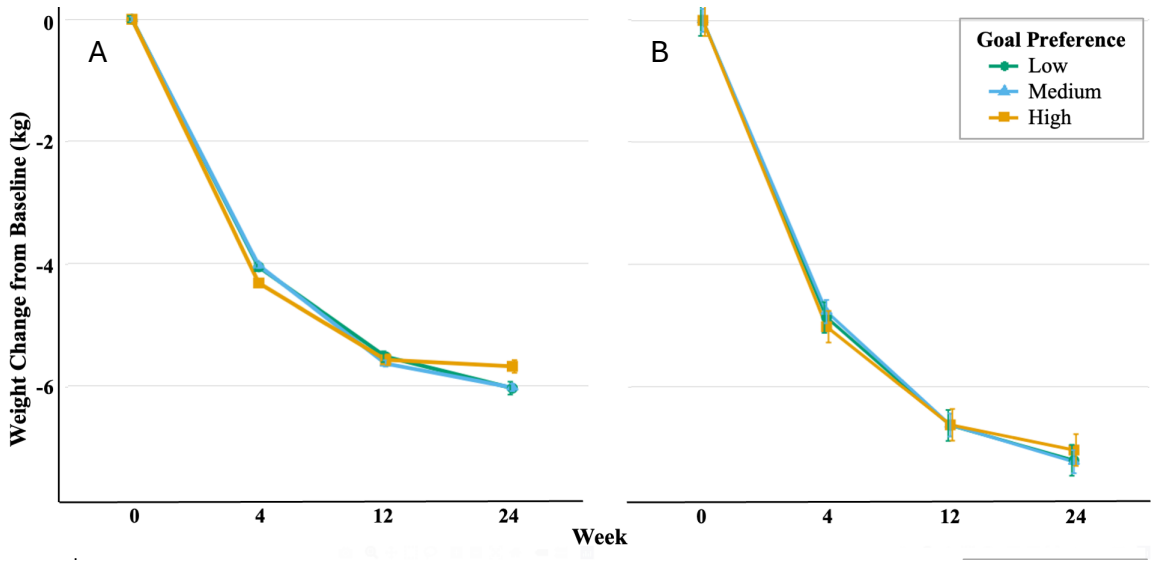

Figure 2.4 : Mean adjusted weight change for each type of goal preference using A) all available data (n = 26,158) or B) completers (n = 2,194). Weight change (kg) at 4, 12, and 24 weeks calculated from mixed effects models, adjusted for age, gender, IMD, and Type 2 and/or pre-diabetes. Values represent mean (standard error of mean).

2.4.3.3 Percentage Weight Loss Goal

I examined the association between goal preference and weight over a 24-week period. At baseline, those who set goals of <5% weighed 7.99kg less (95% CI: 7.09, 8.90; *P*<.001) and those who set goals of >10% weighed 0.99kg less (95% CI: 0.51, 1.47; *P*<.001), compared to goals of 5-10% (***Table 2.9***).

On average those who set goals of 5-10% had a weight change of -3.28kg at 4 weeks; -3.83kg at 12 weeks; and -3.27kg at 24 weeks. Those who set goals of >10% lost significantly more weight at all time points compared to those who set goals of 5-10%. At 24 weeks, those who set goals of >10% lost 5.21kg more (95% CI: 5.01, 5.41; *P*<.001)

compared to those who set goals of 5-10%. Furthermore, those who set goals of >10% continued to lose weight after the programme ended up until 24 weeks, whereas those who set goals of <10% regained some of the weight loss after programme end. A sensitivity analysis using completers only, found a similar pattern of weight change over 24 weeks for each percentage category. ***Figure 2.5*** depicts the results as mean weight change for each percent weight loss goal category.

Table 2.9 : Results of mixed effects model for the association between percent weight loss goal and weight using all available data (n = 28,391) or completers (n = 2,514)

Variables	All Data (n = 28,391)			Completers (n = 2,514)		
	Coef	95% CI	P-value	Coef	95% CI	P-value
Percent Category (ref = 5-10%)						
<5%	-7.99	(-8.9,-7.09)	***<0.001***	-2.13	(-6.49,2.24)	0.34
>10%	-0.99	(-1.47,-0.51)	***<0.001***	0.35	(-1.1,1.8)	0.64
Week (ref = 0)						
4	-3.28	(-3.36,-3.2)	***<0.001***	-3.85	(-4.09,-3.62)	***<0.001***
12	-3.83	(-3.94,-3.71)	***<0.001***	-4.54	(-4.78,-4.3)	***<0.001***
24	-3.27	(-3.42,-3.12)	***<0.001***	-4.18	(-4.42,-3.94)	***<0.001***
Interaction terms						
<5*Week4	0.37	(-0.01,0.75)	0.05	-0.18	(-1.08,0.73)	0.70
<5*Week12	0.43	(-0.08,0.93)	0.10	-0.33	(-1.24,0.57)	0.47
<5*Week24	0.59	(0.0,1.18)	0.05	-0.14	(-1.04,0.77)	0.77
>10*Week4	-2.01	(-2.13,-1.88)	***<0.001***	-1.64	(-1.94,-1.34)	***<0.001***
>10*Week12	-3.69	(-3.86,-3.53)	***<0.001***	-3.50	(-3.8,-3.2)	***<0.001***
>10*Week24	-5.21	(-5.41,-5.01)	***<0.001***	-5.04	(-5.34,-4.73)	***<0.001***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes. 8,403 participants had missing IMD values

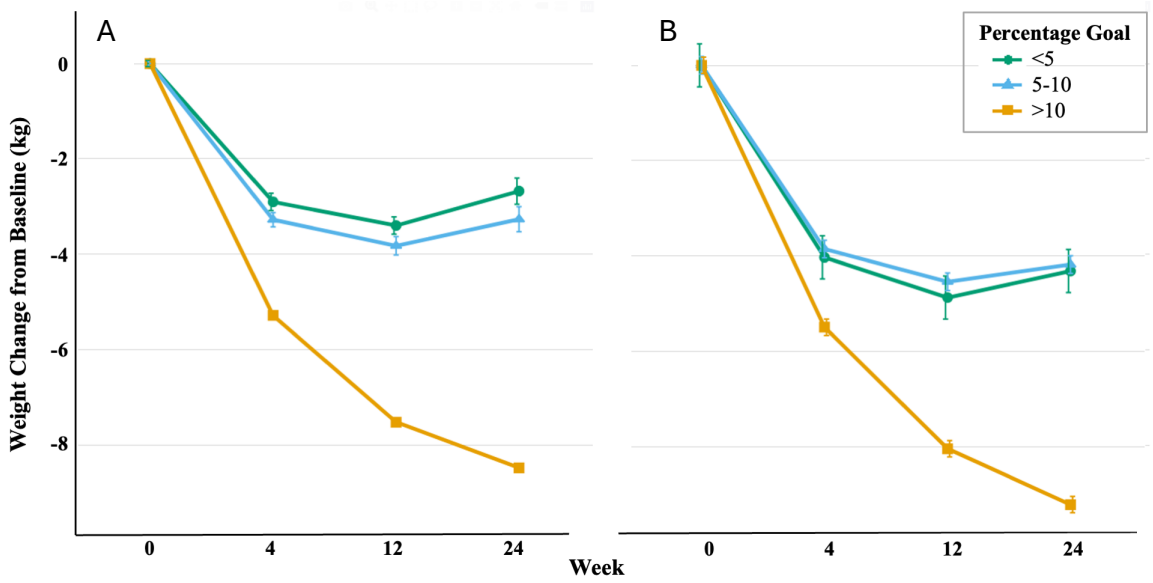

Figure 2.5 : Mean adjusted weight change for each percent weight loss goal category using A) all available data (n = 28,391) or B) completers (n = 2,514). Weight change (kg) at 4, 12, and 24 weeks calculated from mixed effects models, adjusted for age, gender, IMD, and Type 2 and/or pre-diabetes. Values represent mean (standard error of mean).

2.4.3.4 Sensitivity Analyses

Further sensitivity analyses using the missing-indicator method (***Appendix 2.2***) and with adjustment for baseline weight (***Appendix 2.3***) also showed similar results for each aspect of goal setting.

2.4.4 Association Between Goal Setting and Weight Change as Mediated by Engagement

Tracking was the most frequent form of engagement at every time point, though engagement of all types declined over time (***Figure 2.6***). The three measures of engagement (learn, track, and support) were summed to a composite measure of total engagement which will be considered as a mediator variable.

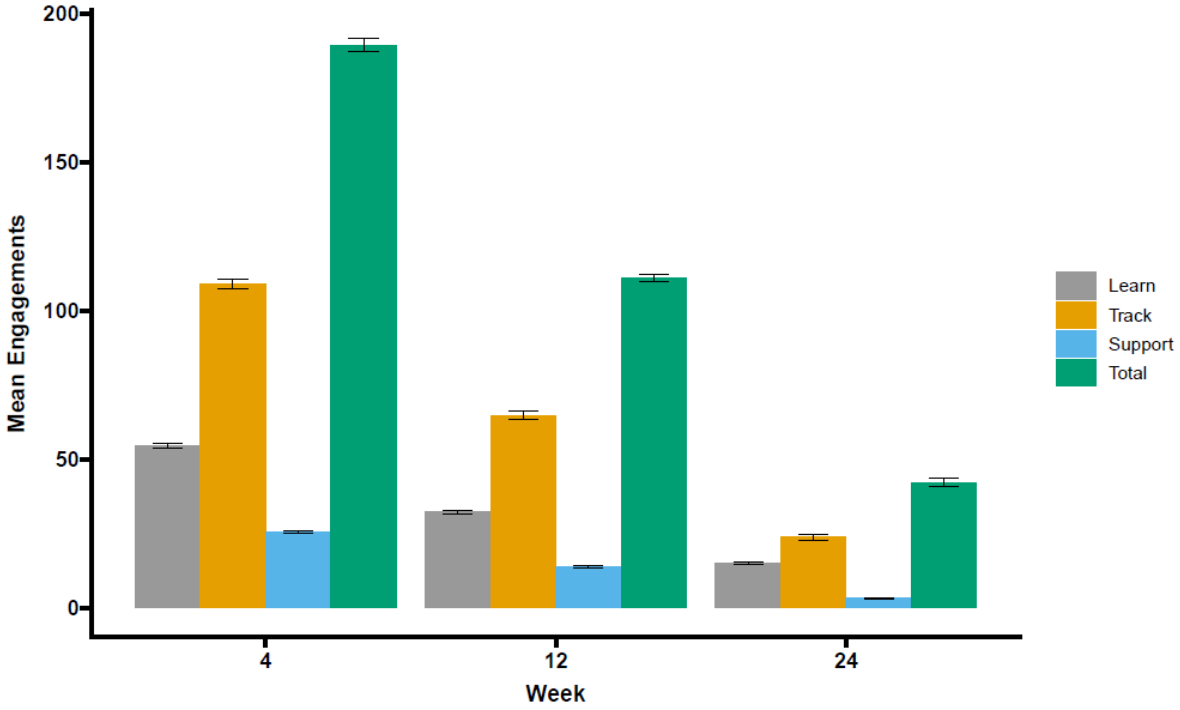

Figure 2.6 : Mean learn, track, support, and total engagements at 4, 12, and 24 weeks. Values are mean engagements from 0-4 weeks, 4-12 weeks, and 12-24 weeks. Errors bars are 95% confidence intervals.

I conducted a mediation analysis to investigate whether total engagement mediated the association between goals and weight loss.

Step 1 of the mediation analysis replicates the primary analysis showing a significant effect of motivation type on weight loss (***Table 2.10***). Step 2 revealed that the type of motivation significantly predicted engagement. Step 3 shows that, with additional adjustment for engagement, engagement affected weight change independently of type of motivation. For each additional 100 engagements, participants lost 0.21kg more weight (95% CI: -0.22, -0.19). At the same time there was still a significant effect of motivation on weight. At 24 weeks, health lost 1.41kg more than appearance, and fitness lost 0.36kg more than appearance. Therefore, engagement can be considered an

independent predictor of weight loss but not a mediator of the association between motivation and weight.

Percent weight loss goal significantly predicted engagement but was not a mediator in the association between percent weight loss goal and weight (***Table 2.11***). For each additional 100 engagements, participants lost 0.16kg more weight (95% CI: -0.17, -0.15). However, there was still a significant effect of percent weight loss goal on weight. At 24 weeks, people who set goals of >10% lost 4.84kg more than those who set goals of 5-10%, showing that engagement was not a major mediator of the difference in weight change between motivation groups.

Table 2.10: Mediation analysis results for the association between weight loss motivation and weight, as mediated by total engagement.

Variables	Step 1 - Association with weight			Step 2 - Association with total engagement			Step 3 - Association with weight adjusted for engagement		
	Coef	95% CI	P-value	Coef	95% CI	P-value	Coef	95% CI	P-value
Motivation (ref = appearance)									
Fitness	6.06	(5.41,6.71)	***<0.001***	-3.55	(-16.12,9.02)	0.58	6.06	(5.41,6.71)	***<0.001***
Health	14.81	(14.29,15.33)	***<0.001***	-1.27	(-11.24,8.69)	0.80	14.81	(14.29,15.33)	***<0.001***
Self-efficacy	10.08	(9.51,10.66)	***<0.001***	0.69	(-10.45,11.84)	0.90	10.08	(9.51,10.66)	***<0.001***
Week (ref = 0)									
4	-3.80	(-3.91,-3.7)	***<0.001***	200.73	(194.81,206.66)	***<0.001***	-3.18	(-3.28,-3.07)	***<0.001***
12	-5.24	(-5.38,-5.11)	***<0.001***	319.49	(313.56,325.42)	***<0.001***	-3.96	(-4.11,-3.81)	***<0.001***
24	-5.57	(-5.73,-5.4)	***<0.001***	361.77	(355.85,367.7)	***<0.001***	-3.88	(-4.07,-3.7)	***<0.001***

Interaction terms									
Fitness*Week4	-0.22	(-0.42,-0.02)	***0.03***	-19.89	(-31.72,-8.06)	***<0.001***	-0.24	(-0.44,-0.05)	***0.02***
Fitness*Week12	-0.41	(-0.68,-0.14)	***<0.001***	-27.63	(-39.46,-15.8)	***<0.001***	-0.42	(-0.69,-0.16)	***<0.001***
Fitness*Week24	-0.38	(-0.7,-0.05)	***0.03***	-27.40	(-39.23,-15.57)	***<0.001***	-0.36	(-0.68,-0.04)	***0.03***
Health*Week4	-0.73	(-0.89,-0.58)	***<0.001***	-10.55	(-19.81,-1.29)	***0.03***	-0.77	(-0.92,-0.62)	***<0.001***
Health*Week12	-1.12	(-1.32,-0.91)	***<0.001***	-12.17	(-21.44,-2.91)	***0.01***	-1.15	(-1.35,-0.95)	***<0.001***
Health*Week24	-1.40	(-1.65,-1.15)	***<0.001***	-6.44	(-15.7,2.82)	0.17	-1.41	(-1.65,-1.16)	***<0.001***
Self-efficacy*Week4	-0.25	(-0.44,-0.07)	***0.01***	-13.83	(-24.39,-3.28)	***0.01***	-0.27	(-0.45,-0.09)	***<0.001***
Self-efficacy*Week12	-0.06	(-0.31,0.19)	0.63	-34.36	(-44.92,-23.81)	***<0.001***	-0.14	(-0.38,0.11)	0.26
Self-efficacy*Week24	0.08	(-0.22,0.39)	0.59	-39.88	(-50.43,-29.33)	***<0.001***	-0.05	(-0.35,0.25)	0.75
Total engagement (per 100 engagements)							-0.21	(-0.22,-0.19)	***<0.001***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes

Table 2.11: Mediation analysis results for the association between percent weight loss goal and weight, as mediated by total engagement.

Variables	**Step 1 - Association with weight**			**Step 2 - Association with total engagement**			**Step 3 - Association with weight adjusted for engagement**		
	Coef	95% CI	P-value	Coef	95% CI	P-value	Coef	95% CI	P-value
Percent Category (ref = 5-10%)									
<5%	-7.99	(-8.9,-7.09)	***<0.001***	-3.44	(-19.59,12.72)	0.68	-7.99	(-8.9,-7.09)	***<0.001***
>10%	-0.99	(-1.47,-0.51)	***<0.001***	0.01	(-8.49,8.51)	1.00	-0.99	(-1.47,-0.51)	***<0.001***
Week (ref = 0)									
4	-3.28	(-3.36,-3.2)	***<0.001***	169.66	(165.11,174.22)	***<0.001***	-2.83	(-2.92,-2.75)	***<0.001***
12	-3.83	(-3.94,-3.71)	***<0.001***	255.55	(251.0,260.1)	***<0.001***	-2.95	(-3.07,-2.82)	***<0.001***
24	-3.27	(-3.42,-3.12)	***<0.001***	280.64	(276.09,285.19)	***<0.001***	-2.17	(-2.33,-2.00)	***<0.001***
Interaction terms									

<5*Week4	0.37	(-0.01,0.75)	0.05	-96.48	(-111.8,-81.15)	***<0.001***	0.31	(-0.06,0.68)	0.11
<5*Week12	0.43	(-0.08,0.93)	0.10	-139.85	(-155.17,-124.52)	***<0.001***	0.34	(-0.15,0.84)	0.17
<5*Week24	0.59	(0,1.18)	0.05	-147.50	(-162.82,-132.18)	***<0.001***	0.51	(-0.07,1.09)	0.09
>10*Week4	-2.01	(-2.13,-1.88)	***<0.001***	96.58	(88.52,104.64)	***<0.001***	-1.93	(-2.05,-1.81)	***<0.001***
>10*Week12	-3.69	(-3.86,-3.53)	***<0.001***	197.83	(189.77,205.9)	***<0.001***	-3.49	(-3.65,-3.33)	***<0.001***
>10*Week24	-5.21	(-5.41,-5.01)	***<0.001***	258.99	(250.93,267.06)	***<0.001***	-4.84	(-5.04,-4.64)	***<0.001***
Total engagement (per 100 engagements)							-0.16	(-0.17,-0.15)	***<0.001***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes.

2.4.5 Association Between Goals and Drop-Out of Programme

There was a lower likelihood of drop-out for those motivated by health, compared to those motivated by appearance at all time points (***Table 2.12***). At 24 weeks, those motivated by fitness reasons were less likely to drop-out compared to appearance. There was a lower likelihood of drop-out for those who preferred medium goals, compared to those who preferred high or low goals at 4 and 12 weeks. There was also a lower likelihood of drop-out for those who preferred medium goals at 24 weeks, compared to high goals. Finally, those who set lower percentage weight loss goals were more likely to drop-out at 4, 12, and 24 weeks.

Table 2.12: Association between goals and likelihood of drop-out of programme at 4, 12, and 24 weeks.

	Drop-out at 4 weeks		Drop-out at 12 weeks		Drop-out at 24 weeks	
Factor	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Percent weight loss goal (ref = 5–10%)						
<5%	2.71 (2.45, 3.01)	***<0.001***	1.60 (1.44, 1.77)	***<0.001***	1.32 (1.17, 1.5)	***<0.001***
>10%	0.40 (0.37, 0.44)	***<0.001***	0.46 (0.44, 0.49)	***<0.001***	0.40 (0.38, 0.42)	***<0.001***
Goal Preference (ref = medium)						
Low	1.20 (1.10, 1.30)	***<0.001***	1.17 (1.09, 1.25)	***<0.001***	1.07 (1.00,1.16)	0.058
High	1.13 (1.04, 1.22)	***0.002***	1.17 (1.09, 1.24)	***<0.001***	1.20 (1.11, 1.29)	***<0.001***
Motivation (ref = appearance)						
Fitness	0.94 (0.85, 1.03)	0.179	0.93 (0.86, 1.00)	0.053	0.92 (0.85, 1.00)	***0.038***
Health	0.90 (0.83, 0.98)	***0.012***	0.88 (0.83, 0.94)	***<0.001***	0.84 (0.78, 0.89)	***<0.001***
Self-efficacy	1.09 (1, 1.18)	***0.041***	1.04 (0.97, 1.11)	0.289	1.05 (0.98, 1.14)	0.161

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes. Abbreviations: CI: confidence interval; OR: odds ratio.

2.5 Discussion

2.5.1 Principal Results

The Second Nature programme was broadly successful for weight loss irrespective of demographic characteristics and goal setting. The programme led to clinically meaningful weight loss at 24 weeks of 6.40 kg (equivalent to 6.8%) among participants that continued to weigh themselves. Differences in relation to demographic characteristics or goal setting were small. Health and fitness motivations were associated with greater weight losses and lower likelihood of drop-out, compared to appearance at 24 weeks. Setting weight loss goals of >10% was associated with an average 5.21 kg greater weight losses than setting the more common 5-10% goal, and an average 60% lower odds of drop-out at 24 weeks. There was no clear association between goal preference and weight loss. Engagement with programme components decreased over time and higher engagement was a significant independent predictor of weight loss, but not a mediator of the effect of goals on weight loss.

2.5.2 Comparison With Prior Work

In contrast to the present study, previous research on weight loss motivations has typically found health to be the primary motivating factor, with appearance cited less frequently (162, 181). The differences observed here could be due to the recruitment strategy and resultant selection bias. Patients recruited from medical centres in a research setting may be more likely to give health as their reason for weight loss, compared to this analysis of data in a community setting where participants were self-

funding programme attendance. However, consonant with previous research, I found that health motivation was associated with greater weight loss than appearance (181, 185). This could be explained by self-determination theory and goal contents (191). Goal contents are distinguished by the extent to which they fill basic psychological needs. Intrinsic goals (e.g., to improve health) are more closely related to the fulfilment of psychological needs, whereas extrinsic goals (e.g., to improve appearance), are not essential to well-being and personal development. Research has shown that extrinsic goals provide motivation in the short-term, whereas intrinsic goals are more beneficial for long-term results (192). Although health or fitness motivators cannot be easily categorised as intrinsic or extrinsic, the present results suggests that the underlying motivational reason may be more important than increasing overall motivation. Weight loss motivation may also differ across different demographic groups, which could explain previously observed differences in outcomes (182, 193).

The finding that participants who set larger weight loss goals lost more weight at 24 weeks, challenges current UK clinical guidelines which encourage a weight loss goal of 5-10% weight loss (37). In fact, the present study supports previous findings demonstrating that setting a higher weight loss goal is associated with greater weight loss at 12 months than lesser goals (173), and a systematic review which reports goal difficulty as one of the main factors which makes goal setting effective (194). The present study also found that participants who set goals of >10% continue to lose weight after programme end, whereas those who set goals of <10% regained some weight up to 24 weeks. For some people, setting a larger weight loss goal may be more motivating, and it has been suggested that higher goals are more self-relevant and provide a sense of

direction and purpose (195). Higher goals have also been associated with greater effort in the weight loss attempt (171), as is predicted by goal setting theory which suggests that goals have an energising function, causing greater effort directed towards more challenging goals (156). These findings suggest that recommendations on setting realistic weight loss goals should be reconsidered.

Goal preference had no clear association with weight loss. As the primary outcome was weight, I was only able to consider participants who submitted weight readings. It could be that those who stopped weighing themselves or dropped out were unsuccessful in their weight loss attempts. This temporal sequence of events has been shown previously, whereby users tend to gain weight and reduce their weight loss efforts prior to ceasing weight tracking (196). Thus, the lack of association with goal preference could be driven by differences in attrition, as those who liked to set high goals were 1.2 times more likely to drop-out by 24 weeks (P<.001). The association between higher weight loss expectations and greater attrition has also been shown previously (168). It is possible that when goals are perceived as too ambitious individuals experience impaired performance, which discourages a person's belief in their ability to control their weight, leading to abandonment of weight management behaviours (164, 165, 197). Alternatively, the bespoke health questionnaire, completed as part of the enrolment process, may not have accurately measured goal preference, particularly as this is a subjective measure, shown by a lack of correlation between the goal preference and percentage weight loss goal variables.

The mediation analysis found that participants who engaged more with programme components tend to lose more weight, as reported previously (133, 136, 198), but this is independent of the type of goal set. Therefore, engagement can be considered an independent predictor of weight loss but not a mediator of the association between goals and weight. Maintaining engagement and retaining participants over time is key to the success of digital weight loss interventions. The modification of goal setting via pre-treatment recommendations may be a means to maintain engagement which is worth further exploration.

2.5.3 Strengths & Limitations

To date, no study in a community setting has explored the association between goals and weight loss on this scale and detail, with three different aspects of goal setting reported. The use of this dataset allows for greater confidence than other studies in terms of the robustness and generalisability of the findings. Strengths include the large sample, the pre-registration of the analysis plan, and prospective design. Although the population sample is predominantly female, this is broadly representative of enrolment in most private weight management services (124, 199).

The limitations of this study largely reflect the challenges associated with analyses of a population in an uncontrolled, community setting. The observational nature means causal relationships cannot be determined, and randomised controlled trials are required to confirm these results. There was a large proportion of missing weight readings as participants are not actively encouraged to weigh themselves or engage with the programme after the initial programme ended at 12 weeks. Many participants

cancelled their subscription after completing the core 12-week programme, as shown in ***Figure 2.2***, which is reflected in the availability of weight data at 24 weeks. Similar proportions of missing weight data have been reported previously for self-funded participants enrolled in the same programme (151). I aimed to mitigate the issue of missing weight readings by using mixed-model repeated-measures analyses, allowing use of all available data with weight readings assumed missing at random. The sensitivity analyses did not lead to different conclusions. However, participants who continue to register weight readings are likely to be more motivated, and to have lost weight, resulting in self-selection bias. Although the exposure groups did not meaningfully differ by demographic characteristics, I cannot rule out the possibility that they may have differed by other factors that were not measured here, such as ethnicity. Further research is needed to extrapolate these findings to more demographically diverse populations, particularly men and those from more deprived backgrounds. The sample only included participants who were paying to participate in the programme, meaning this population are likely to be more self-motivated to lose weight. Payment for participation may have influenced participants' commitment, engagement, and their initial motivation for starting programme. As such, the generalisability of these findings to non-paying populations remains unknown.

2.5.4 Implications & Further Research

Current guidelines recommend weight losses of 5-10%, but encouraging individuals to set larger goals may lead to improved weight loss outcomes and better retention in weight loss programmes. Future randomised controlled trials testing the effect of pre-

treatment counselling to set larger weight loss goals on programme success are warranted. Investigating whether there is an upper limit for the association between higher weight loss goals and achieved weight losses would also be relevant for future research.

Although, further research cannot realistically change participants' primary motivation for weight loss, two randomised controlled trials have shown that weight loss interventions tailored to specific types of weight loss motivation, achieve greater weight loss compared to controls (200, 201). Motivating factors for weight loss may be used to predict who is most likely to be successful and who may need more support, particularly as lack of participant motivation is commonly used to explain poor intervention outcomes (186). Without more complete weight data, it is not possible to establish the long-term outcomes of all participants in this cohort. Further research is needed to find ways of maintaining engagement, as retaining participants over time is likely critical for the optimal effectiveness digital weight loss programmes.

2.5.5 Conclusions

Setting larger weight loss goals and being motivated for health or fitness reasons were associated with greater weight loss and reduced likelihood of drop-out. However, due to the observational nature of this analysis, randomised controlled trials testing the effect of setting these types of goals are needed to confirm causality.

Chapter 3 : The effectiveness and safety of a self-managed mobile application based on self-regulation theory to support weight loss among adults living with obesity: a large-scale pragmatic randomised controlled trial

3.1 SUMMARY

This chapter outlines the development and evaluation of a purpose-built mobile application grounded in self-regulation theory. Self-regulation theory describes how individuals adapt their behaviour to meet goals by repeatedly monitoring progress, evaluating outcomes, and adjusting strategies without the need for continuous external support. Building on preliminary work by a previous DPhil student and in collaboration with a software engineer, I helped to develop an app incorporating core self-regulation components (self-weighing, action planning, and weekly reflection) to support weight loss without human contact.

A two-arm randomised controlled trial was used to assess the effectiveness of the self-regulation app compared to a control, where participants were given simple advice to lose weight. UK adults aged ≥18 years living with obesity were recruited via online social media advertisements and allocated 1:1 to receive access to a purpose-built mobile

application based on self-regulation theory or advice to lose weight. Co-primary outcomes were change in weight and the proportion of participants achieving ≥5% weight loss at 26 weeks. Whether the intervention had adverse effects on symptoms of disordered eating was also assessed. Analyses were conducted on both an intention-to-treat and per-protocol basis, using linear mixed effects and analogous logistic models. The trial was registered on clinicaltrials.gov: NCT05787652.

From 13 April to 15 May 2023, 1,607 participants were randomly assigned to control (n=806), or intervention (n=801). Weight was reported by 632 (39.3%) participants at 26 weeks. Intention-to-treat analyses showed mean (SD) weight change was -3.99 kg (6.5) in the intervention group compared to -2.16 kg (4.5) in the control group at 26 weeks: adjusted mean difference -1.85kg (95% CI: -2.53, -1.17kg, p<0.001). Participants in the intervention group were more than two times as likely to lose ≥5% of their body weight compared to control (adjusted odds ratio [OR]: 2.11, 95% CI: 1.48, 3.03, p<0·001). Per-protocol analyses showed participants using the app lost an additional -2.18kg (95% CI -2.89, -1.48; p<0.001) compared to control at 6 months, and the odds of losing ≥ 5% were 2.44 (95% CI: 1.67, 3.59, p<0·001). The proportion of participants scoring above the threshold for symptoms of disordered eating was lower in the intervention group relative to control at 26 weeks (adjusted OR: 0.51, 95% CI: 0.29, 0·91, p=0.024).

In conclusion, an app with no human contact, designed to foster self-regulatory behaviours, increased weight loss and improved the symptoms of disordered eating measured in people living with obesity. These findings suggest it could be safely deployed at population-level to support effective weight management.

3.2 INTRODUCTION

Following the exploration of a supported digital intervention in ***Chapter 2***, I had the opportunity to design and evaluate a fully automated alternative. This was an unexpected opportunity that arose during my DPhil and allowed me to assess whether a scalable, self-guided intervention could achieve meaningful weight loss outcomes. It also gave me hands-on experience in app development and in managing a definitive randomised trial, alongside serving as a useful point of comparison with the Second Nature programme which includes human-based coaching.

There is an abundance of mobile applications claiming to promote weight loss, but many lack a solid theoretical grounding or have a high-quality evaluation of their effectiveness beyond anecdotal reports or observational studies (202, 203). Current evidence supports the effectiveness of interventions that provide intensive in-person or digital behavioural support from another person (see ***Chapter 1*** for a more detailed discussion). Several reviews have found that digital interventions with some level of human contact (e.g., a coach or counsellor) are more effective than fully automated interventions (117, 128). However, this added human support increases costs, places greater demands on healthcare resources, and limits scalability. In contrast, self-directed interventions have been shown to independently promote weight loss and enhance interventions involving personal contact (130). However, evidence for these types of low or very low intensity interventions is limited and scepticism remains surrounding their effectiveness (89, 90).

A common feature of many mobile weight loss applications is that they support self-regulation, with regular weighing, monitoring of behaviour, and encourage weight loss strategies. Self-regulation theory, as described by Kanfer and Karoly, explains how individuals modify their behaviour to achieve specific goals, without the need for continuous external support (204). The theory states that this process involves several steps. First, individuals measure their current state, i.e., their current weight (known as self-monitoring). Next, they contextualise it with previous states and compare it against the goal state they want to achieve, i.e., their weight loss target. This comparison leads to an evaluation of previous behaviour, and if the evaluation is positive, individuals are likely to repeat those behaviours again. Conversely, if the evaluation is negative, and the current state does not indicate progress toward the goal, individuals may inhibit these unsuccessful behaviours. Individuals continue this cycle of measuring, contextualising, comparing, and evaluating behaviours until their current state aligns with their goal, i.e., they reach their target weight. This iterative process allows individuals to experiment with different techniques, helping them find effective and sustainable strategies. For example, in the context of weight loss, an individual might discover that not eating between meals helps them lose weight and decide to continue that behaviour until they reach their target weight.

It has been argued that the self-regulation process occurs naturally without external support once self-monitoring is performed (204, 205). However, whilst interventions involving regular self-monitoring of bodyweight have been shown to be effective for weight loss (206, 207), self-weighing alone does not typically lead to completion of the

self-regulatory cycle (208, 209). Qualitative evidence suggests that individuals naturally reflect on their previous behaviour only around half of the time following self-weighing, and the planning of specific weight loss actions was uncommon (208). The study also demonstrated that the frequency of making specific action plans was a significant predictor of weight loss. Similarly, a systematic review found that programmes incorporating additional behavioural components alongside self-weighing were more effective than self-weighing alone (210). Self-regulation theory does also acknowledge that factors such as the clarity of the goal, external support, perceived ability, and the consequences of not reaching the goal can influence the likelihood of successful self-regulation (204). Taken together, this suggests that weight loss programmes could be improved by supporting people in performing self-regulation, including making specific time-bound plans about how weight loss actions would be enacted (211).

As such, prompting self-regulation through self-monitoring, providing feedback, goal setting, and specific action planning have all been found to be associated with effectiveness in dietary and physical activity interventions (78, 80). In a previous pilot study conducted by members of my team, participants were guided through an iterative self-regulatory cycle where they performed daily self-weighing and were encouraged to experiment with different weight loss strategies each day, reflect weekly on the strategies they used, and continue to use those they found useful (209). At eight weeks the intervention led to 3·20 kg (95% CI -4·49, -1·92) greater weight loss than the control who engaged in self-weighing alone. Although the pilot showed promising results in terms of acceptability, feasibility, and indicative effectiveness, further evidence is required to

show the intervention is safe and effective in the long-term within a more representative sample before widespread implementation. Furthermore, in the pilot study, engagement with the intervention involved in-person enrolment into the trial and regular emails with a sole researcher, which may have supported engagement over and above a truly self-supported weight loss attempt.

For this study, it was important to consider potential concerns associated with weight loss programmes, particularly behaviours that may inadvertently contribute to disordered eating. One commonly cited risk is frequent self-weighing, which some argue could provoke obsessive behaviours or psychological distress (212, 213). Another is the high degree of dietary restraint characteristic of many weight loss diets, which overlaps with traits often associated with eating disorders (214). According to Cognitive Behavioural Theory, eating disorders or disordered eating behaviours can arise from an excessive focus on eating, body shape, and weight, leading to body dissatisfaction and rigid dietary rules aimed at achieving specific weight goals (214). In the context of weight management, self-regulation involves behaviours such as daily self-weighing, structured reflection with an emphasis on weight outcomes, and adherence to specific dietary rules. Whilst these types of self-regulatory behaviours do have a theoretical basis for potentially exacerbating disordered eating tendencies in vulnerable individuals, a systematic review of self-regulatory interventions found no evidence to suggest that promoting self-regulation leads to disordered eating (212). Nonetheless, the evidence remains limited and insufficient to entirely rule out meaningful risks, underscoring the

importance of monitoring unintended adverse effects on disordered eating behaviours when evaluating such approaches.

This present study built upon the pilot study by adapting the self-regulation intervention for delivery via a mobile application with no in-person contact. This approach enhances the scalability of the intervention and reduces the potential for bias associated with direct communication between the researcher and participants. The primary objective of this study was to examine the effectiveness of this digitally delivered self-regulation intervention to support weight loss, compared to a control where participants were simply advised to lose weight. A secondary objective was to assess the safety of the intervention by monitoring symptoms of disordered eating. Additionally, I conducted a comprehensive process evaluation to explore whether the intervention effectively engaged participants.

3.3 METHODS

3.3.1 STUDY DESIGN

A two-arm, parallel-group, individually randomised, controlled superiority trial was conducted among adults living with obesity. The trial assessed the effectiveness of a purpose-built, digitally delivered self-regulation mobile application (Adults Regulating Their weight Everyday with Mobile Internet Support [ARTEMIS]) in supporting weight loss, compared to standard advice for weight loss. The trial took place between April and December 2023. Participation lasted for 26 weeks from baseline to final follow-up. All study procedures were conducted remotely via the Research Electronic Database Capture (REDCap) web application or the purpose-built study app (intervention only). The trial was approved by the Central University Research Ethics Committee of the University of Oxford (R82050/RE001) and prospectively registered on clinicaltrials.gov: NCT05787652.

3.3.2 PARTICIPANTS

Participants were recruited online through advertisements on social media (Google, Facebook, Twitter, and Instagram) between 13 April and 15 May 2023. Advertisements linked to the study landing page, where potential participants were presented with a participant information sheet (***Appendix 3.1***). Potential participants were then provided a link to the study website where they could consent to participate. Following consent, eligibility was assessed through a brief online screening form. To be eligible potential

participants had to be aged ≥18 years, with a BMI ≥30 kg/m^2 (≥27·5 kg/m^2 for non-European ethnicities). Complete eligibility criteria are detailed in ***Table 3.1.***

Table 3.1: Complete eligibility criteria

Inclusion	Exclusion
• Aged ≥18 years • BMI ≥30 kg/m^2 (≥27·5 kg/m^2 for non-European ethnicities) • Full-time resident in the UK and not intending to move outside the UK in the next 12 months • Able to access the internet with a smartphone or tablet • Able to access and use a digital weighing scale	• Unable to understand the English language • Currently signed up with an intention to attend, or had in the previous three months attended, a weight management programme • Currently participating in another weight management study • Lost >5kg in the previous six months • Previously undergone bariatric surgery or scheduled to have bariatric surgery • Currently pregnant or planning pregnancy in the next 12 months • Currently or previously diagnosed with an eating disorder • Recently diagnosed with a disease, or expected to undergo treatment for a disease, associated with substantial weight loss e.g., cancer treatment

If eligible, potential participants were invited to complete a short baseline questionnaire which captured contact details; socio-demographic characteristics; anthropometric measures (reporting of objectively assessed body weight with photograph verification, and self-reported height); a six-item disordered eating questionnaire (a modified Eating Disorders Examination – Questionnaire Short Form [EDE-QS]));(215, 216) and responses

to three questions regarding overall health, quality of life, and body satisfaction on 5-point Likert scales from 1 (poor) - 5 (excellent).

3.3.3 Randomisation and Masking

Participants were randomised 1:1 using a computerised algorithm with a simple randomisation schedule built into REDCap. The allocation sequence was unknown to researchers or participants i.e., group allocation was concealed until randomisation was performed. It was not possible to blind participants or the research team to treatment allocation post-randomisation as the control group received no intervention, however follow-up was completed remotely with no in-person contact.

3.3.4 App Development

The ARTEMIS intervention built upon prior work conducted by a previous DPhil student in the team as part of the PREVAIL study. Briefly, the DPhil student conducted initial research which involved a systematic evaluation of comparable weight management apps available on the market, identifying best practices, and highlighting key gaps in existing digital interventions (217). This work informed the development of the intervention framework and programme content (196, 208), and culminated in a pilot study to assess its effectiveness and acceptability (209, 218).

Building on this prior research, I adapted the intervention manual developed during the PREVAIL study into a comprehensive document that served as the foundation for the ARTEMIS app's primary content. The manual was adapted to align with the new digital

format of the intervention, as well as reformulating the action categories, the specific individual actions, and their associated descriptions. I created two animations to provide participants with an introduction when they first logged into the app. These animations introduced the theory of the self-regulation process and explained how the ARTEMIS app was designed to guide users through this process step by step.

The app's technical development was undertaken in collaboration with an external software engineer, Nick Goodall, who was responsible for translating the content into a functional and user-friendly digital interface. I provided detailed content materials to the programmer, including the intervention's theoretical framework, action categories, and user journey, which served as a blueprint for the app's design. Initial wireframes and app mock-ups were then reviewed by two researchers and me. The development process progressed iteratively through several review cycles. Each cycle involved testing with the core study team and amongst the wider members of the Health Behaviours team for 2-4 weeks to and resolve technical or usability issues. Feedback from these cycles informed the subsequent revisions, culminating in a beta version of the app that was ready for user testing.

To ensure the app's usability and functionality from a user perspective, a Patient and Public Involvement (PPI) workshop was conducted to evaluate the beta version. The workshop provided valuable insights into the app's design, navigation, and overall user experience. Participants generally reported positive experiences, highlighting that the app was intuitive, user-friendly, and easy to navigate. However, feedback also revealed several suggestions for additional features, such as step tracking, integration with

wearable devices, and access to personalised coaching. While these features could enhance user engagement, they were deliberately excluded in this study to evaluate the specific effect of the self-regulatory components of the intervention and to maintain scalability. Future iterations of the app could incorporate these features to align with user preferences.

The feedback gathered during the PPI workshop informed the final revisions, leading to the completion of the final version of the ARTEMIS app. The app is designed to guide participants through the self-regulation process in a stepwise, iterative manner, as detailed in ***Figure 3.1*** and below.

Figure 3.1: Overview of the self-regulation cycle and corresponding ARTEMIS app components designed to guide participants through each stage of the cycle

3.3.5 PROCEDURES

The intervention aimed to guide participants through each stage of the self-regulatory cycle on a daily basis, and was delivered in an automated, self-directed format without human involvement. It supported participants to experiment with evidence-based weight loss strategies to find helpful ones for them and encouraged their repeated use.

Only participants randomised to the intervention arm were granted access to the ARTEMIS app, which they were instructed to download via the Apple or Google Play stores and log in using a unique passcode issued at randomisation. After logging in, participants were met with two short explanatory animated subtitled videos outlining the rationale of the approach and how to use the app. Participants entered their height, weight, preferred daily notification time, and selected a category of weight loss actions to try for the week (e.g., eating in a structured way, being more active as part of daily life). There were eight categories, relating to diet, physical activity, and sleep, which could be selected by participants and rotated weekly. Within each category were several evidence-based actions that could be chosen by participants and rotated daily (***Figure 3.2*** & ***Appendix 3.2***).

Figure 3.2: Overview of action categories (selected weekly) and individual actions (selected daily)

Each day, participants were prompted by a push notification at a time they had selected, to weigh themselves, record their weight in the app, choose a specific weight loss action from their selected category to perform that day, and make an action plan about how, when, and where they would perform that action. Participants repeated this process every day, each time selecting a different action from their selected action category. At the end of each week, participants received a progress report which contained

information on their weight change during the week, displayed on a regression line through daily weight readings, and their progress since beginning the intervention. Participants were asked to reflect on the usefulness of the individual strategies used that week and save those that they felt were helpful to their '*toolbox*' (***Figure 3.3***).

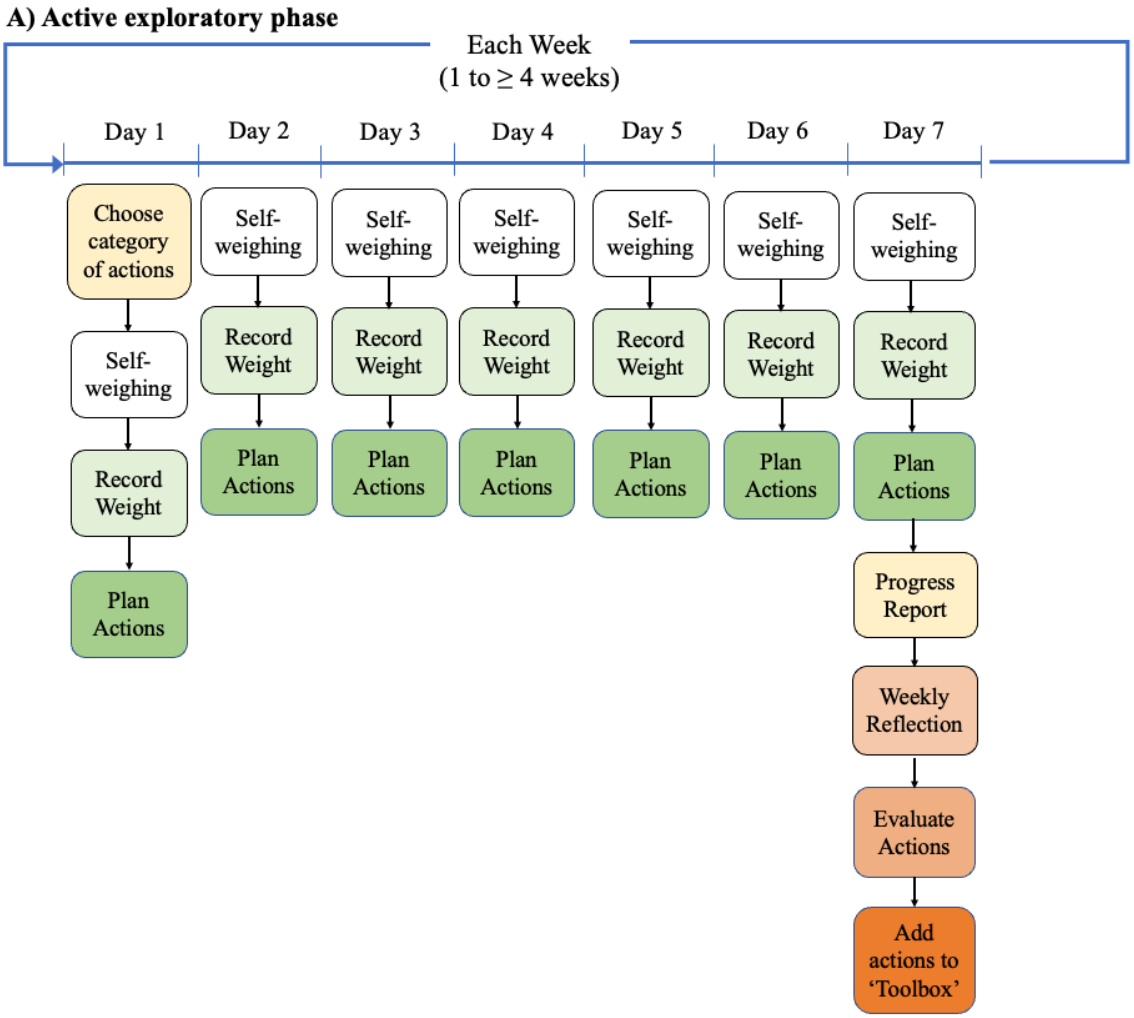

Figure 3.3: Summary of intervention procedures during the 'active exploratory phase' (weeks one to at least week four) where participants could try new weight loss actions each day.

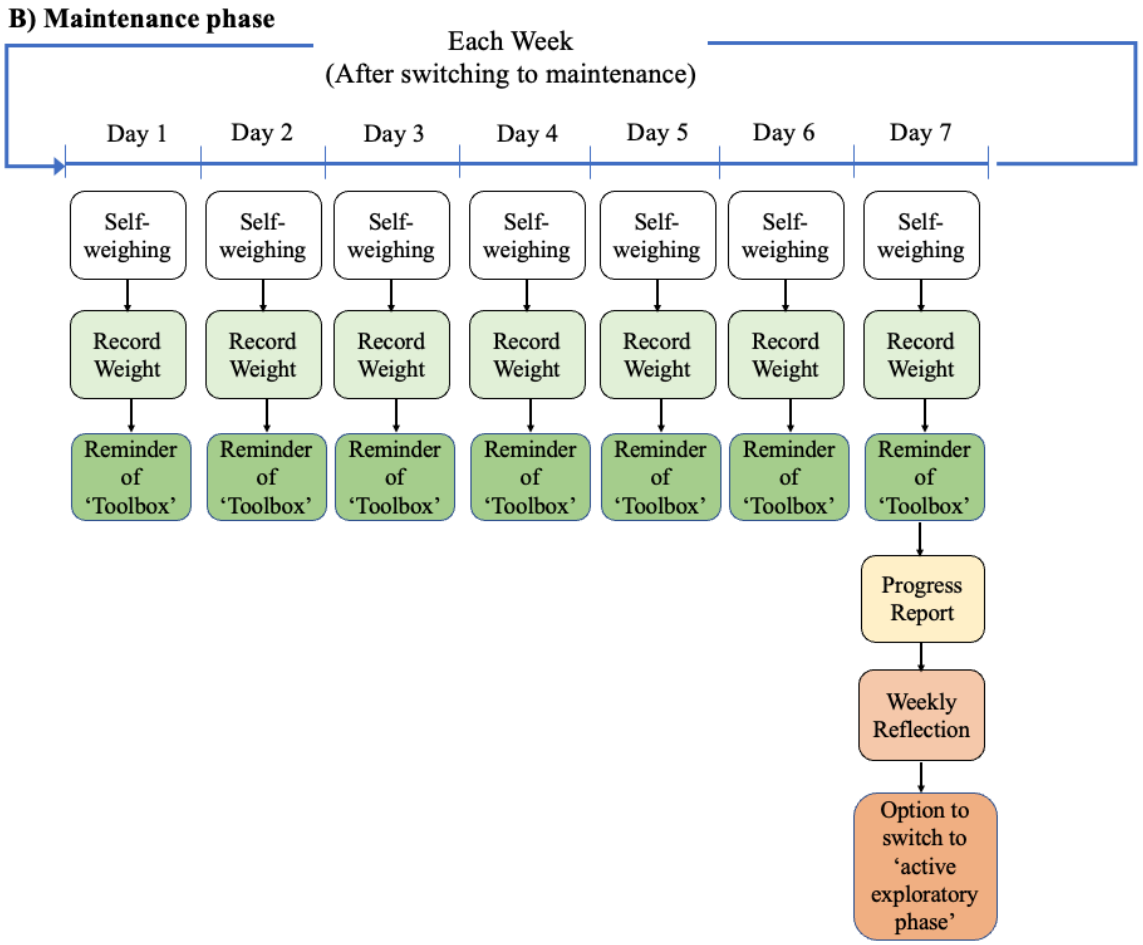

Figure 3.4: Summary of intervention procedures during the 'maintenance phase' (optional switch after week four) where participants used actions from their 'toolbox'.

After the fourth week, participants could choose to continue to experiment with new strategies or switch to the 'maintenance phase' and use the existing strategies already in their '*toolbox*' (***Figure 3.4***). In the maintenance phase, participants were still prompted via push notification to return to the app every day to track their weight, reminded of the actions in their '*toolbox*', and to plan how they could perform these actions. At the end

of each week participants received a progress report and were asked to reflect. Participants could switch back to experimentation at any time.

Participants randomised to the control received no intervention but were advised that they may wish to lose weight on their own.

Follow-up data were collected at 12- and 26-weeks, while app data were collected continuously throughout the trial and collated at each follow-up. At each follow-up participants were asked to complete the same weight, eating disorder symptoms, and general health measures as at baseline, as well as a study specific weight management questionnaire regarding the specific actions they used to manage their weight since the previous assessment (***Appendix 3.3***). At the final assessment, participants were asked to rate the usefulness of the app to assist in weight loss on a scale of 1 (not useful) to 10 (very useful). Participants received payment for completing the assessments: either a £5 or £8 voucher after completing the 12-week assessment, and an £8, £12, or £20 voucher after completing the 26-week assessment. The variation represents ethically approved increases in reimbursement in attempt to improve participant retention (see ***section 3.3.8***)

3.3.6 Outcomes

3.3.6.1 Primary Outcomes

The co-primary outcomes were change in body weight from baseline to 26 weeks, and the proportion of participants achieving ≥ 5% weight loss at 26 weeks.

3.3.6.2 Secondary Outcomes

Change in body weight from baseline to 12 weeks, and the proportion of participants achieving ≥5% weight loss at 12 weeks.

3.3.6.3 Adverse Effects

The most commonly used instrument to assess disordered eating is the Eating Disorder Examination Questionnaire (EDE-Q). This is 28 items in length and is not suitable for a trial such as this where there is little to no engagement of the participants with the research. Therefore, it was suggested that a short-form version of the modified Eating Disorders Examination - Questionnaire Short Form (EDE-QS) was used for the purposes of this trial (215, 216). The questionnaire was adapted to remove items, which, in this context, will signify participants are adhering to the intervention, but retain those that assess the degree to which participants are over-concerned with weight, shape, and overly rigid rules for eating and exercising (the core psychopathology of eating disorders). Using only these items maximised the questionnaire's sensitivity for detecting adverse outcomes.

Adverse effects will be measured as the proportion of participants scoring above threshold (>7) on the EDE-QS between baseline and 12- and 26- weeks (***Appendix 3.3***).

3.3.6.4 Process Measures

In this study, I chose to conceptualise engagement in relation to each stage of the self-regulation cycle so that I could examine which stages were most strongly associated with

outcomes. App engagement was assessed through the number of days with any app engagement; daily weight readings; daily actions selected; daily action plans; weekly reflections completed; and the percentage of actions successfully completed. Both intervention and control participants also reported their actions to lose weight, including use of weight management programmes.

Perceived barriers to completion of daily action plans were assessed using free-text responses to the following question in the app: '*Please tell us why you were unable to perform your action yesterday*'. This question was asked when respondents indicated they were unable to complete their previously selected action.

3.3.7 Statistical Analysis

The study originally aimed to recruit 1,294 participants, which allowed for 25% dropout. This gave 90% power to detect a 1·5kg difference in mean weight change, which has previously been shown to be cost-effective (219), with a type 1 error rate of 2·5% for co-primary outcomes. All statistical analyses were conducted in R (version 4·3·3). A statistical analysis plan was published on ClinicalTrials.gov (NCT05787652), preceding analysis. Before analysis of outcomes, I assessed the association between baseline variables and loss to follow-up at 26 weeks. Baseline BMI and IMD were associated with loss to follow-up and included as covariates in subsequent analyses.

3.3.7.1 Primary Analysis

I conducted intention-to-treat analyses using linear mixed effects models for repeated measures to assess weight change from baseline to 26 weeks. Week and the interaction between week and treatment group were added as fixed effects, and participant ID as a random effect. I used analogous logistic models to assess the proportion of participants achieving ≥5% loss in body weight. Pre-specified exploratory subgroup analyses were conducted by age, gender, level of educational attainment, employment status, IMD, and ethnicity.

Sensitivity analyses examined assumptions regarding missing data by 1) imputing the last-measured weight (last observation carried forward (LOCF)); 2) carrying forward the baseline weight (baseline observation carried forward (BOCF)), and 3) restricting analysis to participants with complete weight data at all time points (completer analysis).

A linear mixed effects model was also used for the per-protocol analysis. I defined per-protocol as participants that successfully completed at least one weigh-in and action on at least four separate weeks and had at least one action in their action toolbox, reflecting those who engaged meaningfully with the app as intended. A post-hoc sensitivity analysis was conducted excluding participants who did not have a valid baseline or follow-up weight verification photograph.

3.3.7.2 Secondary Analysis

The 12-week outcomes were assessed with the primary outcome in the linear mixed effects model.

3.3.7.3 Adverse Effects

Analysis of change in the proportion of participants scoring above the threshold (>7) on the modified EDE-QS was assessed using mixed effects logistic regression.

3.3.7.4 Exploratory Analysis

I assessed the actions participants used to manage their weight, including accessing other weight management programmes. These actions were classified as no action, self-help measures (alterations to diet and physical activity), and other effective action (attending a behavioural or other online weight loss programme; taking weight loss medication; or following a meal-replacement weight loss programme; and using the ARTEMIS app or learned strategies from the app among the intervention group). A sensitivity analysis was conducted which excluded participants who used another effective strategy for weight loss. Responses to the health, quality of life, and body satisfaction questions were summarised descriptively and an ordinal logistic regression used to compare treatment groups.

To assess whether engagement predicted weight change from baseline to 26 weeks, I used linear regression with weight change as the dependent variable and each engagement measure as a predictor in independent models.

The free-text responses to the daily action completion question were analysed qualitatively using conventional content analysis. Responses were coded and then grouped into broader categories of shared meaning.

3.3.8 Deviations from Protocol

Retention was monitored throughout the trial. Due to lower than anticipated completion rates after 20% of participants had received an initial follow-up reminder the following alterations were made following Research Ethics Committee approvals:

- The incentive payment for 12-week follow-up was increased from £5 to £8, and for 26-week follow-up from £8 to £12, and later £20
- A fourth follow-up email and SMS reminder were sent to participants at 12-week follow-up to notify them of the above change
- The requirement for photo verification at 12- and 26-week follow-up was removed
- A larger sample size was recruited to account for additional dropouts
- Final follow-up was moved from 52 to 26 weeks due to low retention, prior to conducting any analyses. Consequently, most participants did not rate the usefulness of the app, so I was unable to analyse these data.
- The definition of per-protocol analysis was altered from participants who successfully switched to maintenance as the app did not collect the necessary data to allow this.

The clinicaltrials.gov registration was updated to reflect these deviations from the initial protocol.

3.4 RESULTS

3.4.1 SAMPLE

Between 13 April and 15 May 2023, 6,156 screenings were conducted. Of these, 1,678 records were eligible and randomly allocated to either control (n=839) or intervention (n=839). Duplicate sign-ups were identified and removed (n=71), resulting in a final sample of 1,607 unique participants: n=806 randomised to control, and n=801 to intervention. Six hundred and ninety-six (43·3%) participants were followed up at 12 weeks and 632 (39·3%) at 26 weeks (***Figure 3.5***). Overall, 48% of participants provided at least one follow-up weight reading. At 12 weeks, 489 (70%) of followed-up participants had a valid weight verification photograph and 528 (84%) at 26 weeks.

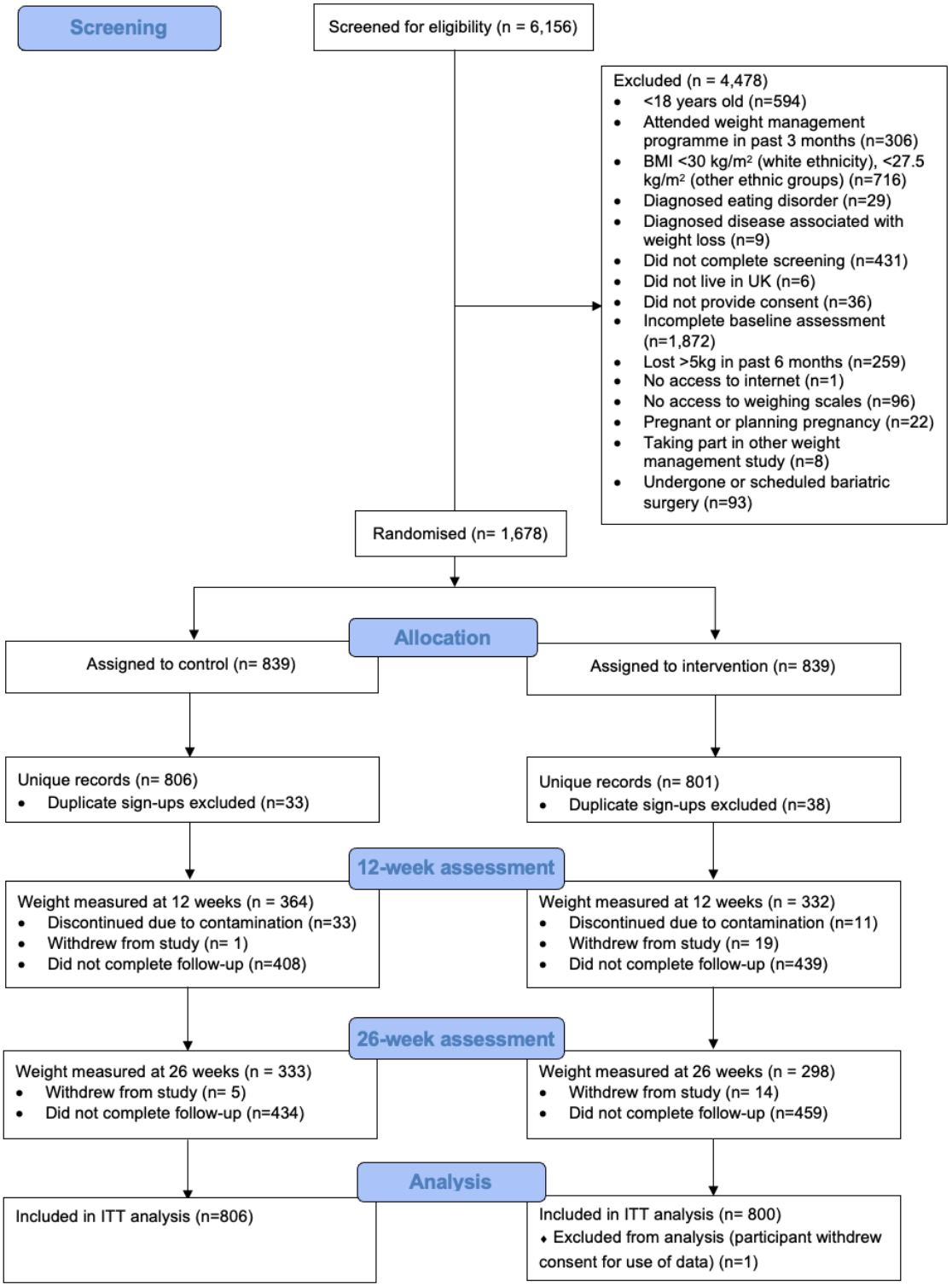

Figure 3.5: CONSORT flowchart. Note: completion of 26-week assessment was not dependent on completion of 12-week assessment.

The mean (SD) BMI of participants was 38 (6) kg/m^2, and 38% of participants scored above threshold on the modified disordered eating questionnaire. Mean (SD) age was 47 (11) years, the majority of participants were female (93%), and of a white ethnic group (88%). Sixty-one percent had an undergraduate or postgraduate degree. Further baseline characteristics are summarised in ***Table 3.2***.

Table 3.2: Baseline characteristics of participants (n=1,606)

Characteristics	**Control (n=806)**	**Intervention (n=800)***	**Total (n=1,606)**
Age, years, mean (SD)	46 (11)	47 (11)	47 (11)
Gender, n (%)			
Female	743 (92·2)	756 (94·5)	1,499 (93·3)
Male	63 (7·8)	44 (5·5)	107 (6·7)
BMI, kg/m^2, mean (SD)	38 (6)	38 (6)	38 (6)
Ethnicity, n (%)			
Asian or Asian British	46 (5·7)	39 (4·9)	85 (5·3)
Black or Black British	31 (3·8)	21 (2·6)	52 (3·2)
Mixed or multiple ethnic groups	14 (1·7)	23 (2·9)	37 (2·3)
White	706 (88)	705 (88)	1,411 (88)
Other	7 (<1)	6 (<1)	13 (<1)
Prefer not to say	2 (<1)	6 (<1)	8 (<1)
IMD decile, n (%)			

1-3 (most deprived)	188 (24)	189 (24)	377 (24)
4-7	333 (43)	323(42)	656 (42)
8-10 (most affluent)	259 (33)	261 (34)	520 (33)
Missing	26 (<1)	27 (<1)	53 (<1)
Highest Educational Qualification, n (%)			
No formal qualifications	13 (1·6)	14 (1·8)	27 (1·7)
GCSE/O-level	99 (12)	97 (12)	196 (12)
A levels/BTEC	182 (23)	191 (24)	373 (23)
Undergrad/postgrad degree	498 (62)	483 (60)	981 (61)
Prefer not to say	14 (1·7)	15 (1·9)	29 (1·8)
Employment Status, n (%)			
Employed	588 (73)	539 (67)	1,127 (70)
Self-employed	44 (5·5)	53 (6·6)	97 (6·0)
Unemployed	13 (1·6)	16 (2·0)	29 (1·8)
Looking after home and family	35 (4·3)	40 (5·0)	75 (4·7)
In education or training	16 (2·0)	18 (2·3)	34 (2·1)
Retired	62 (7·7)	86 (11)	148 (9·2)
Long-term sick or disabled	34 (4·2)	29 (3·6)	63 (3·9)
Other	14 (1·7)	19 (2·4)	33 (2·1)
Proportion scoring >7 on EDE-QS, n (%)	286 (35)	318 (40)	604 (38)

*One participant in the intervention group withdrew consent for use of their data.

Abbreviations: A-level: Advanced level; BMI: body mass index; BTEC: business and technology education council; EDE-QS: eating disorders examination – questionnaire short form; GCSE: general certificate of secondary education; IMD: index of multiple deprivation; O-level: ordinary level.

3.4.2 Primary Outcomes

Mean (SD) weight change at 26 weeks was -3·99 (6·5) kg in the intervention group, and -2·16 (4·5) kg in the control group (***Figure 3.6***).

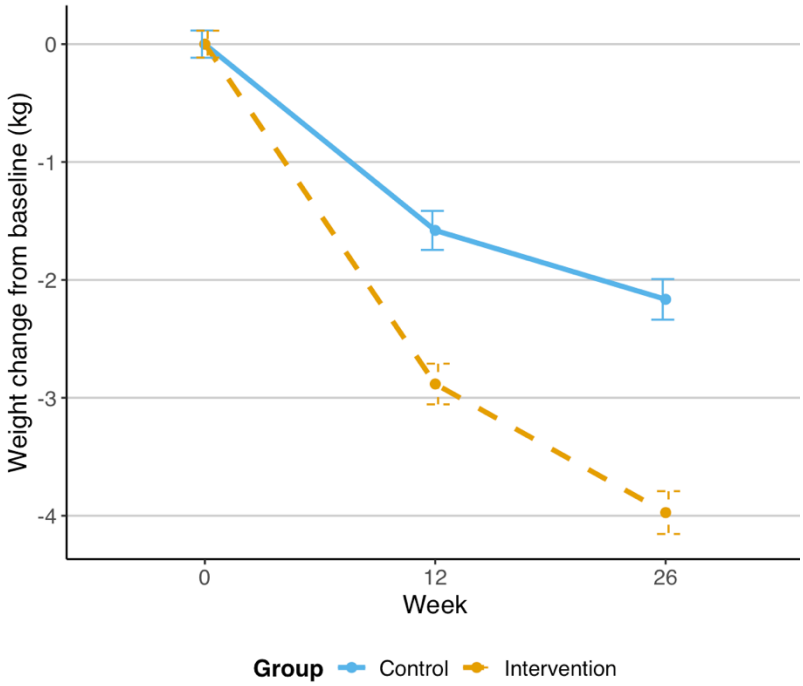

Figure 3.6: Mean weight change over 26 weeks in intention-to-treat sample using all available data. Values represent mean (standard error).

Adjusted mean difference in weight change between the intervention and control was -1·85kg (95% CI: -2·53, -1·17; p<0·001) in the intention-to-treat population using all available data in mixed-effects models for repeated measures. Among participants followed up at 26 weeks, 34·9% of the intervention (n=104) and 20·4% of the control group (n=68) lost ≥5% of their baseline body weight (adjusted OR: 2·11; 95% CI: 1·48, 3·03; p<0·001) (***Table 3.3***)

Table 3.3: Co-primary outcomes by randomised group in intention-to-treat sample using all available data

Timepoint	Variable	Mean (SD) change from baseline				Adjusted difference (95% CI)	*P*-value
		Control	n	Intervention	n		
12 weeks	Weight (kg)	-1·59 (3·7)	364	-2·88 (4·5)	332	-1·42 (-2·08 to -0·77)	***<0·001***
	n (%) losing ≥5% weight	50 (13·7)	364	88 (26·5)	332	2·27* (1·55 to 3·35)	***<0·001***
26 weeks	Weight (kg)	-2·16 (4·5)	334	-3·99 (6·5)	298	-1·85 (-2·53 to -1·17)	***<0·001***
	N (%) lost ≥5% weight	68 (20·4)	334	104 (34·9)	298	2·11* (1·48 to 3·03)	***<0·001***

*Odds ratio.

In the intervention group, 367 (37·5%) participants met the definition of per-protocol and analyses showed a -2·18kg difference between the intervention and control (95% CI -2·89, -1·48; p<0·001) at 26 weeks. Of the 367 participants who met the definition of per-protocol, 221 participants were followed up at 26 weeks, of these, 38·5% (n=85) lost ≥5% of their baseline body weight (adjusted OR: 2·44, 95% CI: 1·67, 3·59; p<0·001) (***Table 3.4***).

Table 3.4: Co-primary outcomes by randomised group in per-protocol sample

Week	Variable	Mean (SD) change from baseline				Adjusted difference (95% CI)	*P*-value
		Control	n	Intervention	n		
12 weeks	Weight (kg)	-1·59 (3·7)	364	-3·15 (4·3)	263	-1·60 (-2·27 to -0·94)	***<0·001***
	n (%) losing ≥5% weight	50 (13·7)	364	73 (27·8)	263	2·27* (1·55 to 3·35)	***<0·001***
26 weeks	Weight (kg)	-2·16 (4·5)	334	-4·40 (6·3)	221	-2·18 (-2·89 to -1·48)	***<0·001***
	n (%) lost ≥5% weight	68 (20·4)	334	85 (38·5)	221	2·44* (1·67 to 3·59)	***<0·001***

*Odds ratio.

In pre-specified sub-group analyses, there was no evidence that the effects of the intervention on weight change (***Figure 3.7***) or on the odds of losing ≥ 5% body weight (***Figure 3.8***), differed by gender, ethnicity, employment status, educational attainment, IMD, or age.

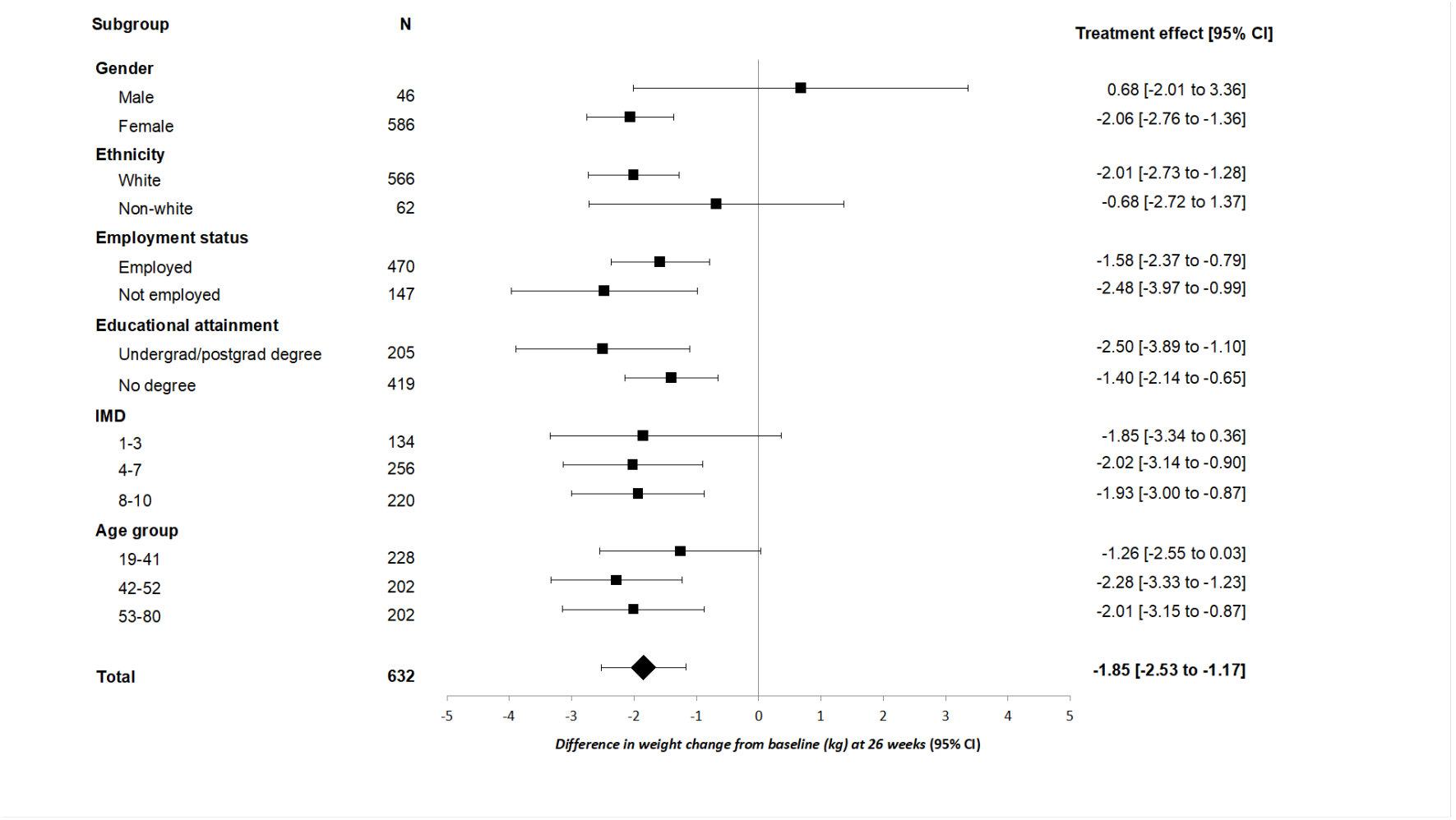

Figure 3.7: Difference in weight change from baseline to 26 weeks between intervention and control by selected sub-groups

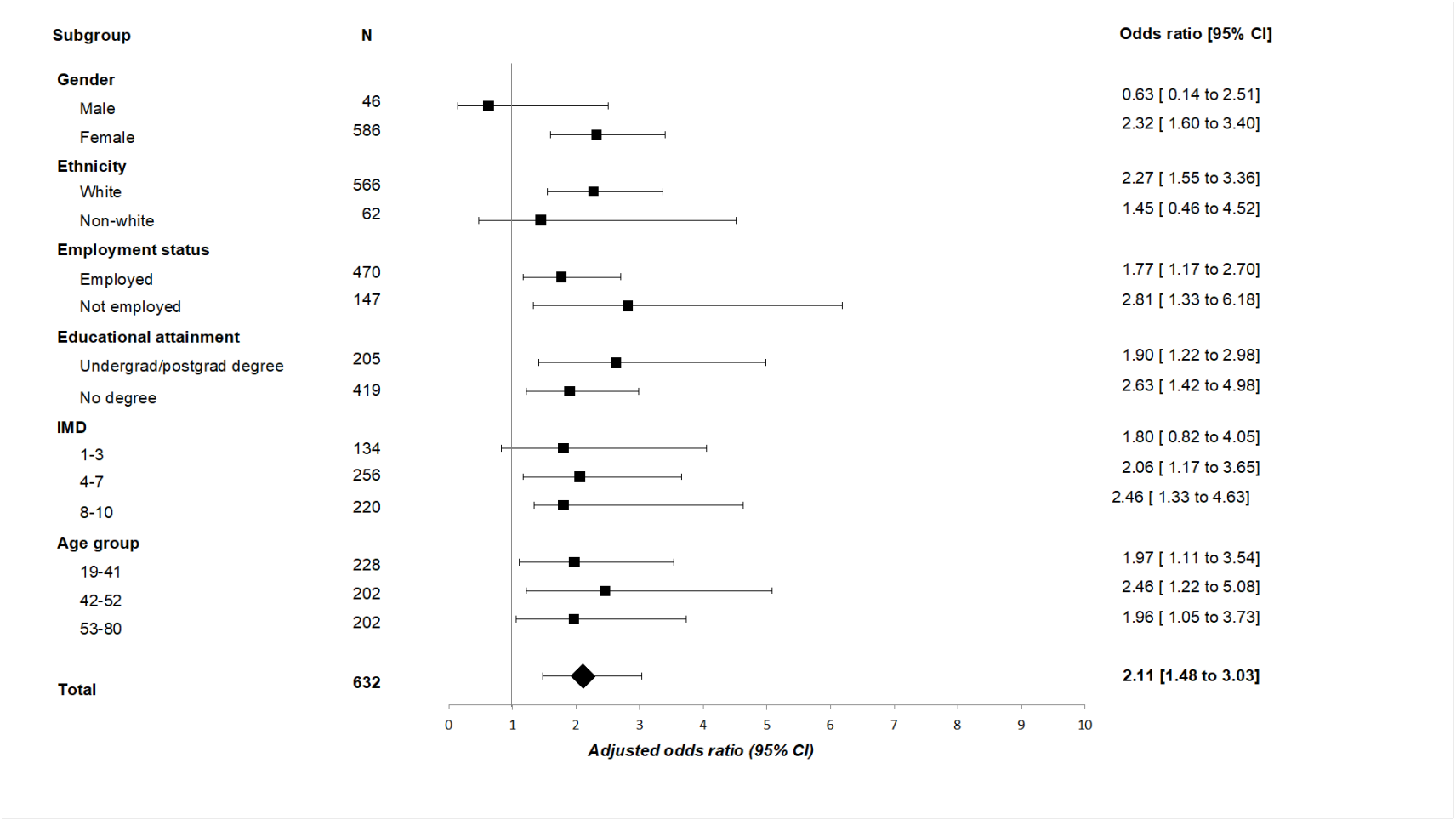

Figure 3.8: Adjusted odds ratio of losing >5% baseline body weight at 26 weeks by selected sub-groups

Sensitivity analyses on loss to follow-up using LOCF, BOCF, and completers only did not change the conclusion that the intervention led to significantly greater weight loss than control (***Table 3.5*** & ***Table 3.6***). Post-hoc sensitivity analyses excluding participants who did not have a valid baseline or follow-up weight verification photograph, also did not change the conclusion that the intervention led to significantly greater weight loss than control (***Appendix 3.4***).

Table 3.5: Adjusted difference in weight between treatment groups under different missing data approaches.

		BOCF		**LOCF**		**Completers only**	
Week		Control (n=806)	Intervention (n=800)	Control (n=806)	Intervention (n=800)	Control (n=301)	Intervention (n=266)
12 weeks	Mean (SD) weight change	-0·72 (2·61)	-1·19 (3·22)	-0·72 (2·61)	-1·19 (3·22)	-1·53 (3·68)	-2·92 (4·55)
	Adjusted difference (95% CI)	-0·51 (-0·83 to -0·19)		-0·48 (-0·79 to -0·16)		-1·49 (-2·23 to -0·73)	
	P-value	***0·002***		***0·003***		***<0·001***	
26 weeks	Mean (SD) weight change	-0·9 (3·09)	-1·49 (4·39)	-1·04 (3·26)	-1·71 (4·54)	-2·19 (4·6)	-3·86 (6·44)
	Adjusted difference (95% CI)	-0·65 (-0·97 to -0·33)		-0·67 (-0·98 to -0·35)		-1·78 (-2·54 to -1·03)	
	P-value	***<0·001***		***<0·001***		***<0·001***	

Adjusted mean difference (kg) (95% CI) calculated using linear mixed effects models with fixed effects for condition, week, and group*week interaction, and a random effect for participant. IMD and baseline BMI were included as covariates as baseline values were predictive of missingness in the data. Abbreviations: BOCF: baseline observation carried forward; LOCF: last observation carried forward.

Table 3.6: Adjusted odds of losing >5% baseline body weight between treatment groups under different missing data approaches.

		BOCF		LOCF		Completers only	
Week		Control (n=806)	Intervention (n=800)	Control (n=806)	Intervention (n=800)	Control (n=301)	Intervention (n=266)
12 weeks	n (%) losing ≥5% weight	50 (6·2)	88 (11·0)	50 (6·2)	88 (11·0)	40 (13·3)	74 (27·8)
	Odds ratio (95% CI)	1·97 (1·36 to 2·89)		1·86 (1·30 to 2·70)		2·77 (1·78 to 4·35)	
	P-value	***<0·001***		***<0·001***		***<0·001***	
26 weeks	n (%) losing ≥5% weight	68 (8·4)	104 (13·0)	78 (9·7)	118 (14·8)	62 (20·6)	90 (33·8)
	Odds ratio (95% CI)	1·69 (1·21 to 2·37)		1·61 (1·19 to 2·19)		2·05 (1·39 to 3·04)	
	P-value	***0·002***		***0·002***		***<0·001***	

Adjusted odds ratio (95% CI) calculated using logistic regression models. IMD and baseline BMI were included as covariates as baseline values were predictive of missingness in the data. Abbreviations: BOCF: baseline observation carried forward; LOCF: last observation carried forward.

3.4.3 Secondary Outcomes

At 12 weeks, the adjusted mean difference in weight change between the intervention and control groups was -1·42kg (95% CI: -2·08 to -0·77; p<0·001) (***Table 3.3***). Among participants followed up at 12 weeks, more than twice as many participants in the intervention group lost ≥5% of their baseline body weight compared to the control group (adjusted OR: 2·27; 95% CI: 1·55, 3·35; p<0·001).

3.4.4 Risk of Adverse Outcomes

The intervention group showed significantly lower odds of an EDE-QS score above the threshold (>7) compared to the control group at both 12 and 26 weeks (***Table 3.7***).

Table 3.7: Adverse outcomes by randomised group.

Timepoint	Variable	Control	n	Intervention	n	Adjusted difference (95% CI)	*P*-value
12 weeks	n (%) >7 on the EDE-QS	111 (29·8)	373	63 (18·6)	338	0·28* (0·16 to 0·48)	***<0·001***
26 weeks	n (%) >7 on the EDE-QS	84 (24·9)	337	65 (21·7)	300	0·51* (0·29 to 0·91)	***0·024***

*Odds ratio.

Abbreviations: EDE-QS: Eating Disorders Examination - Questionnaire Short Form.

3.4.5 Process Outcomes

3.4.5.1 App Engagement

In the intervention group 735/801 (91·8%) participants logged into the app at least once. Overall engagement with the intervention (as measured by total number of days with any activity), as well as greater engagement with each of the intervention components, were associated with greater weight change at 26 weeks (***Table 3.8***).

Table 3.8: App engagement and association with weight change from baseline to 26 weeks per 1 standard deviation increase in each engagement measure.

Engagement measure	Mean (SD)	Association with weight change at 26 weeks (n=295)		
		B	95% CI	P-value*
Days with any activity	45·5 (61·7)	-1·09	-1·69, -0·50	***<0·001***
Daily weight readings	40·4 (58·2)	-1·11	-1·69, -0·53	***<0·001***
Daily actions selected	28·0 (39·9)	-1·10	-1·67, -0·53	***<0·001***
Daily action plans	27·5 (39·7)	-1·11	-1·68, -0·53	***<0·001***
Percentage of actions successfully completed	33·2 (29·5)	-1·20	-2·00, -0·41	***0·003***
Weekly reflections	7·7 (10·6)	-1·02	-1·64, -0·40	***0·001***

*Significance defined based on a Bonferroni-corrected p value of 0·0083 (0.05/6).

3.4.5.2 Actions Used to Manage Weight

At 26 weeks, 337 (41·8%) control participants and 300 (37·5%) intervention participants reported on the actions they used to lose weight since their previous assessment (***Table 3.9***). Eighty (26·7%) intervention participants reported using the ARTEMIS app, and a further 87 (29%) reported using strategies learned from the ARTEMIS app but were not actively using the app. Overall, between the 12- and 26-week follow-up, almost twice as many participants in the intervention (61·3%) compared to control (32·9%) took effective

action to lose weight (including using the ARTEMIS app or learned strategies from the app among the intervention group).

Table 3.9: Participant self-reported actions* used to manage weight at 12- and 26-weeks.

Actions	12 weeks		26 weeks	
	Control (n=369)	Intervention (n=336)	Control (n=337)	Intervention (n=300)
Taking action to manage weight, n (%)	247 (66·9)	275 (81·8)	195 (57·9)	204 (68·0)
No action, n (%)	122 (33·1)	61 (18·2)	142 (42·1)	96 (32·0)
Actively using the ARTEMIS app, n (%)	-	157 (46·7)	-	80 (26·7)
Using learned strategies from the ARTEMIS app, but not actively using app, n (%)	-	96 (28·6)	-	87 (29·0)
Other Effective action, n (%)	125 (33·9)	99 (29·5)	111 (32·9)	76 (25·3)
Using another online or app-based weight loss programme	77 (20·9)	57 (17·0)	70 (20·8)	40 (13·3)
Attending a weight loss programme where I see someone face-to-face	16 (4·3)	18 (5·4)	15 (4·5)	14 (4·7)
Using weight loss medication	24 (6·5)	14 (4·2)	13 (3·9)	16 (5·3)

Using a meal replacement programme	23 (6·2)	22 (6·5)	23 (6·8)	14 (4·7)
Other (e.g., surgery)	0 (0)	1 (<1)	2 (<1)	0 (0)
Self-help strategies, n (%)	117 (31·7)	41 (12·2)	76 (22·6)	40 (13·3)

*Answers were not mutually exclusive, i.e., participants could select more than one action that they used to manage their weight.

Pre-specified sensitivity analysis excluding participants who used another effective strategy for weight loss showed an adjusted mean difference weight change between intervention and control of -2·40kg (95% CI: -3·27, -1·53kg; p<0·001) at 26 weeks. Similarly, 37·2% of the intervention group and 14·4% control group lost ≥5% of their baseline body weight (adjusted OR: 3·53; 95% CI: 2·14, 5·97; p<0·001) (***Table 3.10***).

Table 3.10: Sensitivity analysis excluding those who utilised any other effective actions for weight loss.

Week	Variable	Mean (SD) change from baseline				Adjusted difference (95% CI)	P-value
		Control	n	Intervention	n		
12 weeks	Weight (kg)	-1·71 (3·7)	199	-2·72 (4·2)	210	-1·19* (-2·03 to -0·36)	***0·005***
	n (%) losing ≥5% weight	24 (12·1)	199	51 (24·3)	210	2·34† (1·38 to 4·04)	***<0·001***
26 weeks	Weight (kg)	-1.55 (4·2)	180	-3·97 (6·4)	188	-2·40* (-3·27 to -1·53)	***<0·001***
	N (%) lost ≥5% weight	26 (14·4)	180	70 (37·2)	188	3·53† (2·14 to 5·97)	***<0·001***

*Adjusted mean difference (kg) (95% CI) calculated using linear mixed effects models with fixed effects for condition, week and group*week interaction, and a random effect for participant. IMD and baseline BMI were included as covariates as baseline values were predictive of missingness in the data.

†Odds ratio.

3.4.5.3 Self-Reported Barriers to Daily Action Planning

Within the intervention group, there were 2,399 valid responses provided to the question regarding reasons incompletion of daily action plans. The most common barriers to performing daily weight loss actions were: 1) being too busy/not having enough time; 2) forgetting; 3) work commitments, and; 4) eating out or social plans (***Table 3.11***).

Table 3.11: Codes and subcategories from content analysis for self-reported barriers to daily action planning.

Subcategory	Codes
Time-management & confliction priorities	Too busy or lack of time
	Work commitments
	Family Responsibilities
	Prioritising or distracted by other tasks
	Not convenient
Physical challenges	Illness
	Physical limitations/ discomfort
	Hormonal changes
	Controlling blood sugar
	Too tired
Motivational factors	Lack of motivation
	Lack of willpower or self-control
	Didn't keep on track
Dietary Challenges	Cravings

	Hunger/fullness
	Snacking
	Comfort/pleasure eating & drinking
	Cheating/taking a break from diet
	Binging
	Temptation
Social Influences	Social plans/eating out
	Guests/visitors
	Social expectations/pressure
	Special occasions
Environmental Influences	Travel
	On holiday
	Weather
	Food availability
	Weekend
	Environmental structure
Psychological Factors	Stress & mental health
	Boredom
	Personal life crisis
	Mindfulness & mindless eating
	Difficulty breaking habits
Planning & Organisation	Planning/preparation
	Need a reminder
	Forgot

	Change to plans or routine
	Went out or away from the house
Programme-related factors	Doubt about the effectiveness of action
	App issues
	Unsuitable or irrelevant action
	Action too difficult or disliked action
	Just didn't do action
	Partially performed action
	Performed suitable alternative
Other	Don't know
	Unknown/other

3.4.5.4 Self-Reported Rating on Health, Quality of Life, and Body Satisfaction

At 26 weeks, there was no evidence of a difference in self-reported rating of health (OR: 1·27; 95% CI: 0·96, 1·70; p=0·09) or quality of life (OR: 1·13; 95% CI: 0·85, 1·50; p=0·41) between the intervention and control groups. The odds of reporting higher body satisfaction were significantly higher in the intervention group compared to control at 12 (OR: 1·88; 95% CI: 1·42, 2·50; p<0·001), and 26 weeks (OR: 1·80; 95% CI: 1·35, 2·42; p<0·001) (***Table 3.12***).

Table 3.12: Participant self-reported rating of heath, quality of life, and body satisfaction answered of a 5-point Likert scale.

Variable	Self-reported rating	Baseline		12 weeks		26 weeks	
		Control (n=806)	Intervention (n=800)	Control (n = 373)	Intervention (n=338)	Control (n=337)	Intervention (n=300)
Health	Excellent, n (%)	12 (1·5)	7 (<1)	4 (1·1)	8 (2·4)	8 (2·4)	8 (2·7)
	Very Good, n (%)	79 (9·8)	82 (10·3)	57 (15·3)	54 (16·0)	42 (12·5)	52 (17·3)
	Good, n (%)	311 (38·6)	283 (35·4)	145 (38·9)	140 (41·4)	133 (39·5)	119 (39·7)
	Fair, n (%)	302 (37·4)	339 (42·3)	132 (35·4)	108 (40·0)	118 (35·0)	93 (31)
	Poor, n (%)	102 (12·7)	89 (11·1)	35 (9·4)	28 (8·3)	36 (10·7)	28 (9·3)
	Odds ratio* (95% CI)	-	0·94 (0·78 to 1·12)	-	1·19 (0·91 to 1·56)	-	1·27 (0·96 to 1·70)
	P value	-	0·47	-	0·21	-	0·09
Quality of life	Excellent, n (%)	14 (1·7)	19 (2·4)	15 (4·0)	14 (4·1)	15 (4·5)	19 (6·3)
	Very Good, n (%)	132 (16·4)	107 (13·4)	85 (22·7)	83 (24·6)	73 (21.7)	63 (21·0)
	Good, n (%)	323 (40·1)	307 (38·4)	151 (40·5)	139 (41·1)	137 (40·7)	128 (42·7)

	Fair, n (%)	263 (32·6)	286 (35·8)	100 (26·8)	87 (25·7)	89 (26·4)	71 (23·7)
	Poor, n (%)	74 (9·2)	81 (10·1)	22 (5·9)	15 (4·4)	23 (6·8)	19 (6·3)
	Odds ratio* (95% CI)	-	0·85 (0·72 to 1·03)	-	1·12 (0·86 to 1·47)	-	1·13 (0·85 to 1·50)
	P value	-	0·09	-	0·41	-	0·41
Body satisfaction	Very satisfied, n (%)	1 (<1)	2 (<1)	1 (<1)	1 (<1)	0 (0)	3 (1)
	Satisfied, n (%)	5 (<1)	3 (<1)	16 (4·3)	19 (5·6)	7 (2·1)	28 (9·3)
	Neither satisfied nor dissatisfied, n (%)	23 (2·9)	25 (3·1)	37 (9·9)	50 (14·8)	44 (13·1)	48 (16)
	Dissatisfied, n (%)	303 (37·6)	286 (35·8)	141 (37·8)	165 (48·8)	150 (44·5)	132 (44)
	Very dissatisfied, n (%)	474 (58·8)	484 (60·5)	178 (47·7)	103 (30·5)	136 (40·4)	89 (29·7)
	Odds ratio* (95% CI)	-	0·94 (0·77 to 1·14)	-	1·88 (1·42 to 2·50)	-	1·80 (1·35 to 2·42)
	P value	-	0·52	-	***<0·001***	-	***<0·001***

* Odds ratio (95% confidence interval) calculated using ordinal logistic regression model to compare between treatment group.

3.5 DISCUSSION

3.5.1 PRINCIPAL RESULTS

A self-regulation theory-based mobile application led to 1.85 kg greater weight loss, doubled the odds of losing ≥ 5% body weight, halved the odds of symptoms of disordered eating, and improved body image compared with simple advice to lose weight at 26 weeks. Importantly, the intervention was entirely automated with no in-person coaching or support. The intervention appeared to achieve its effects through engagement with the app, which participants partially used in favour of other effective weight loss strategies that were more commonly used by participants in the control group.

3.5.2 COMPARISON WITH PRIOR WORK

Previous trials of digital weight loss interventions combined with more intensive in-person or remote support have demonstrated effectiveness in promoting weight loss among adults with excess weight or obesity, as well as hypertension or diabetes. On average, participants in the intervention group achieved a weight loss of 2.9 kg (95% CI: 3.5, 2.3) at 26 weeks, compared to 1.0 kg (95% CI: 1.9, 0.1) in the usual care control group (220). Similarly, a web-based weight loss intervention with remote nurse support led to an additional weight loss of 1·97 kg compared to usual care in adults with obesity and comorbidities such as hypertension, high cholesterol, or diabetes (221). In comparison to the pilot trial, the mean difference in weight loss between the control and intervention

was smaller in the present study. However in the pilot, participants communicated directly with a sole researcher, which may have introduced researcher bias and enhanced the weight loss effect, whereas the lack of in-person contact in the present study eliminated these potential biases (209).

The effectiveness of low intensity interventions has faced scepticism (89, 90). Digital interventions with some degree of human contact tend to be more effective that fully automated ones, which likely contributes to the moderate effect size observed here (117, 128). However, studies of other self-management interventions have reported similar differences in weight loss, with a 1.85 kg greater loss at 6 months compared to other self-help interventions or minimal controls (129). Overall, the evidence from this study suggests that an entirely self-managed mobile application which required no professional input or additional healthcare resources, produced broadly comparable weight loss to more resource-intensive interventions.

This study also found no evidence that the treatment effect on weight loss at 26 weeks differed by age, gender, educational attainment, employment status, IMD, or ethnicity. However, national weight management programmes, such as the NHS DPP and the NHS Digital Weight Management Programme, have reported some demographic disparities in outcomes. Older participants achieved greater weight loss in both programmes, and individuals from Black and Asian ethnic groups consistently lost less weight than White participants (105, 113). Socioeconomic disparities were evident in the NHS DPP, where participants from more deprived areas had lower completion rates and smaller weight reductions (105). In contrast, the digital programme achieved comparable weight

reductions across socioeconomic groups, which likely reflects the tailored triage system, that proactively allocates participants to the different intensities of support to improve completion rates (113). Notably, a comparison of digital and face-to-face NHS DPP delivery revealed that both approaches achieved similar outcomes for participants from deprived areas, but ethnic disparities were more pronounced in the digital format (222). Overall, while digital delivery is unlikely to exacerbate health inequalities, targeted recruitment, engagement, and support strategies - particularly for ethnic minority groups - are essential to ensure equitable effectiveness across the wider populations (104). In this study, whilst the sample was skewed towards more affluent and White participants, the absence of subgroup differences in outcomes is encouraging, as it suggests the intervention may not exacerbate existing disparities.

Participants in the control group who were followed up lost over 2 kg, which is a somewhat larger weight loss than is typical for minimal intervention control groups (223). As a result, the difference in weight loss between the intervention and control groups was reduced. For participants, the absolute weight loss is usually more meaningful than relative differences between interventions, as a 2 kg loss in the control group and a 4 kg loss in the intervention group both represent significant weight loss improvements. Such outcomes may reflect the motivational effects of trial participation itself, where regular follow-ups, self-monitoring, and awareness of participation can encourage behavioural changes even in control groups (223). Additionally, a third of control group participants reported using effective weight loss interventions, which is roughly three times the rate observed in a general population of individuals living with obesity, who were not

specifically selected based on their motivation to lose weight and exhibited higher follow-up rates (224). For individuals actively seeking support for weight loss, the intervention resulted in greater weight loss and reduced reliance on additional weight loss activities compared to those attempting to lose weight without support. Control group participants were also more likely to self-fund or pursue other publicly funded weight loss interventions, underscoring the intervention's role in encouraging self-directed weight management efforts.

The intervention showed no evidence of adverse effects on eating behaviours when delivered to a general population sample, despite initial concerns that a focus on self-weighing and self-regulatory behaviours might encourage obsessive or over-controlling thoughts and actions (212-214). In fact, I observed an improvement in the symptoms of disordered eating measured and improved body satisfaction at 12- and 26- weeks. The study sample exhibited higher than average symptoms of disordered eating at baseline, which was potentially influenced by the recruitment method, which relied on social media advertisements. (215). Although this may contrast with perceived concerns surrounding weight loss programmes, these findings add to the growing body of evidence suggesting that behavioural weight loss interventions could in fact improve disordered eating symptoms (225). For example, a recent systematic review of 38 studies including 3,364 participants, found that weight loss interventions consistently improved disordered eating scores (226). In this trial, a modified version of the EDE-QS was used, omitting items that would inevitably show an increase when individuals with obesity intentionally restricted food intake for weight loss. This adjustment aimed to enhance the

questionnaire's specificity for detecting genuine changes in concerning symptoms of eating disorders within the context of this weight loss trial, but this means the results should be interpreted and generalised with caution.

Previous research suggests that few individuals naturally complete the self-regulation process (12). Existing interventions aimed at promoting self-regulatory behaviours have demonstrated significant weight loss effects compared to control groups, but they often fail to incorporate all the key components of the self-regulation process. For example, some interventions educate participants on self-regulation theory but lack practical support for specific action planning (227-229), which is a key component that had been linked to weight loss that is seldom put into practice (12). Other interventions that promote action planning often overlook the iterative nature of self-regulation, which limits the ability to adjust plans based on progress toward goals (230, 231). Additionally, many existing interventions rely on resource-intensive, face-to-face sessions, making them less scalable (209, 232). In contrast, the intervention in this study utilised a purpose-built mobile application designed to guide participants through the entire self-regulation cycle while minimising any additional intervention components. Delivered remotely, the app offers a more scalable solution. Notably, overall engagement with the self-regulation process and each intervention component was positively associated with weight loss, providing further evidence for the efficacy of self-regulation theory in supporting weight loss. This also highlights the importance of user engagement with the intervention, showing that active participation in each stage of the self-regulation process is crucial for achieving weight loss outcomes.

3.5.3 STRENGTHS & LIMITATIONS

This trial tested the effectiveness of the ARTEMIS intervention in a large, community sample of 1,607 people living with obesity, with a long follow-up of 26 weeks. The remote nature of the trial allowed for greater convenience for participants and allowed the research team to rapidly recruit and collect data from a large population sample. This also allowed me to evaluate the effectiveness of the intervention in a real-world setting, providing a more accurate representation of its impact if implemented on a wider scale.

The sample was predominantly female, white, and well educated, which is broadly representative of enrolment in most private weight management services but limits the generalisability of the findings to the wider population (124, 199, 233). While a somewhat representative sample of minority ethnic groups was included in the sample, they form a small minority of the middle aged and older population, meaning these exploratory subgroup analyses were underpowered to detect such differences and so there is only weak evidence to suggest that the treatment effect is similar across all ethnic groups.

Retention was anticipated as a challenge, so efforts were made to minimise the demands of follow-up and compensate individuals for their time. Despite this, only 40% of participants were followed up at 26 weeks and 48% provided at least one weight reading after baseline, showing that retention and follow-up remain a challenge in remote trials. The follow-up rates in this study were low compared to clinical trials with selected participants and in-person contact, but typical of trials of digital interventions, where attrition rates range from 9-86% (142), and from 9-89% in digital weight loss

interventions specifically (234). I aimed to mitigate the issue of missing weight readings by using mixed models for repeated measures, allowing use of all available data with weight readings assumed missing at random. I also employed sensitivity analyses with different assumptions for missing data which did not change the conclusions that the intervention was effective but did reduce the size of the intervention effect. Weight was self-reported, meaning there is a risk that the outcome measures were not accurately reported. This risk was mitigated by asking participants to provide a photograph of their scales to validate their reported readings, as well as checking any implausible weight readings with data entered in the app.

3.5.4 Implications & Further Research

Despite the large number of mobile applications supporting weight loss, many lack theoretical grounding or substantial evidence of effectiveness beyond anecdotal reports or observational studies. Current evidence supports the effectiveness of interventions which incorporate intensive in-person or digital behavioural support from another person, but this increases costs and limits scalability. This large, pragmatic randomised controlled trial provides evidence supporting the benefits of a fully self-managed, self-regulation intervention designed to help adults with obesity lose weight. The intervention proved effective without any adverse effects, making it a viable option for delivery through healthcare providers or other public or private channels for individuals seeking self-managed weight loss support. As such, I am currently in discussions with the

Department of Health and Social Care, who have expressed interest in ARTEMIS as a scalable treatment option.

Notably, the intervention was entirely automated, requiring no in-person coaching or professional support, and achieved weight loss results broadly comparable to more resource-intensive programmes. This approach reduces the need for healthcare resources and given the evidence that it works for most people with no significant disparities, it presents a broadly scalable solution. However, engagement was modest, and ARTEMIS is likely to attract individuals who are already relatively motivated and digitally enabled. The intervention also requires a high level of individual agency, which may not be suitable for everyone, but even if only a small proportion of users continue to engage with the mobile app, its wide reach and minimal resource demands could lead to a significant population-level impact. Whilst the sample was skewed towards more affluent and White participants, the absence of subgroup differences in outcomes is encouraging, as it suggests the intervention may not exacerbate existing disparities.

Future research should focus on comparing the effectiveness and cost-effectiveness of the intervention with other digital weight loss interventions, particularly those that are more resource intensive. Although I conducted exploratory subgroup analyses in this study, the sample size was insufficient to detect significant differences between ethnic groups, meaning these results should be interpreted with caution, and an assessment of the effectiveness of the intervention across diverse populations is still required. Additionally, further investigation is needed to assess the effectiveness of the

intervention when provided as part of routine primary care appointments for individuals with obesity, relative to standard care.

3.5.5 Conclusions

An entirely self-managed mobile application with no human support, which was designed to promote self-regulation, increased weight loss and improved the symptoms of disordered eating measured in people living with obesity. These findings suggest that the intervention could be safely deployed at population-level to support effective weight management.

Chapter 4 : Enhancing engagement and adherence in a commercial digital weight loss programme: the development and optimisation of a complex intervention guided by the Multiphase Optimisation Strategy Framework

4.1 SUMMARY

This chapter describes the preparatory work I carried out to develop a set of candidate components aimed at increasing engagement, and in turn, weight loss, in the Second Nature programme. As part of my iCASE studentship, I spent three months on placement with Second Nature, where I observed health coaches and interviewed participants to understand key barriers to engagement. This experience helped me to understand the programme in depth and identify small changes that might enhance its effectiveness.

I took a systematic, research-led approach to testing these potential changes by applied the Multiphase Optimisation Strategy (MOST) framework. This chapter outlines the work conducted in the preparation phase of MOST, including selection and development of

candidate intervention components, development of a conceptual model, and the definition of the optimisation objective. The development process followed four steps: scoping the literature; understanding the problem and user preferences; filtering and refining potential intervention options; and translating findings into app features.

The four components selected for testing were: (1) an introductory video call with the health coach, (2) drop-in webchat sessions, (3) goal-setting statements, and (4) food diary review plus feedback. The intervention theory and conceptual model were grounded in the supportive accountability model, which posits that human support can improve adherence to digital interventions by fostering a sense of accountability to another person. This preparatory work laid the foundation for an optimisation trial (***Chapter 5***), which aimed to identify the optimal combination of components for enhancing engagement and weight loss within the Second Nature programme.

Note: parts of this chapter have been published in a peer-reviewed journal article.

- **Wren GM** et al. Optimising a digitally delivered behavioural weight loss programme: study protocol for a factorial cluster randomised controlled trial. Trials. 2024. 25(1):477. https://doi.org/10.1186/s13063-024-08320-5

4.2 INTRODUCTION

4.2.1 DEVELOPING AND EVALUATING COMPLEX INTERVENTIONS

Whilst a fully automated intervention like ARTEMIS (***Chapter 3***) offered clear benefits in terms of scalability, retention was low. The modest effect sizes and engagement levels observed therefore prompted me, in this chapter, to explore whether more supportive components could enhance outcomes in digital programmes.

Complex interventions, which are defined as interventions that consist of multiple interacting components, are generally more effective than single-component approaches (235, 236). Digital behaviour change interventions typically integrate multiple components into a single package delivered to participants, meaning they are inherently complex interventions by design.

There are several published frameworks to help guide the process of developing and evaluating complex interventions. The UK Medical Research Council (MRC) Complex Intervention Framework highlights the importance of using relevant theory in intervention design (236). The MRC guidance suggests a flexible process of four interrelated phases: development, feasibility, evaluation, and implementation (237). The development phase involves developing a new intervention or adapting an existing one (238). The feasibility phase addresses key uncertainties, often using predefined progression criteria to determine readiness for further research (237, 239). The evaluation phase typically involves a trial, with parallel group randomised controlled trials (RCT) commonly used to

compare the intervention's effectiveness against a suitable comparator, such as usual care (237).

However, RCTs have several limitations when it comes to evaluating complex interventions (240). Although a standard RCT can provide evidence about whether the intervention as a whole works better than a control or a comparator intervention, such designs cannot determine the effectiveness of individual components or how their interactions may drive the observed effect (241). RCTs are also resource-intensive yet provide limited information beyond the effectiveness of an intervention package as a whole. Using a RCT to evaluate new features individually would require conducting numerous individual studies over a long period of time, a process that would lag behind the pace of technological advancement. As a result, it calls into question whether relying on RCTs as the default standard for evaluating complex interventions is truly the most effective approach (242).

New frameworks for developing behavioural interventions have emerged, including the Multiphase Optimisation Strategy (MOST), which offers a means to address some of these limitations (243). MOST involves multiple phases of randomised trials to establish the optimal combination of individual intervention components. As it relies on randomised experimentation, bias is minimised, and causal relationships can be identified, increasing confidence in the results. By using this framework, it is possible to increase the efficacy of behavioural interventions, and when paired with the scalability of digital health interventions, this has the potential to provide considerable public health impact.

4.2.2 Multiphase Optimisation Strategy

MOST is an engineering-inspired framework which uses highly efficient randomised experimentation to identify an optimised combination of intervention components *before* testing this intervention package in a standard RCT (148, 243). This systematic approach is particularly well-suited for digital interventions due to its emphasis on efficiency, resource management, and iterative testing (243). MOST progresses through three distinct phases: the preparation phase, optimisation phase, and evaluation phase (***Figure 4.1***).

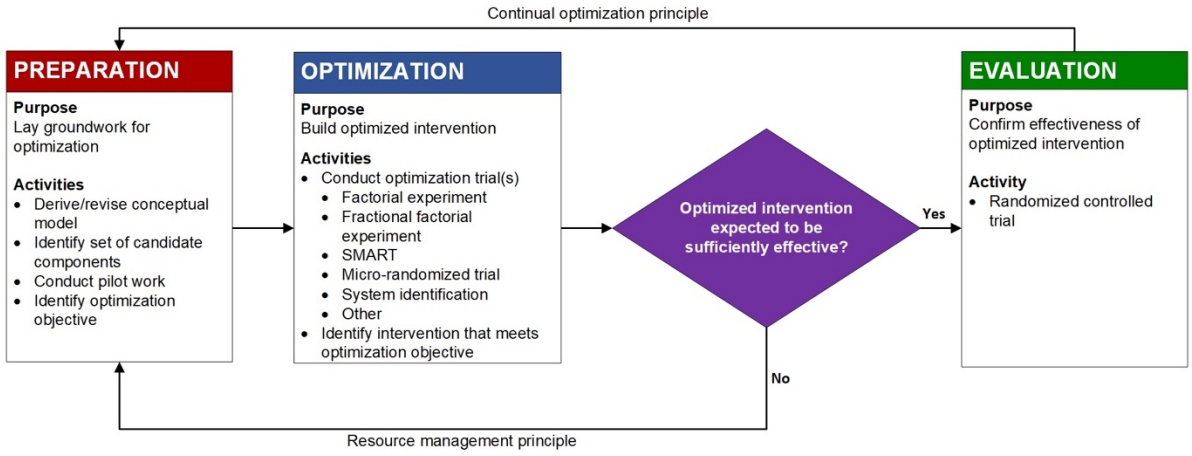

Figure 4.1: Outline of Multiphase Optimisation Strategy (MOST), taken from Collins et al. (148)

4.2.2.1 Preparation Phase

The preparation phase focusses on laying the foundation for the optimisation of the intervention. This phase involves three main tasks: developing a conceptual model, identifying candidate intervention components, and defining an optimisation objective

(242, 244). The development and revision of a conceptual model should be informed by theory and empirical evidence and visually demonstrate the expected mechanisms of the intervention (245). The conceptual model in MOST goes a step further than a traditional logic model by hypothesising the causal pathways through which each intervention component is expected to influence the outcome (244). Each intervention component should be designed to target a specific mediator within the conceptual model, ensuring independence to help with decision-making when it comes to identifying the optimised intervention package (244).

After establishing the conceptual model, the next step is to develop or identify candidate components. While this process may share similarities with a typical intervention development process, MOST requires some further key considerations. These may include, but are not limited to, granularity and independence. Granularity refers to the size and scope of each component, which may depend on the research question and available resources. The independence of each component means that one component's function doesn't rely on another component being present. It is also important to consider how individual components form a cohesive intervention package to prevent participants from receiving a fragmented intervention or encountering significant duplication across components.

Developing affordable and scalable interventions is a central goal of MOST, and implementation considerations start in the preparation phase by specifying an optimisation objective (244, 245). The optimisation objective is explicitly defined in the preparation phase to balance effectiveness with any constraints on resources. This

objective can include any constraint relevant to the intervention, such as cost, or the time required to participate in or deliver the intervention.

4.2.2.2 Optimisation Phase

The optimisation phase employs rigorous experimental designs to systematically test the effects of individual intervention components and their interactions (148). This empirical evidence guides the selection of components for inclusion in the optimised intervention package, adhering to the pre-defined optimisation objective (246). MOST doesn't specify a particular experimental design for the optimisation phase. However, the resource management principle is a core part of the MOST framework and suggests that selecting a design should be based on its efficiency in using resources to answer the specific research question (242, 247).

A factorial experiment is commonly used for the optimisation phase as this design can estimate the effects of components both individually and in combination (248, 249). This data can be used to inform decision-making about which components to include in final intervention package (246, 250). If the optimised intervention demonstrates effectiveness, researchers will typically proceed to the evaluation phase to confirm its effectiveness. However, if the optimisation trial results indicate minimal or no impact of the components on the outcome, it may be more beneficial to revisit the preparation phase. This would involve revising the conceptual model and potentially developing new candidate components, consistent with the resource management principle of MOST (246).

4.2.2.3 Evaluation Phase

The final phase involves a formal evaluation of the effectiveness of the optimised intervention package compared to a suitable control condition, typically by means of a RCT (148). If the RCT indicates that the optimised intervention is effective, then the intervention could be implemented in its intended setting. If the RCT shows the optimised intervention to be ineffective, or even if it finds the optimised intervention to be effective, it may still be possible to improve the intervention. The MOST framework embraces the principle of continuous optimisation, enabling the revisiting of the preparation phase to further refine the intervention based on new insights and knowledge gained during the evaluation phase (251).

4.2.3 Optimising Digital Interventions: Integrating Frameworks and Behaviour Change Theory

Developing effective digital health interventions requires a rigorous approach that integrates established frameworks with behaviour change theory. As discussed in ***Chapter 1***, incorporating such theory not only enhances intervention effectiveness but also aids in understanding mechanisms of action (252).

Despite the multitude of mobile apps available for weight loss in commercial markets, the quality of their content remains suboptimal (203, 253). Specifically, many mobile health apps have been developed in the absence of evidence-based features, do not involve health care experts in their development process, and have not undergone rigorous scientific testing (254-256). As such, it has been argued that mobile health

development would benefit from collaboration between commercial app developers and behaviour change experts (154). My iCASE studentship and collaboration with Second Nature, was the perfect opportunity to bridge this gap by integrating evidence-based behaviour change strategies into a commercially available mobile health app.

4.2.4 RATIONALE FOR THIS STUDY

The MOST framework offers an efficient design particularly suited to testing components within a technology-supported obesity intervention, as demonstrated in previous research (149). By leveraging the MOST framework, the development of more effective behavioural interventions can be accelerated and, when paired with the scalability of digital health interventions, this approach offers considerable potential for making a significant impact on public health.

During my placement at Second Nature, I identified potential small changes that could alter the effectiveness of their overall intervention. However, these changes were expected to have small effects individually, which would not justify a standalone trial. Second Nature currently employs an iterative process to trial new components. Whereas I adopted a more research-driven approach, by applying the MOST framework to explore whether it could be used to optimise the effectiveness of their existing digital behavioural weight loss programme.

This chapter details the work undertaken during the preparation phase of MOST which laid the groundwork for the optimisation phase (***Chapter 5***). Key activities that I conducted in the preparation phase involved reviewing relevant literature, undertaking

user interviews, selecting the candidate intervention components, and developing a conceptual model. ***Figure 4.2*** provides a visual representation of the development process, which is described further in subsequent sub-sections.

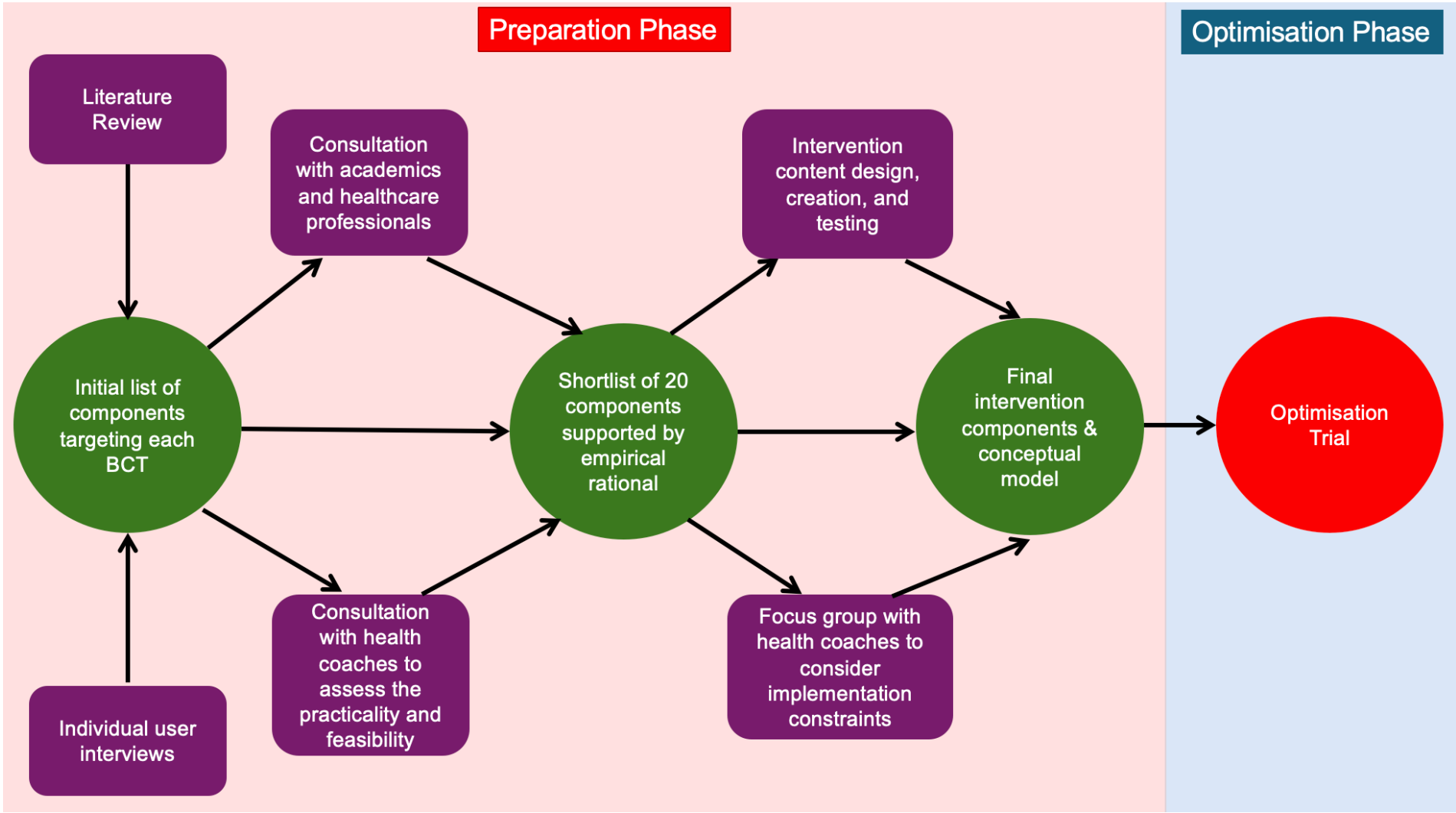

Figure 4.2: Overview of the intervention development process and alignment with the phases of the MOST framework

4.3 The Complex Intervention: Current Second Nature Programme Description

The core intervention, delivered primarily to participants via a smartphone application, is the 'core' phase of the Second Nature programme (***Figure 4.3***). The 'core' phase consists of a 17-week behaviour change programme aiming to support people to have a healthier diet and increase their physical activity.

Note: The Second Nature programme and its contents evolved over the course of my DPhil. It is described here as it was at the time of this study.

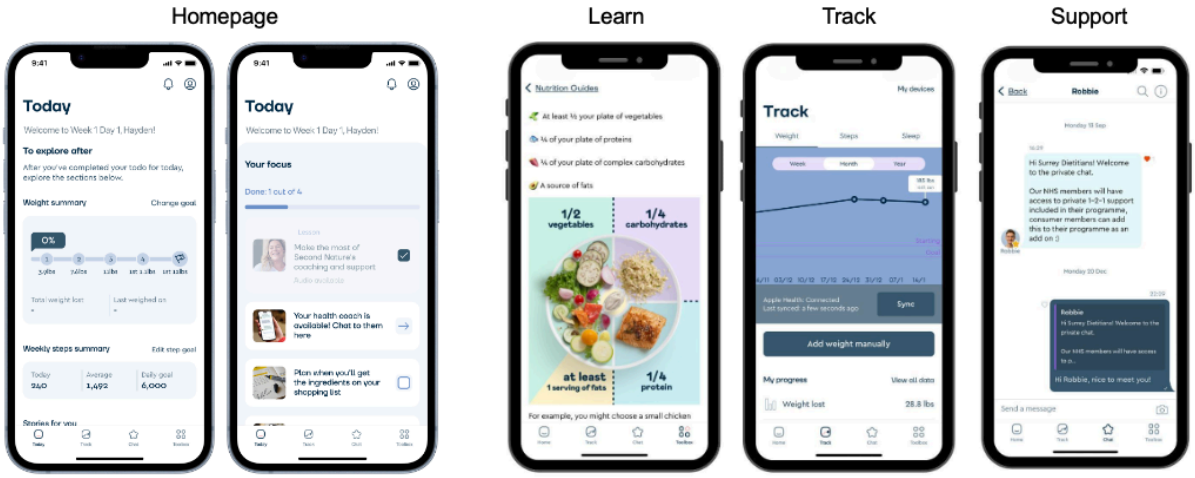

Figure 4.3 : Example Second Nature programme content.

Second Nature provides a 12-month programme consisting of three 4-month phases: 1) 'Core' (weeks 1-17), where participants receive support from their peers and health coach, and acquire knowledge of nutrition and habit formation 2) 'Growth' (weeks 18-35), where participants gain a deeper understanding of their new behaviours and

reinforce their new habits, and 3) 'Maintain' (weeks 36-52) where participants practice the skills they've learned to maintain their weight loss.

At the start of the programme, each participant receives a hard-copy instructional handbook and recipe book. The 'core' 17-week programme consists of mentoring from a registered dietitian or nutritionist (a health coach) who delivers personalised support via a text-based messaging service within the app. The messaging support is provided both privately and within a group chat of around 30 other people. The minimum standard frequency for group messages is as follows: weeks 1-4: four messages per week; weeks 5-8: three messages per week; weeks 9-15: two messages per week; weeks 16-17: three messages per week. The group chat is monitored daily by the health coach, any comments or questions are answered within the day's coaching window, and further conversation is facilitated where possible. The private chat is only visible to the health coach and the participant and allows participants to ask specific questions on topics such as health-related issues and personalised dietary requirements. Educational information, delivered by plain text, audio, and videos can be accessed by participants through the app. The educational information covers topics which focus on nutrition, mindset, exercise, and sleep (***Table 4.1***). All content within the app can be translated into other languages as required by the user. Participants can record and view their weight and step count within the tracking section of the app, which can also be viewed by the participant's health coach. Participants who have low engagement (defined as < 10 interactions with the app in the previous week) receive automated messages to encourage participation.

During the 'Growth' phase, users can still access all features of the app however, their group is merged with another group and their health coach may change. The intensity of the programme decreases during 'Growth', the message frequency is a minimum of two messages per week, and participation is encouraged less frequently.

Table 4.1. Educational content during each week of the Second Nature programme.

Week	Topic	Description
1	Kickstart week	Introduction to the programme and healthy habits.
2	The psychology of eating	The 'why' behind certain food choices and overcoming the common obstacles to weight loss.
3	Unpacking nutrition	Introduction to nutrition recommendations and common dieting myths.
4	The relationship between weight and health	Set point theory, weight loss plateaus, and ways of measuring progress.
5	Breaking and making habits	Habit formation, the value of 'tiny habits', and stopping unhelpful habits.
6	Appetite and cravings	Managing cravings and understanding factors that influence appetite.
7	Mindset	Thinking traps, strategies to overcome common thought patterns, and an introduction to body image.
8	Stress and emotions	How stress and emotions affect food choices; introduction to mindfulness and emotional eating.
9	Exercise	Common barriers to exercise and strategies to incorporate more exercise into daily life.
10	Hunger and fullness	The biology and psychology of hunger and fullness and how to be more mindful of fullness cues.

11	Nutrition myths	Counting macros, protein intake, alcohol, sweeteners, and reducing risk of heart disease.
12	Sleep	The impact of sleep on weight loss and strategies to improve sleep quality.
13	Motivation	Types of motivation and how to find and maintain motivation.
14	Taking back control	Preparing for challenging situations, social pressure, and impulsive food decisions.
15	Reflect and progress	Tools for the next phase of the programme including building self-belief and managing the food environment.
16	Accepting thoughts and emotions	Overcoming emotional eating, accepting difficult thoughts, and managing feeling of restriction.
17	Moving forwards	Reflecting on the journey so far before moving to the next phase of the programme.

4.4 Intervention Component Selection and Development

The selection and development of the intervention components followed a structured, multi-step process aimed at ensuring that the components were evidence-based, user-centred, and practically feasible. This process involved four key steps: scoping the literature, understanding the problem and user preferences, filtering and refining potential intervention options, and translating findings into app features. The final intervention components were developed in collaboration with the industry partner, Second Nature, and were shaped by both user needs and organisational constraints. Given the resources allocated to this trial by Second Nature, the aim was to identify four intervention components hypothesised to enhance engagement with the programme

and subsequent weight loss. I was unable to modify the core elements of the programme or access engineering resources to modify the app, so the components had to be tested as adjuncts to the core programme.

4.4.1 STEP 1: SCOPING THE LITERATURE

To ensure the intervention was grounded in evidence, the development process began with a rapid review of the literature. The primary aim was to understand the factors associated with engagement and weight loss success in digital weight loss programmes, focusing predominantly on existing reviews identified through backward citation.

4.4.1.1 Factors Associated with Engagement and Weight Loss Success in Digital Weight Loss Programmes

I began by searching for systematic reviews using the terms “weight loss”, “obesity”, “behavioural”, “lifestyle”, “engagement”, “adherence”, “digital”, “mobile apps” and their variations were used, as well as backward citation. I then collated and summarised the factors associated with weight loss and engagement (***Table 4.2***).

Recent conceptual models of engagement have identified various factors that influence engagement and its relationship with intervention effectiveness (discussed further in ***Chapter 1***). These factors include the programme-related factors (content and delivery), contextual influences (setting and population), and psychological characteristics (motivation and self-efficacy) (131, 144). For this review, I specifically focused on programme-related factors, since these are modifiable within the context of this study.

Table 4.2: Summary of factors associated with weight loss and engagement in digital behavioural weight loss programmes. Factors associated with engagement (E), weight (W), or both (B).

Factor	Explanation	Evidence	Refs	Associated with
Goal setting	The process of defining specific, measurable, achievable, relevant, and time-bound objectives.	Digital interventions can support goal setting. Goal setting is a common BCT used to support motivation and progress tracking.	(78, 144, 257, 258)	B
Social support	Opportunities for users to connect with peers and receive support and encouragement from others.	Access to social support is highly valued by users, enhances accountability, and promotes engagement. Peer support can improve efficacy of interventions.	(78, 89, 128, 144, 147, 257-259)	B
Rewards	Incentives and rewards for engaging with the app or achieving goals.	Positive reinforcement strategies such as rewards increase engagement.	(144, 257, 260)	E
Structured programmes & frequent contact	Structured programmes with regular check-ins, and weekly lessons.	Programmes with a clear structure (e.g., regular lessons, check-ins) and frequent contact (e.g., weekly sessions, regular feedback) lead to better weight loss outcomes and increased engagement. This structured approach	(78, 85, 128)	B

		fosters a sense of accountability.		
Personalisation	Tailoring interventions to individual needs, goals and circumstances.	Participants value tailored information and personal targets, dislike generic feedback. Interventions that adapt to individual needs are more engaging. Personalisation of content and feedback is a key feature of effective interventions.	(117, 128, 144, 147, 258)	B
Individualised Feedback	Receiving personalised feedback regarding performance.	Individualised feedback may increase engagement levels. Feedback messaging is a frequently used tool in apps. Personalised feedback is important for weight management as it enhances self-awareness and promotes sustained behaviour change.	(89, 117, 128, 144, 147, 257)	B
Programme engagement	Overall engagement with the intervention is associated with higher weight loss.	High levels of engagement correlate with improved weight loss outcomes.	(89, 138)	W
Self-monitoring	Tools that enable users to track their weight, health behaviours, and progress.	Self-monitoring is an essential component of digital health technologies. It is associated with weight loss, adherence and	(78, 89, 117, 128, 138, 144, 147, 257, 261)	B

		promotes behavioural self-regulation.		
Reminders and prompts	Reminders and notifications to use the app or engage in healthy behaviours.	Reminders, particularly push notifications, can have a positive impact on engagement	(147, 257, 259)	E
Health information	Providing educational content with relevant and practical content.	Educational content builds knowledge and supports informed decision-making.	(144, 147, 261)	B
Human contact/support	The presence of human interaction within the intervention, such as personal coaching or counselling.	Blended approaches that include human contact are proposed to improve accountability, which is associated with increased engagement and weight loss compared to full automated interventions	(115, 117, 259)	B
Support from a health professional	Access to health professionals and practitioners within the app.	Health professional input is associated with greater trust and improved outcomes.	(89, 128, 144, 259, 261)	B

4.4.1.2 Evidence-Based Strategies to Address these Challenges

The BCT Taxonomy, encompassing 93 established techniques, served as a foundational framework for identifying potential intervention components (77). As a starting point for the intervention development process, I made an initial list of potential intervention components based on the BCT taxonomy, targeting factors associated with weight loss

and engagement identified in ***Table 4.2***. These intervention components were categorised into broad themes: feedback and reinforcement, goal setting, social support, incentives & rewards, environmental restructuring, self-monitoring & prompts, cognitive restructuring.

4.4.2 Step 2: User Interviews to Understand Barriers To Success and User Preferences in the Second Nature Programme

To complement the evidence from the literature, a user-centred approach was adopted to identify specific barriers to success within the Second Nature programme. During a three-month internship at Second Nature, I was involved in conducted 27 individual interviews with current programme participants to understand key challenges to programme success.

The three main barriers identified were as follows:

1) **Lack of personal connection.**

Many participants expressed that the digital format of the programme made it challenging to establish a strong sense of connection with their assigned health coach. They reported that interactions often felt impersonal which reduced their sense of feeling supported with their weight loss efforts. Most participants shared that they valued the idea of a coach but felt that infrequent or generic communication did not foster the sense of accountability to their coach they were seeking. Without a more personal connection, participants were less likely to seek help when facing challenges, which ultimately

affected their engagement with the programme. This lack of clarity left many participants uncertain about how to interact with their coach, unsure of what to expect from the relationship, and often waiting passively for the coach to initiate contact instead of proactively reaching out with any issues they were facing.

2) **Difficulty sustaining motivation due to insufficient accountability mechanisms.**

While participants appreciated the flexibility and convenience of an app-based programme, many highlighted the absence of structured accountability mechanisms. Several participants compared the programme to in-person services such as Weight Watchers or Slimming World, where scheduled sessions provided a sense of commitment to attend and an opportunity to share progress within either a coach or community that they felt accountable to. The lack of these structured elements made it easier for participants to deprioritise the programme in their daily lives. Additionally, during periods of slower progress or setbacks, participants found it difficult to stay motivated and committed to the programme without mechanisms such as peer accountability, group meetings, or regular one-on-one check-ins.

3) **Limited personalised feedback.**

Participants noted that generic advice from their health coach or automated tips received through the educational articles in the app, often failed to address their unique circumstances. Some of these circumstances included their specific lifestyles, dietary preferences, or challenges. Without tailored guidance, participants found it hard to

relate to the programme or to implement its suggestions effectively within their current lifestyle. This lack of personalisation left some users feeling that the programme was not well-suited to their individual needs, meaning they would disengage from the app and stop participating in the programme altogether.

4.4.3 Step 3: Filtering and Refining Potential Intervention Components

Building on the insights from Steps 1 and 2, the comprehensive list of candidate components based on the 93 BCTs was narrowed to 20 viable options through expert consultation with academics and healthcare professionals with knowledge of the factors associated with successful outcomes and research into barriers to success. To be shortlisted, each component was required to have robust empirical evidence base and a clear rationale in addressing barriers identified through the literature review and user interviews in Steps 1 & 2. The filtering process also involved input from Second Nature health coaches to assess the practicality and feasibility of delivering these techniques within the existing programme structure. The resulting shortlist included 20 components which are summarised in ***Table 4.3***.

Table 4.3: Summary of 20 shortlisted candidate intervention components

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
Feedback & Reinforcement	Motivational emails or texts	Motivational emails or text highlighting health benefits of target behaviours and prompting participants to engage with activities in the app.	Tailored text messages increased adherence to weight loss programme and could enhance weight loss (262, 263).	Prompts/cues, information about health consequences, information about social & environmental consequences, information about emotional consequences	Requires app changes: No	No	Yes
	Congratulating success	Congratulate the person for each week they lose weight or each day they meet their step goal. Or add function in app to congratulate others in your group on their successes.	Members enjoy receiving recognition for success in areas such as diet, exercise, and actual weight loss. This recognition in turn sometimes provides encouragement	Social reward	Requires app changes: Yes	Yes	Yes

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
			and motivation to persist (264).				
	Success stories	Testimonials/videos shared from other successful users. Motivational quotes from users about healthy eating, physical exercise, losing weight, using the app.	Members read personal accounts of how other members have succeeded in losing weight. This sometimes provides encouragement and motivation (264).	Information about others' approval	Requires app changes: Yes	Yes	Yes
	Food diary review plus feedback	Participants are reminded to complete a food diary. Health coach reviews and provides personalised feedback on food diary entries.	Dietary self-monitoring improves weight loss (206), and that dietary self-monitoring combined with feedback leads to greater weight loss than self-monitoring alone (265).	Feedback on performance	Requires app changes: No	Yes	Yes
Goal Setting	Higher weight loss goal	Participants counselled to set a higher weight loss goal - increase weight loss goal by 50%.	Setting higher weight loss goals is associated with improved weight loss and better retention (173, 194). See ***Chapter 2***.	Goal setting (outcome)	Requires app changes: No	No	Yes

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
	Goal Setting and reflection statements	Participants set their own weight loss goals, process goals (like daily steps), and specific actions. They are asked to reflect on their progress towards the goals on a weekly basis.	Self-determined motivation, fostered through goal setting, is associated with better weight management (192), and that monitoring goal progress is an effective strategy for promoting goal attainment (266).	Goal Setting (process)	Requires app changes: No	Yes	Yes
Social Support	Health coach introductory call	The addition of one call with the health coach at the start of the programme. Health coach to introduce themselves and their qualifications/experience to build rapport and connection with the participant.	Previous systematic review evidence has shown that providing dietitian or therapist contact is associated with improved weight loss (69, 267). Supplementing weight management with brief human support could improve usage and outcomes (268).	Social support (practical), Credible source	Requires app changes: No	Yes	Yes

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
	Booster calls	Addition of 'booster' calls with health coach at times of low engagement.	Greater number of treatment sessions results in greater weight loss (269, 270). There is comparable efficacy of telephone and in-person coaching for achieving weight loss (271).	Social support (practical)	Requires app changes: No Implementation challenges: engagement is generally low so would require substantial health coach resource	Yes	Yes
	Buddy support	Allocate a buddy to each participant (someone with similar motivations/ experiences) versus the group chat function.	Engaging peers together in weight loss has been found to augment treatment retention and weight loss outcomes (272).	Social support (unspecified)	Requires app changes: Yes	Yes	Yes
	Group call	Test addition of one group call at the start of the programme. Participants may feel more connected	Engaging peers together in weight loss has been found to augment treatment	Social support (unspecified)	Requires app changes: No	Yes	Yes

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
		to group, facilitating greater accountability.	retention and weight loss outcomes (272).				
	Drop-in Webchat Sessions	Participants have a dedicated time each week that they can drop-in to the webchat and interact with their health coach to ask specific questions, receive feedback and personalised support.	Contact with a dietitian or therapist, and in particular more frequent contact, is associated with improved weight loss (69, 267).	Social support (practical), Credible source	Requires app changes: No	Yes	Yes
Incentives & Rewards	Incentive for behaviours	Inform that participants will receive free membership if they use the app/monitor their weight/engage with group chat/reach other behavioural goal.	Outcome-based and goal-directed financial incentives were similarly effective for weight loss (273).	Material incentive (behaviour)	Requires app changes: No	No	Yes
	Incentive for weight loss	Inform the participant that they will receive a free month subscription if and only if a certain amount of weight is lost.	Financial incentives have shown mixed results in relation to weight loss outcomes (274-276). Outcome-based and goal-directed financial	Incentive (outcome)	Requires app changes: No	No	Yes

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
			incentives were similarly effective for weight loss (273).				
Environmental Restructuring	Recipe Box	Provide recipe box with ingredients and recipe cards for the first week of the programme.	Food provision in behavioural interventions for weight loss has been shown to significantly enhance weight loss and compliance (277, 278).	Instruction on how to perform behaviour, Adding objects to the environment	Requires app changes: No Implementation challenges: requires lots of logistical input	Yes	Yes
	Provision of scales	Provision of Bluetooth scales.	Providing scales is hypothesised to increase the rate of self-weighing and self-regulation behaviours (279). A pilot study has shown that the provision of smart scales improved weight loss (280).	Adding objects to environment, Self-monitoring of outcome	Requires app changes: No Implementation challenges: participants generally get to choose to pay for the scales	No	Yes

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
Prompting and self-monitoring	Prompt weight tracking	Prompt participants to record their weight as soon as they wake up. Can set a reminder for 15 mins after they normally wake up.	Regular weighing (self-monitoring) associated with more successful weight loss (206, 213).	Prompts/cues, self-monitoring of outcome	Requires app changes: Yes	No	Yes
	Prompt behaviours	Add function of prompts to app for performing desired behaviour at a particular time e.g., prompt meal planning on Sunday evening, prompt going for a walk during lunch break.	Research has found that weight management interventions using BCT associated with self-regulation or control theory (281) appear to lead to more weight loss (80, 81).	Prompts/cues, Habit formation	Requires app changes: Yes	Yes	Yes
	Visibility of weight records	Option to view the weight/activity/engagement of other members of the group switched on/off.	Systematic review showed that behavioural weight management programmes which included BCTs that compare participants' behaviour with others were associated with greater weight loss (69).	Social comparison	Requires app changes: Yes	No	Yes

Category	Component	Explanation	Evidence/Literature	BCT	Feasibility	Aligns with business objectives	Empirical rationale
Cognitive restructuring	Changing self-identity	Ask participants to articulate their new identity as a 'healthy eater and an active person'. Or they are encouraged to think of themselves as a role model to their children. They must think and log this every day.	One important mechanism underlying health behaviour change is identity-based motivation (282). Qualitative evidence that a shift in identity occurs in successful weight loss maintenance (283).	Identity associated with changed behaviour, identification of self as role model.	Requires app changes: No Implementation challenges: would require intensive behavioural counselling	No	Yes
	'I will' statement	Participants asked to write down an "I will" statement to affirm or reaffirm a strong commitment e.g. I will track my weight every day or cook three meals a day at home.	Behavioural contracts, have potential for facilitating short-term, and possibly longer-term weight loss and dietary behaviour change when used alongside a lifestyle intervention (284).	Commitment	Requires app changes: No	Yes	Yes

Abbreviations: BCT: behaviour change technique

4.4.4 Step 4: Translating Findings into Viable App Features

The final stage involved further filtering the 20 shortlisted components to four practical intervention components that could be implemented within the constraints of the Second Nature programme. I co-produced these components by conducting focus groups with the company's health coaches which helped to translate user feedback into viable app features and to understand the practicality of introducing these components into the programme.

Each component was designed to address specific barriers identified in Step 1 & 2 while adhering to the following implementation constraints:

Constraint 1: The component must be practically feasible to implement

Each component was assessed for its practicality and ease of integration within the existing programme structure. Given the constraints of the study, engineering resources were unavailable meaning no app modifications were possible. As a result, components needed to be delivered by health coaches or through mechanisms external to the app. This required features that could be implemented without any app modifications and without adding excessive workload to the health coaches or research team.

Constraint 2: The component must align with Second Nature's business objectives

All proposed components were evaluated to ensure alignment with Second Nature's strategic and operational goals. This included considering their compatibility with the company's priorities for implementation and the capacity of the existing team of four

health coaches. Components were prioritised based on their empirical evidence base, potential to enhance engagement with the programme and weight loss outcomes, whilst supporting the organisation's long-term objectives.

See ***Table 4.3*** for a summary of these considerations for each component.

4.5 THE FOUR CANDIDATE INTERVENTION COMPONENTS

Following the selection process the following four intervention components were selected:

4.5.1 HEALTH COACH INTRODUCTORY VIDEO CALL

Within the category of social support, the health coach call and the group call were both options that could be feasibly implemented in the programme (***Table 4.3***). To address the barrier identified in Step 2, 'lack of personal connection', the health coach call was selected with the aim of strengthening user-health coach connections. Previous evidence has shown that telephone coaching produces comparable weight loss to in-person coaching (271), and supplementing a web-based programme with coaching calls improved engagement and weight loss outcomes in those that take up the call (268). Here, the digitally delivered programme will be enhanced with an introductory video call with the health coach.

4.5.2 Coaching Drop-In Webchat Sessions

Within the category of social support, coaching drop-in webchat sessions were selected as they could be feasibly implemented in the programme (***Table 4.3***), and they address all three barriers identified in Step 2. In support of this component, systematic reviews have shown that contact with a dietitian or therapist, and in particular more frequent contact, is associated with improved weight loss (69, 267). Similarly, human-delivered online coaching sessions have been shown to increase user engagement and was associated with a significantly higher chance of clinically meaningful weight loss (285). In this component, participants will be offered regular, scheduled 1-to-1 coaching drop-in time with their health coach delivered in the chat function of the app.

4.5.3 Goal Setting Statements

This component was selected to address the barrier identified in Step 2, 'insufficient accountability mechanisms', and it could be feasibly implemented in the programme (***Table 4.3***). Goal setting is integral to fostering accountability, particularly by involving the participant in the definition of goals and expectations (286). Previous literature has proposed that self-determined motivation, fostered through goal setting, is associated with better weight management (192), and that monitoring goal progress is an effective strategy for promoting goal attainment (266). In the current Second Nature programme, participants set only one weight loss goal at the start of the programme. Here, participants will be asked to complete goal setting statements alongside reflection of the actions made towards their goals each week.

4.5.4 Food Diary Review Plus Feedback

Within the category of feedback and reinforcement, the food diary review plus feedback component was an option that would be feasibly implemented in the programme (***Table 4.3***). This component was selected to address two of the barriers identified in Step 2, as it aims to create accountability mechanisms and facilitate personalised feedback.

Previous evidence has shown that dietary self-monitoring improves weight loss (206), and that dietary self-monitoring combined with feedback leads to greater weight loss than self-monitoring alone (265). This may promote self-regulatory behaviours, which has been associated with improved weight loss in numerous dietary and physical activity interventions (78, 80, 209). However, adherence to dietary self-monitoring tends to decline over time as individuals may find it tedious (206). Therefore, dietary self-monitoring in the short term may help participants establish initial habits before transitioning to more intuitive strategies for maintaining progress. To balance effectiveness with participant burden, I chose to prompt participants to complete their food diary at three times in the programme.

4.6 The Conceptual Model

The theory for the conceptual model is based on the supportive accountability model (286). The model suggests that human support can improve adherence to digital interventions by fostering a sense of accountability to another person. This model argues that individuals are more likely to adhere to an intervention when they feel accountable

to a coach they trust and see as benevolent and having relevant expertise, and who sets clear process-focused expectations, establishes goals, and monitors their progress.

Based on this theory, each of the four candidate intervention components are hypothesised to improve weight loss beyond the core programme, an effect that could, in part, be mediated through enhanced engagement with the programme (***Figure 4.4***). When individuals are provided with components that provide social support (health coach introductory video call or coaching drop-in webchat sessions) as well as components that provide accountability (coaching drop-in webchat sessions, goal setting statements, and food diary review), they will experience adequate supportive accountability, which in turn should increase programme engagement and subsequent weight loss. A detailed explanation of the theoretical underpinning of each component is described below.

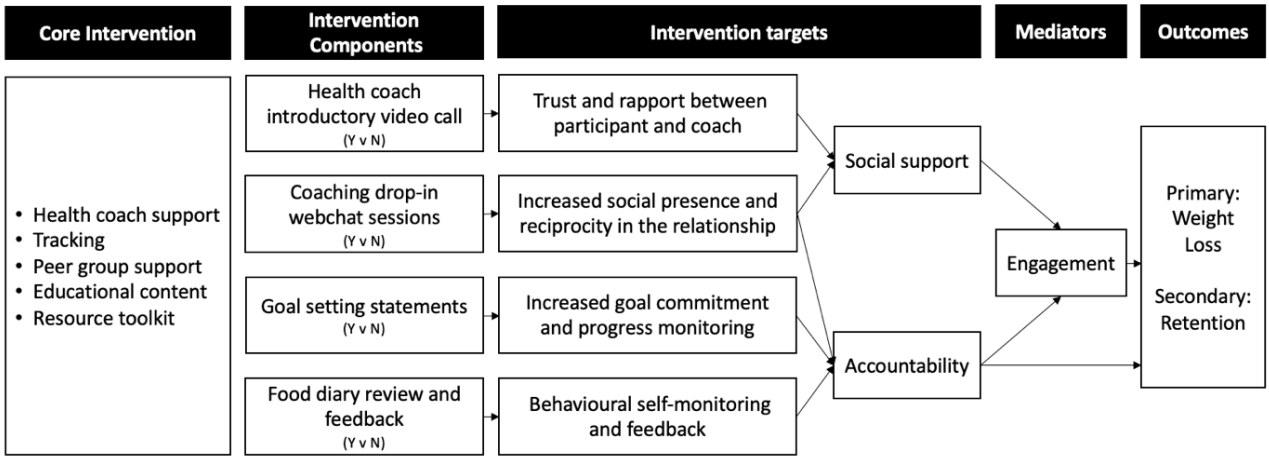

Figure 4.4: Conceptual model for the optimisation of a digital behavioural weight loss programme, incorporating four new intervention components which target supportive accountability.

4.6.1 Health Coach Introductory Video Call

This component falls in the broader concept of social support, intended to help participants establish a personal connection with their health coach and build trust and rapport, which are important for creating a supportive relationship. By establishing a personal connection with the coach, participants may feel more comfortable seeking future guidance and support from their coach which will increase ongoing programme engagement. The health coach will present their qualifications as a registered dietitian or nutritionist, establishing their expertise and relevant experience, thereby reinforcing instrumental legitimacy.

4.6.2 Coaching Drop-In Webchat Sessions

These regular, scheduled 1-to-1 coaching drop-in sessions allow for regular interaction with the health coach, further reinforcing social presence. The opportunity to ask questions and receive personalised support contributes to the perception of reciprocity in the relationship, as the user derives a clear benefit from engaging in the sessions. Additionally, the timely responses received during these sessions can reinforce the perception of the coach as trustworthy and attentive, supporting relational legitimacy.

4.6.3 Goal Setting Statements

Participants will be asked to complete goal setting statements alongside reflection of the actions made towards their goals each week. Goal setting is integral to fostering accountability, particularly by involving the participant in the definition of goals and

expectations (286). Involving the participant in the definition of goals and the planning of specific actions, reinforces their involvement in defining expectations, which increases their commitment to the process. The regular prompts for reflection and potential goal adjustment encourage self-monitoring and a focus on the process, which are key aspects of the supportive accountability model.

4.6.4 Food Diary Review Plus Feedback

This component relates to the performance monitoring and feedback component of the supportive accountability model. The model emphasises that feedback should be process focused and framed in terms of benefit to the participant. By maintaining a food diary and receiving feedback, participants may enhance their engagement with self-monitoring of their eating behaviours, particularly in the short term, to support the development of initial healthy habits. Focusing the feedback on dietary strategies, rather than weight loss, ensures the feedback process focused. The personalised feedback from the health coach based on the food diary entries supports the perception of reciprocity in the relationship, as the user receives tangible benefits from their interaction.

4.7 The Optimisation Objective

The objective is to select the set of intervention components and component levels in which each component is making a contribution to the overall effect, and any inactive

components have been eliminated. I therefore will aim to identify the combination of intervention components with the greatest effect, as judged through weight loss.

4.8 Development of Intervention Materials

Finally, the intervention materials for the four selected candidate components were developed. These materials were designed to reflect the specific content, structure, and delivery format of the Second Nature programme. Development required close collaboration with the Second Nature team to ensure consistency with their platform and practices. The intervention content can be found in ***Appendix 4***.

4.9 Discussion

This chapter describes the work I conducted during the preparation phase of MOST, to identify four candidate intervention components that were hypothesised to improve engagement and subsequent weight loss in a commercial digital behavioural programme. The components were identified using behaviour change theory and a review of the literature, combined with insights from user interviews and collaboration with the commercial provider, Second Nature.

The intervention theory is grounded in the supportive accountability model, which hypothesises that additional human support may increase adherence to digital interventions through accountability to another person (286). By incorporating supportive accountability, these intervention components aim to emulate some of the benefits of face-to-face interventions, such as personalised and timely support, while also leveraging the scalability and convenience of digital platforms. This approach has been previously implemented in digital health interventions for depression (287) and weight management (268).

Implementation of the MOST methodology aligns with the need to produce efficient, effective, and scalable multicomponent interventions. This is particularly relevant for digital weight loss interventions where the effect sizes are relatively small, there is variability in outcomes, and suboptimal engagement rates (89, 288), necessitating a more efficient trial design. The subsequent trial will be implemented within a commercial setting, using routinely collected data. In such contexts, traditional RCTs that test

individual components may fail to address the complexities and keep pace with the rapid changes in the field. The MOST framework is better suited to continuous service improvement, driven by routine data collection and analysis.

The MOST framework is limited in that is does not provide detail regarding the development of individual intervention components for a complex intervention (289). To address this limitation, intervention design frameworks such as the Person-Based Approach, the Behaviour Change Wheel, and Intervention Mapping, offer guidance on determining the content, format, and delivery of intervention components (187, 290, 291). These frameworks can be effectively integrated into the preparation phase of MOST (292), and my approach broadly aligns with Intervention Mapping (290).

I chose to follow a structured, multi-step process aimed at ensuring that the components were evidence-based, user-centred, and practically feasible. This process mirrors with the six-stage intervention mapping process which involves: 1) assessing the problem; 2) identifying intervention targets; 3) selecting theory-based intervention methods; 4) developing intervention materials; 5) planning for implementation of the intervention; 6) developing an evaluation plan (290). It is noted that these stages can be moved between iteratively, and stakeholder engagement is highly encouraged throughout. However, due to resource and business constraints, strict adherence to the Intervention Mapping approach would not have been feasible. Instead, the intervention development process was adapted to meet the requirements of working with a commercial partner, ensuring components were evidence-based, feasible, and aligned with both user and

organisational needs. By narrowing options and co-producing final features with health coaches, the components were tailored for both effectiveness and practicality.

If successful, this application of the MOST framework could offer a practical approach for commercial digital health providers to generate robust evidence on the effectiveness of specific intervention components. Over time, this may support the identification of generalisable conclusions about which components contribute most meaningfully to outcomes such as engagement and weight loss. This approach could reduce reliance on large, resource-intensive RCTs to test components that are expected to yield only modest effects, while supporting continuous service improvement in real-world digital settings.

Chapter 5 : Optimising a digitally delivered behavioural weight loss programme: a factorial cluster randomised controlled trial

5.1 SUMMARY

This chapter presents the optimisation phase of MOST framework, which was used to systematically test the four candidate intervention components developed in ***Chapter 4***. I used a 2^4 factorial cluster design to identify the most effective combination of four intervention components which enhanced weight loss over a 24-week period. I also examined which components contributed to improved participant retention and engagement with the programme.

A total of 1,335 adults enrolling in a commercial weight management programme were randomised to one of 16 experimental conditions. The four components tested were: (1) an introductory video call with a health coach, (2) drop-in webchat sessions with the health coach, (3) goal-setting statements, and (4) food diary review plus feedback. All participants received the core Second Nature programme along with zero to four of the additional components. The primary outcome was weight change at 16 weeks. Secondary outcomes, measured at 4, 16, and 24 weeks, included cancellation of

subscription and programme engagement, defined as the number of interactions with the app's main functions. Fidelity and acceptability were assessed using component adherence data and self-report questionnaires. Selection of components for the enhanced programme was based on whether they produced at least a minimal improvement in weight loss defined as ≥0.75 kg either alone or in combination with other components at 16 weeks.

Weight data were available for 52% of participants at 4 weeks, 26% at 16 weeks, and 20% at 24 weeks. The health coach introductory video call was the only component to lead to a significant positive effect on weight loss at 24 weeks, resulting in an average additional loss of 1.0 kg compared to those who did not receive the call. In contrast, the food diary review and feedback component had significant adverse effects on weight loss at both 16 and 24 weeks and were associated with lower engagement. Engagement tended to be lower in conditions that included multiple components, particularly when the food diary was present. Although no component or combination met the pre-defined optimisation objective of ≥ 0.75 kg additional weight loss at 16 weeks, the findings offer insight to inform future intervention development by identifying components that may be further refined and tested in subsequent studies.

Overall, the findings suggest that brief, early human contact could meaningfully enhance the effectiveness of digital interventions, while effortful components that lack adequate support may reduce engagement or increase dropout. The results reinforce the importance of delivering low-burden, well-timed support, while highlighting an ongoing challenge of sustaining engagement even in the medium term.

5.2 INTRODUCTION

As outlined in ***Chapter 4***, the MOST framework provides a structured approach to developing more effective interventions (148). Although MOST does not recommend a specific experimental design for the optimisation phase, factorial experiments are commonly employed due to their ability to evaluate the individual and combined effects of multiple intervention components (248, 249). By identifying which components, either alone or in combination, contribute meaningfully to the desired outcome, researchers can make informed decisions to construct an optimised intervention package that balances effectiveness within defined resource constraints.

The potential of the MOST framework in the context of digital weight management interventions has been demonstrated in two key studies. The Opt-IN study, was the first to apply the MOST framework to develop a scalable, optimised version of a technology-supported weight loss programme (149, 293). This study employed a 2^5 factorial design to evaluate five intervention components (coaching calls, primary care provider reports, text messaging, meal replacements, and buddy training). By testing all possible combinations simultaneously, the study identified a subset of components that contributed meaningfully to weight loss whilst balancing cost-effectiveness. Similarly another optimisation trial, yet to publish its findings, aimed to test five components (virtual reality for skills training, interactive video feedback, tailored intervention to promote physical activity, skills for dysregulated eating, and social support combined with friendly competition) in an internet-based behavioural weight loss programme using a 2^4 factorial design (294). Notably, a key distinction of that study was its emphasis on

identifying effective components that could be delivered entirely without human involvement, allowing for a fully automated intervention that could be disseminated at scale with minimal cost to patients or providers.

Together, these studies demonstrate the value of the MOST framework in guiding optimisation to develop more efficient and scalable digital weight loss interventions. However, they also highlight a key trade-off in digital behavioural interventions. While human support can enhance engagement and outcomes, it adds cost and complexity. To address this, the present study evaluated whether low-intensity human-supported components, combined with components that support accountability, could meaningfully improve outcomes in a commercial digital weight loss programme.

The intervention theory was grounded in the supportive accountability model, which posits that human support can improve adherence to digital interventions through accountability to another person (286). By incorporating supportive accountability, these intervention components aim to emulate some of the benefits of face-to-face interventions, such as personalised and timely support, while also leveraging the scalability and convenience of digital platforms. This approach has been previously implemented in digital health interventions for depression (287) and weight management (268).

Unlike traditional RCTs that evaluate a fixed intervention package at a single time point, the MOST framework supports continuous service improvement through routine data collection and iterative refinement. In line with this, the current study conducted the first factorial optimisation trial in collaboration with an industry partner to assess which of

four intervention components most effectively enhanced their digital behavioural weight loss programme. This approach is particularly well-suited to industry settings where rapid scalability and cost-efficiency are essential.

The primary objective of this study was to determine if one or more of four new components added to a commercial weight loss programme led to greater weight loss. The four components tested were: 1) an introductory video call with the health coach (No vs. Yes), 2) drop-in webchat sessions with the health coach (No vs. Yes), 3) goal setting statements (No vs. Yes), and 4) food diary review plus feedback (No vs. Yes). Secondary objectives were to: a) identify which, if any, intervention components increase retention and, b) identify which, if any, intervention components increase programme engagement. The study also aimed to explore the fidelity and acceptability of each of the intervention components.

5.3 METHODS

5.3.1 STUDY DESIGN

The study used a 2^4 factorial cluster design to test all possible combinations of four intervention components (295). The new components were tested as adjuncts to a core digital behavioural weight loss programme, Second Nature (296). Participants were assigned to groups of 28-32 and underwent the programme within these groups. Follow-up in the trial lasted for 24 weeks. Each group was cluster randomised to one of 16 experimental conditions (***Table 5.1***).

A factorial design was chosen as it could be used to estimate the main effects and interactions of the intervention components, which allows for a decision about which components should be retained in the intervention. Another advantage of using a factorial design is its efficiency. In a factorial experiment, power is based on the per-level of a factor sample size (i.e., the number of participants assigned to each level of a component, such as 'Yes' or 'No') not the per-condition sample size, which is fundamentally different than a traditional RCT. Factorial experiments require fewer participants to achieve the same statistical power compared to a RCT, because they test multiple component effects simultaneously, and each factor has its own control group (i.e., the mean of the conditions where that factor is set to 'no') (248). The factorial design achieves its efficiency as all participants are involved in every estimate (249), meaning it can achieve adequate power using a similar sample size to that needed to test a single component (247).

Table 5.1: Experimental Conditions

Experimental Condition	Core intervention	Health coach introductory video call	Coaching drop-in webchat sessions	Goal setting statements	Food diary review plus feedback
1	Y	Y	N	N	N
2	Y	Y	N	N	Y
3	Y	Y	N	Y	N
4	Y	Y	Y	N	N
5	Y	Y	N	Y	Y
6	Y	Y	Y	N	Y
7	Y	Y	Y	Y	N
8	Y	Y	Y	Y	Y
9	Y	N	N	N	N
10	Y	N	N	N	Y
11	Y	N	N	Y	N
12	Y	N	Y	N	N
13	Y	N	N	Y	Y
14	Y	N	Y	N	Y
15	Y	N	Y	Y	N
16	Y	N	Y	Y	Y

5.3.2 ELIGIBILITY

The study enrolled adults aged ≥18 years with a BMI >21 kg/m^2 reflecting the usual profile of users of the app. All users that registered to privately access the Second Nature programme during the recruitment window (January to September 2024) were eligible to

participate in the trial. Participants had to be able to access the internet with a smartphone or laptop and willing to install the Second Nature app on their device. Potential users were ineligible to join if they had a past or present diagnosis of an eating disorder or if they were currently pregnant.

5.3.3 Recruitment

Participants were recruited to the trial through the routine sign-up process on the Second Nature website (https://www.secondnature.io/). The programme is primarily advertised through various online channels and platforms, such as social media, email marketing, search engine marketing, and affiliate partnerships. All advertisements link directly to the Second Nature website. Participants may also find the website through a personal web search for phrases relating to weight loss, healthy living, or diet plans. I chose to align the trial start with the first week of January, the peak sign-up period for most weight management providers, to accelerate recruitment.

Figure 5.1 summarises the trial procedures.

	Enrolment	Allocation	*Assessment timepoints*		
TIMEPOINT	***At sign-up***	**0**	***4 weeks***	***16 weeks***	***24 weeks***
ENROLMENT:					
Eligibility screen	X				
Consent	X				
Allocation		X			
INTERVENTIONS:					
[Core programme]			←	→	
[Intervention components]			←	→	
ASSESSMENTS:					
[Socio-demographic characteristics]	X				
[Health-related conditions]	X			X	
[Weight]	X		X	X	X
[Programme drop-out]			X	X	X
[Engagement with app]			X	X	X
[Fidelity measures]			X	X	
[Acceptability questionnaire]				X	

Figure 5.1: Schedule of enrolment, interventions, and assessments

5.3.4 Screening, Consent, and Baseline Assessment

Eligibility criteria were assessed, and baseline data collected, via Second Nature's bespoke self-reported health questionnaire which was completed as part of the sign-up process on the Second Nature website. This was completed prior to commencement of the programme with no additional instruction. During the questionnaire, participants

were asked to self-report demographic characteristics (date of birth and gender); anthropometric measures (body weight and height); health-related conditions (diabetes, physical, and mental health conditions); current pregnancy; and their main priorities and goals for the programme. If the participant was ineligible (based on age, BMI, current pregnancy, and past or present diagnosis of an eating disorder), a pop-up explained that they did not meet the eligibility criteria for the Second Nature programme, they were not able to proceed further, and no identifiable information was collected.

Participants who met the eligibility criteria were able to complete the sign-up process which involved reviewing and accepting the Second Nature Privacy Policy (***Appendix 2.1***). As per the privacy policy, participants consented to being involved in internal and external research and for their data to be used for academic research purposes. As such, Second Nature delivered the intervention, and I received anonymised data for analysis. Participants who accepted the Terms & Conditions and Privacy Policy were then able to complete the sign-up process, where they could purchase the programme and input their personal contact details (name, email, and home postcode). After sign-up, participants received instructions on how to download and set-up the Second Nature app. After downloading the app, participants were asked to weigh themselves using their weighing scales and record their baseline weight reading in the app.

5.3.5 Randomisation

Participants were allocated to closed groups in which they underwent the programme. Allocation occurred through an algorithm which assigned participants to groups based on age and gender. Groups consisted of male only, female only, and mixed gender groups

plus mostly older, mostly younger, and mixed age groups. Only groups that had between 28-32 participants were included in the trial, to ensure a similar number of participants were included in each experimental condition. Groups in which the number of participants fell outside this range continued to the standard Second Nature programme.

Each eligible group was cluster randomised to one of 16 experimental conditions. I used a computerised randomisation software (MinimPy version 2) to randomly allocate the groups with a minimisation algorithm to balance gender and age across the experimental conditions as much as possible. I conducted the randomisation. I was not involved in intervention delivery and had no access to the screening process or group allocation.

Although Second Nature was instructed not to move participants between groups, the programme's usual operations allow participants to restart at any time, and so this did occasionally occur. To minimise the risk of contamination between intervention components, participants who switched groups after their group start date were excluded from the analysis. Participants who moved before their group start date were retained, as they had not yet been exposed to any intervention content.

5.3.6 Blinding

All participants were blind to treatment allocation. Due to the nature of the interventions, the health coaches delivered the intervention could not be blinded but they were not involved in data analysis.

5.3.7 Core Intervention

The core intervention, delivered to all participants primarily via a smartphone application, was the 'core' phase of the Second Nature programme. The 'core' phase consisted of a 17-week behavioural change programme aiming to support people to have a healthier diet and increase their physical activity (described in detail in ***Chapter 4***).

Following sign-up, participants were asked to download the app onto their device, or they could also access the app functions on the Second Nature website and use it throughout the intervention period. Participants had access to the core Second Nature programme for as long as they continued to pay for it within the 24 weeks of the trial. All participants within each experimental condition were in the same programme group and assigned to the same health coach.

Whilst weight monitoring is typically self-directed in the standard Second Nature programme, participants in this trial were prompted by their health coach to weigh themselves at four specific timepoints within the programme (baseline, week 4, week 16, and week 24) to increase the availability of weight data.

5.3.8 Intervention Components

The intervention components were delivered as adjuncts to the standard Second Nature programme during the active 'Core' phase of the programme only (weeks 1-17). How each component was operationalised is described below.

5.3.8.1 Health Coach Introductory Video Call (Y/N)

Participants were either offered one introductory call with their health coach within the first two weeks of the programme or received the core programme without any additional contact. Health coaches were instructed to keep the call to approximately 20 minutes. Three days prior to their programme start date, participants received an email with a link to schedule a timeslot for the call, followed by a reminder message in their group chat. The purpose of the call was for the health coach to introduce themselves, including their qualifications as a registered dietitian or nutritionist, and for the participant to ask any specific questions they may have about the programme. The health coaches were trained on how to perform the calls and provided with a conversation guide to facilitate discussion (***Appendix 4.1***).

5.3.8.2 Coaching Drop-In Webchat Sessions (Y/N)

Participants were either offered or not offered (core programme) a designated 30-minute time slot where their health coach was 'live' in the private chat. This provided a platform for participants to receive timely responses to questions, seek guidance, and receive personalised support, as well as providing regular, ongoing accountability. At the end of the first week of the programme, participants were sent a link in both the private and group chat to schedule a timeslot to 'drop-in' with their health coach for personalised support delivered in the private chat function of the app. Health coaches were able to schedule up to three participants in each 30-minute session. At the scheduled time, the health coach messaged the participant in the private chat to begin the session. These drop-in sessions were offered once a week for the first month and then were participant-

driven thereafter. At the end of each drop-in session, the health coach sent a booking link where the participant could schedule a suitable time for the next drop-in session. The content of the conversation was largely led by the participant; however, the health coach was provided with a conversation guide to prompt conversation if necessary (***Appendix 4.2***).

5.3.8.3 Goal Setting Statement (Y/N)

Participants were either asked to complete a goal setting statement alongside regular reflection with their health coach or did not complete a goal setting statement (core programme). Participants were introduced to the goal setting activity by their health coach in the group chat function and were instructed to complete a template in the journal section of the app (***Appendix 4.3***). The template prompted them to set an outcome goal (e.g., lose 5 kg by the end of the programme); a process goal (e.g., walk 5,000 steps a day); and commit to performing 1-2 actions of their choice (e.g., walk to and from work every day). Participants were then prompted at the end of each week to answer a series of reflection questions around which actions went well or not so well that week, and what they might do differently next week. These reflection questions allow participants to monitor their progress and adjust their strategies accordingly. On a monthly basis, the health coach prompted the participant to review their goal and ask them whether they wish to adjust the goal. If participants wished to adjust the goal, they were provided with a new goal setting template to complete in the journal section of the app.

5.3.8.4 Food Diary Review Plus Feedback (Y/N)

The food diary feature is part of the core Second Nature programme but is self-directed by default and therefore rarely used. In this study, participants either received the standard version, where they had access to the food diary but were not prompted to use it and received no feedback (core programme). Or an enhanced version, where they were prompted weekly to complete a food diary and received personalised feedback from their health coach at three specific timepoints during the programme.

At the beginning of each week, participants randomised to receive the food diary review plus feedback received a reminder to complete their food diary. At the beginning of weeks 3, 6, and 10, the health coach messaged in the group chat offering to review and provide personalised feedback on 1 weeks' worth of entries for that week. Feedback was based on Second Nature's nutritional advice which emphasises the following: 1) Second Nature's balanced plate model (eat three balanced meals per day, portion size guidelines), 2) Base meals on whole foods (limit intake of ultra-processed foods and sugar) 3) Meal timing (leave gaps of 3-5 hours between meals, skipping main meals, snacking), 4) Fluid intake (drink at least 2 litres of water per day, limit alcohol intake, limit caffeine within 4-5 hours of sleep) (***Appendix 4.4***). Health coaches reviewed and sent feedback to each participant via the private chat function of the app. Health coaches were instructed to review all food diaries, even if they were incomplete.

5.3.9 OUTCOMES

5.3.9.1 Primary Outcome

- Weight change between baseline and 16 weeks

5.3.9.2 Secondary Outcomes

- Weight change between baseline and 24 weeks
- Drop-out of programme (defined as programme cancellation) between baseline and 16 weeks
- Drop-out of programme (defined as programme cancellation) between baseline and 24 weeks
- Engagement with the programme between baseline and 16 weeks
- Engagement with the programme between baseline and 24 weeks

5.3.9.3 Exploratory Outcomes

- Weight change between baseline and 4 weeks
- Drop-out of programme (defined as programme cancellation) between baseline and 4 weeks
- Engagement with programme between baseline and 4 weeks

5.3.10 MEASURES

5.3.10.1 Weight

Weight data were either automatically collected using the Bluetooth weighing scales provided at the start of the programme (for those who opted to use them) or was manually inputted into the app if participants were using their own weighing scales. Data for all participants were retrieved from Second Nature's database at baseline, and three further time points following the start of the start of the programme: 4, 16, and 24 weeks. Participants were instructed by a message from their health coach to self-weigh and log their weight in the app at the end of weeks 4, 16, and 24. Participants who did not submit a weight reading were contacted via push notification and group chat 1 day after the follow-up timepoint, via private chat 3 days after the follow-up timepoint, and via phone call 4 days after the follow-up timepoint. Data for all participants were retrieved from Second Nature's database. A single weight reading was extracted for each time point by searching within a specified time period (3-5 weeks for 4 weeks, 14-18 weeks for 16 weeks, and 20-28 weeks for 24 weeks) and the reading closest to the mid-point of each time period was extracted.

5.3.10.2 Programme Drop-Out

Programme drop-out was defined as participants who have chosen to cancel the programme up to and including each follow-up assessment. Cancellation data was extracted from the app aligning with each follow-up assessment: 0-4 weeks, 0-16 weeks, and 0-24 weeks.

5.3.10.3 Engagement

Following the definition used previously in ***Chapter 2***, engagement was measured as the cumulative total number of interactions with the three main components of the app: 'Learn', 'Track', and 'Support'. 'Learn' interactions were defined as the total of number of articles read. 'Track' interactions were defined as the number of times a participant viewed or had a recorded weight or steps reading. 'Support' interactions were defined as the number of messages sent or received in either the private or group chat. Engagement metrics were extracted from the app at three time periods, aligning with each follow-up assessment: 0-4 weeks, 0-16 weeks, and 0-24 weeks. The exact cut-off time point for each period was defined based on the date of the extracted single weight reading. The total number of interactions with the three components of the app from baseline to 16- and 24- weeks was calculated.

5.3.10.4 Process Evaluation Measures

Acceptability

In the penultimate week of the core programme (week 16), participants were asked to complete a questionnaire, which assessed the acceptability of the overall programme and each component using a 5-point Likert scale. Participants were asked about the perceived helpfulness of the overall Second Nature programme to promote weight loss, the perceived helpfulness of each intervention component, and how much effort was associated with each intervention component. Participants received payment of a £5 Amazon voucher for completing the questionnaire.

Fidelity

I assessed whether the intervention components were being delivered as planned by collecting the following measures during the trial period:

- Number of participants attending the health coach introductory call
- Duration of the attended health coach introductory call for each participant
- Number of coaching drop-in session sessions attended per participant, out of a maximum of 17 sessions
- Number of goal setting statements completed per participant, out of a maximum of 16
- Number of reflection statements completed per participant out of a maximum of 16
- Number of food diaries completed per participant out of a maximum of 17 (entries were counted even if incomplete)

5.3.11 Statistical Analysis

5.3.11.1 Sample Size

I conducted the power analysis using the R macro %FactorialPowerPlan (297). The available resource allocated to this trial by Second Nature was 48 groups with an average of 30 participants per group. Considering the resource management principle of MOST (148), and given this allocated sample size, I calculated the available power to detect different effect sizes, as summarised in ***Table 5.2***.

Table 5.2: Power calculations

Cohen's d effect size	Difference in weight	Power
0.25	1 kg	89%
0.22	0.88 kg	81%
0.188	0.75 kg	70%

Power for this study was based on weight change from baseline to 16 weeks. Specifically, the study aimed to assess which intervention components contribute to a more than minimal improvement in weight loss to identify components for inclusion in the optimised intervention. My pre-specified definition of at least a minimal difference in weight loss was ≥ 0.75 kg - alone or in combination with other components - at 16 weeks. I assumed a standard deviation of 4 kg from previous studies, which translated to a component effect size of d = 0.188 (233). From a decision-priority perspective, this optimisation trial aimed to screen components for an optimised intervention that could be tested in a future definitive evaluation, meaning I did not want to overlook a potentially useful component (148, 242). Therefore, the criteria to consider an effect important was set liberally at $p<.10$, which is not uncommon for this phase of MOST methodology (149).

I assumed 70% retention (an average of 21 participants per group), and a cluster size standard deviation of 5 participants, an intraclass correlation of 0.01, and set alpha to 0.1. This sample size provided 70% power to detect a 0.75 kg difference in weight loss - which was my definition of at least the minimal difference - and 90% power to detect any differences of 1 kg or larger. Therefore, this study was powered to detect any main effects

or interactions of these sizes or larger. Of note, the macro assumes effect coding rather than dummy coding, meaning I had essentially the same power to detect interactions as main effects.

5.3.11.2 Statistical Methods

Demographic characteristics of the sample were explored descriptively. Continuous variables were summarised using means and standard deviations. Categorical variables were summarised using counts and percentages.

Primary Objective

For the primary analysis, data were analysed using a linear mixed-effect model with repeated measures, to assess whether each component was associated with weight change across the time points (4-, 16-, and 24-weeks). For each component, I determined whether there was a difference in weight change across each time point using baseline as the reference cell. This was the main effect of each component on weight change and statistically allowed me to investigate component by time interactions, with the 16-week outcome as the primary outcome. Participant ID was added as a random effect to account for repeated measures of weight; time and component were added as fixed effects; and an interaction term of component by time was added. I also assessed interactions between components by adding appropriate multiplicative interaction terms (e.g., component 1 x component 2 x time). To aid with decision making, estimated weight loss was calculated based on a regression models for each experimental condition.

I assessed the sensitivity of the analysis to assumptions about missing data by: 1) imputing the last-measured weight (last observation carried forward, LOCF); 2) carrying forward the baseline weight (baseline observation carried forward, BOCF); and 3) restricting the analysis to participants with complete weight data at all time points (completer analysis).

Planned subgroup analyses categorised participants into three subgroups based on their baseline BMI: 1) participants with a BMI of 21-25kg/m^2, 2) participants with overweight (BMI 25-30 kg/m^2), and 3) participants with obesity (BMI > 30kg/m^2). I also planned to conduct subgroup analyses by age (based on the median age of the study population), gender, tertiles of IMD (with cut points determined from the study population), and presence of pre-diabetes or type 2 diabetes at baseline.

Subgroup effects were tested by adding the relevant stratification variable to the primary model and estimating three-way interactions between time, intervention component, and the stratification variable. This allowed assessment of whether component effects on weight change varied meaningfully across subgroups. Due to the low prevalence of pre-diabetes or type 2 diabetes at baseline (2% of the total sample), subgroup analyses for this variable could not be conducted.

Significance levels were set at $p \leq 0.10$. Effect sizes and 90% confidence intervals were reported for all analyses, given the alpha of 0.10. All analyses were conducted using R (version 4.3.3) with the integrated development environment R Studio.

Secondary Objectives

For the secondary outcomes, the proportion of participants that cancelled the programme from baseline to 4- 16- and 24- weeks was assessed using three independent logistic regression analyses for each time point. Cumulative engagement data were analysed using a linear mixed-effect model with repeated measures, to assess whether each component was associated with engagement across the time points (4-, 16-, and 24-weeks).

Process Evaluation

Descriptive statistics were used to summarise the quantitative intervention component fidelity assessments. Descriptive statistics were calculated for the individual items on the acceptability questionnaire and overall, for each intervention component.

5.3.12 Decision Making

The criteria for selecting components for inclusion in the optimised intervention package was defined a priori. Specifically, components were considered for inclusion if they demonstrated a main or interaction effect with a *p*-value less than 0.1 and contributed at least a minimal improvement in weight loss, defined as $\geq$ 0.75 kg at 16 weeks. Decisions were based on effect estimates from the primary analysis.

Decision-making followed a stepped approach, as described by Collins et al. (250). In line with the principle of 'effect hierarchy', which prioritises main effects and lower-order interactions as the most scientifically meaningful, main effects were examined first to

screen components in or out. Components with meaningful main effects at 16 weeks were tentatively selected for inclusion. Interaction effects were then assessed for those components that showed significant main effects, beginning with two-way interactions and progressing to higher-order terms, to determine whether any combinations of components modified the effectiveness of those selected based on main effects.

Although 16 weeks was the primary decision point, relevant effects observed at 4- and 24- weeks were also considered to support decisions. Once a preliminary set of components was identified based on weight loss outcomes, this set was reassessed in light of secondary outcomes, programme drop-out and engagement. As before, main effects were prioritised, followed by relevant interaction effects, to contextualise decisions and identify potential trade-offs.

Finally, components screened in were assigned to the higher (active) level, and those screened out to the lower (inactive) level, to make up the optimised intervention package.

5.3.13 Data Management

Second Nature was the data owner and controller. Data collected at assessment timepoints throughout the trial were stored on their secure servers with trusted 3rd party suppliers, compliant with the UK General Data Protection Regulation. All identifiable information, which was provided by the participant to Second Nature, was governed by their privacy policy. Data was anonymised by Second Nature after study completion and transferred to the researchers at Oxford via a secure University information governance

approved method for data transfer. The dataset was stored on a university secure server with access held by the study team. Within the University server, all data were stored in password protected folders, accessible only to members of the research team.

5.3.14 Ethics Approval

The investigators ensured that the study was conducted in accordance with the principles of the Declaration of Helsinki, with relevant institutional regulations, with Good Clinical Practice and General Data Protection Regulations. The study was reviewed and received ethical approval by the Medical Sciences Interdivisional Research Ethics Committee of the University of Oxford (Ref: R89540/RE001). Any substantial changes to the protocol were submitted as an amendment to the ethics committee and the Sponsor.

5.4 RESULTS

5.4.1 SAMPLE

Between January and September 2024, 1,335 participants were enrolled and randomised. The number of participants randomised to each experimental condition ranged from 660 to 675, with similar distribution across component levels (***Figure 5.2***). Of those randomised, 697 (52%) participants were followed up at 4 weeks, 352 (26%) participants were followed up at 16 weeks, and 265 (20%) at 26 weeks.

The mean (SD) age of the participants was 50 (12) years, and the mean baseline BMI was 33 (11) kg/m^2. Most of the participants were female (90%) and from IMD deciles ≥ 4 (77%). There were no statistically significant differences in baseline characteristics across the component levels to which participants were assigned (***Table 5.3***).

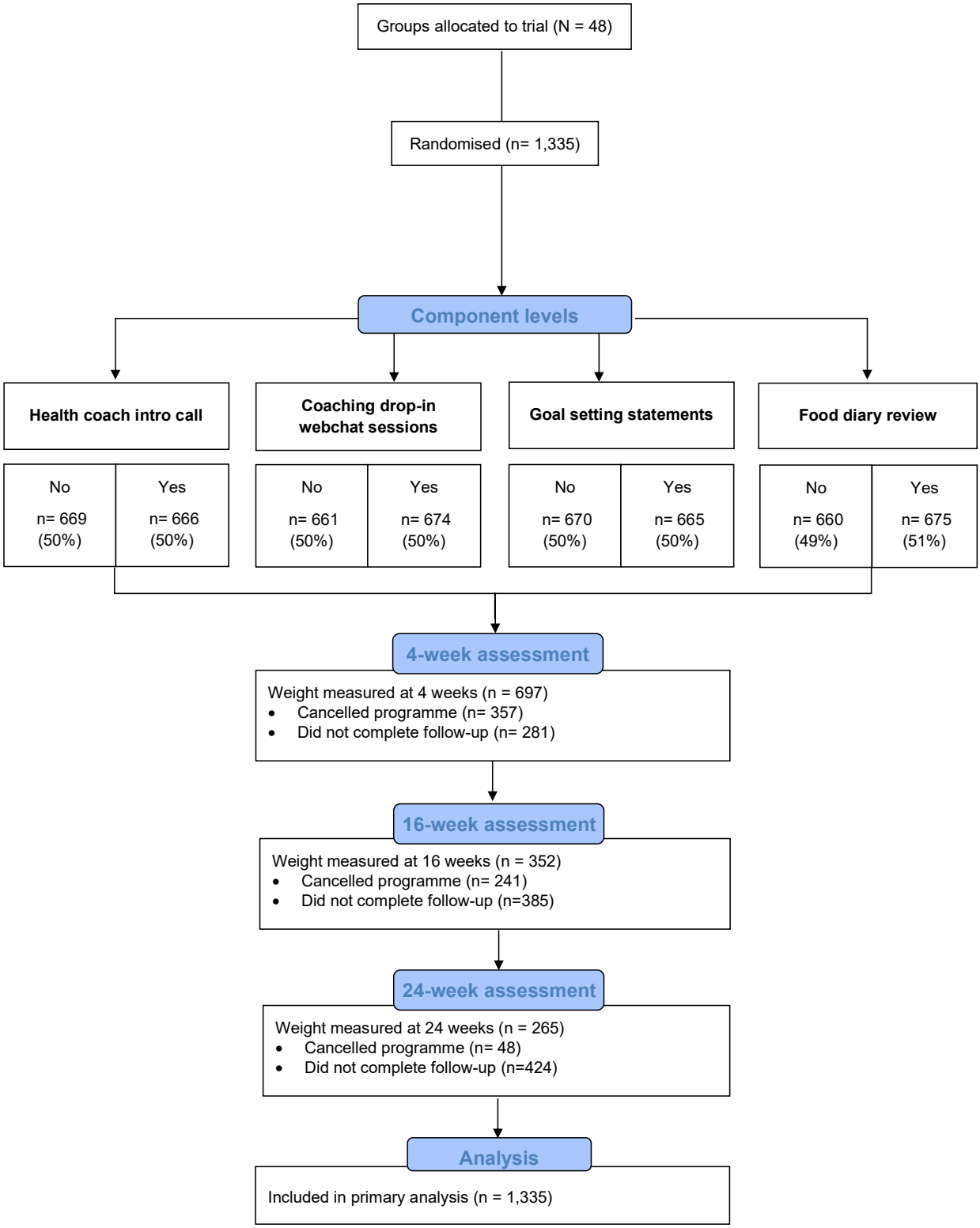

Figure 5.2: Consort flow

Table 5.3: Baseline characteristics of participants by component level

Characteristic	Total (n = 1,335)	Health coach intro call		Coaching drop-in webchat sessions		Goal setting statements		Food diary review plus feedback		P-Value
		No (n = 669)	Yes (n= 666)	No (n = 661)	Yes (n= 674)	No (n = 670)	Yes (n= 665)	No (n = 660)	Yes (n= 675)	
Age, years, mean (SD)	49.7 (12.3)	50.1 (12.3)	49.2(12.4)	50.2 (12.4)	49.1 (12.3)	50.2 (12.1)	49.1 (12.6)	49.8 (12.4)	49.5 (12.3)	0.4
Gender, n (%)										0.13
Female	1,205 (90.3)	602 (90.0)	603 (90.5)	587 (88.8)	618 (91.7)	620 (92.5)	585 (88.0)	595 (90.2)	610 (90.4)	
Male	130 (9.7)	67 (10.0)	63 (9.5)	74 (11.2)	56 (8.3)	50 (7.5)	80 (12.0)	65 (9.8)	65 (9.6)	
BMI, kg/m^2, mean (SD)	32.7 (11.1)	32.9 (12.5)	32.5 (9.4)	32.8 (12.6)	32.6 (9.4)	32.9 (14.0)	32.5 (6.9)	32.9 (12.5)	32.5 (9.4)	> 0.9
IMD decile, n (%)										0.08
1-3 (most deprived)	175 (13.1)	70 (10.5)	105 (15.8)	80 (12.1)	95 (14.1)	83 (12.4)	92 (13.8)	98 (14.8)	77 (11.4)	
4-7	513 (38.4)	267 (39.9)	246 (36.9)	269 (40.7)	244 (36.2)	268 (40.0)	245 (36.8)	239 (36.2)	274 (40.6)	
8-10 (most affluent)	522 (39.1)	270 (40.4)	252 (37.8)	270 (40.8)	252 (37.4)	257 (38.4)	265 (39.8)	263 (39.8)	259 (38.4)	
Missing	125 (9.4)	62 (9.3)	63 (9.5)	42 (6.4)	83 (12.3)	62 (9.3)	63 (9.5)	60 (9.1)	65 (9.6)	
Type 2 or prediabetes, n (%)										0.3
Yes	26 (1.9)	14 (2.1)	12 (1.8)	13 (2.0)	13 (1.9)	20 (3.0)	6 (0.9)	14 (2.1)	12 (1.8)	
No	1,309 (98.1)	655 (97.9)	654 (98.2)	648 (98.0)	661 (98.1)	650 (97.0)	659 (99.1)	646 (97.9)	663 (98.2)	

P values were calculated using 2-tailed *t* tests for continuous variables or chi-squared tests for categorical variables to compare differences between participants in the component levels. Abbreviations: BMI: body mass index; IMD: index of multiple deprivation.

5.4.2 WEIGHT CHANGE

The results presented in ***Table 5.4*** are from the full mixed effects model, which tested all main effects and interactions of the candidate intervention components on weight change over 24 weeks. First, I examined all two-way interactions between time and component (e.g., week x component), which in this model are conceptually equivalent to main effects on weight change. For each component, I looked at weight change from baseline to 4-, 16-, and 24-weeks, with the primary focus on the 16-week timepoint as the primary outcome. Interactions with p-values < 0.10 were considered potentially meaningful. While these are modelled as time-by-component interactions, they can be interpreted as the effect of each component when it is set to 'Yes', vs. when it is set to 'No', on weight change at that timepoint.

The food diary review plus feedback component had a statistically significant negative effect on weight loss at 16 weeks (β = 0.26, 90% CI [0.03, 0.50], p = 0.07) and at 24 weeks (β = 0.37, 90% CI [0.11, 0.64], p = 0.02). The health coach introductory video call had a statistically significant positive effect on weight loss at 24 weeks (β = -0.50, [-0.76, -0.23], p = 0.002).

Because effect coding was used, these estimates reflect half the difference between component set to "yes" and "no" conditions. To aid interpretation for my optimisation objective, I estimated the total weight difference attributable to each component at 16- and 24- weeks. Participants who received food diary review plus feedback (vs. not) had approximately +0.52 kg and +0.74 kg greater weight at 16- and 24- weeks, respectively. Participants who received the health coach call (vs. not) had 1.00 kg greater weight loss

at 24 weeks. See ***Figure 5.3*** for the estimated main effects of each intervention component on weight change over time.

To illustrate the pattern of weight change in the same individuals over time, a sensitivity analysis was conducted using complete cases only (n = 191). The model included only main effects, as the full factorial model was underpowered due to sparse data across higher-order combinations (***Table 5.4***). ***Appendix 5.1*** also shows estimated effects using LOCF and BOCF to assess different missing data assumptions. Overall, the same intervention components had statistically significant main effects on weight over time across all missing data approaches.

I also conducted exploratory subgroup analyses to examine whether the effects of individual intervention components varied by gender, IMD tertile, age, or BMI category (***Appendix 5.2***). The results suggested that goal setting was more effective for males than females at 24 weeks (β = -1.54, 90% CI [-2.74, -0.35], p = 0.034), and that coaching drop-in webchat sessions were less effective for participants < 50 years old compared to those > 50 years old at 16 weeks (β = 0.53, 90% CI [0.04, 1.02], p = 0.076). At 24 weeks, the IMD subgroup analysis suggested that goal setting was more effective in participants from the most deprived (lowest IMD tertile) group compared to those from the moderately deprived (middle tertile; β = 1.74, 90% CI [1.06, 2.42], p < 0.001) or least deprived (highest tertile; β = 2.01, 90% CI [1.30, 2.72], p < 0.001) groups. The food diary had less adverse effect for participants in the lowest IMD tertile compared to those in the highest (β = 0.92, 90% CI [0.21, 1.63], p = 0.034). There was no evidence of differences in

effects by baseline BMI category (i.e., 21-25 vs. 25-30 kg/m^2 or 21-25 vs. ≥30 kg/m^2) for any component.

Table 5.4 : Results of mixed effects models examining effects of candidate components on weight loss over a 24-week period, using all available data (n = 1,335) or completers only (n =191).

Term	All Data (n = 1,335)			Completers only (n = 191)		
	Coef	90% CI	P-value	Coef	90% CI	P-value
Week (ref = 0)						
4	-1.35	(-1.53,-1.18)	***<0.001***	-1.59	(-1.98,-1.21)	***<0.001***
16	-2.63	(-2.87,-2.4)	***<0.001***	-3.09	(-3.47,-2.71)	***<0.001***
24	-2.92	(-3.19,-2.66)	***<0.001***	-3.68	(-4.06,-3.3)	***<0.001***
Week4:CS	-0.02	(-0.19,0.16)	0.88	0.07	(-0.31,0.46)	0.75
Week4:FD	0.05	(-0.13,0.22)	0.67	0.17	(-0.22,0.55)	0.48
Week4:GS	0.03	(-0.15,0.2)	0.81	0.09	(-0.3,0.47)	0.71
Week4:HC	-0.06	(-0.24,0.12)	0.59	-0.04	(-0.43,0.34)	0.85
Week4:CS:FD	-0.05	(-0.22,0.13)	0.66	-	-	-
Week4:CS:GS	0.03	(-0.15,0.2)	0.81	-	-	-
Week4:GS:FD	0.04	(-0.13,0.22)	0.70	-	-	-
Week4:HC:CS	0.02	(-0.16,0.2)	0.84	-	-	-
Week4:HC:FD	0.05	(-0.13,0.23)	0.65	-	-	-
Week4:HC:GS	-0.03	(-0.2,0.15)	0.82	-	-	-
Week4:CS:GS:FD	0.04	(-0.14,0.22)	0.71	-	-	-
Week4:HC:CS:FD	0.04	(-0.14,0.21)	0.74	-	-	-
Week4:HC:CS:GS	0.03	(-0.14,0.21)	0.77	-	-	-
Week4:HC:GS:FD	0	(-0.17,0.18)	0.97	-	-	-
Week4:HC:CS:GS:FD	-0.01	(-0.19,0.17)	0.92	-	-	-
Week16:CS	-0.07	(-0.3,0.17)	0.65	0.04	(-0.34,0.43)	0.86
Week16:FD	0.26	(0.03,0.5)	***0.07***	0.44	(0.05,0.82)	***0.07***
Week16:GS	-0.22	(-0.45,0.02)	0.14	-0.16	(-0.55,0.22)	0.50
Week16:HC	-0.22	(-0.46,0.01)	0.13	-0.30	(-0.69,0.08)	0.20
Week16:CS:FD	-0.18	(-0.41,0.06)	0.23	-	-	-
Week16:CS:GS	0.10	(-0.14,0.33)	0.50	-	-	-
Week16:GS:FD	-0.17	(-0.41,0.06)	0.23	-	-	-
Week16:HC:CS	-0.14	(-0.38,0.09)	0.32	-	-	-
Week16:HC:FD	-0.01	(-0.25,0.22)	0.93	-	-	-

Week16:HC:GS	-0.11	(-0.34,0.13)	0.46	-	-	-
Week16:CS:GS:FD	0.23	(-0.01,0.46)	0.12	-	-	-
Week16:HC:CS:FD	0.04	(-0.2,0.27)	0.80	-	-	-
Week16:HC:CS:GS	0.16	(-0.08,0.4)	0.27	-	-	-
Week16:HC:GS:FD	0.1	(-0.13,0.34)	0.48	-	-	-
Week16:HC:CS:GS:FD	-0.03	(-0.26,0.21)	0.85	-	-	-
Week24:CS	-0.25	(-0.51,0.02)	0.13	-0.33	(-0.71,0.05)	0.16
Week24:FD	0.37	(0.11,0.64)	***0.02***	0.44	(0.05,0.82)	***0.06***
Week24:GS	-0.07	(-0.34,0.19)	0.65	-0.15	(-0.53,0.24)	0.53
Week24:HC	-0.5	(-0.76,-0.23)	***0.002***	-0.61	(-1.0,-0.22)	***0.01***
Week24:CS:FD	-0.5	(-0.77,-0.24)	***0.002***	-	-	-
Week24:CS:GS	-0.11	(-0.37,0.16)	0.52	-	-	-
Week24:GS:FD	-0.14	(-0.4,0.13)	0.41	-	-	-
Week24:HC:CS	-0.2	(-0.46,0.07)	0.23	-	-	-
Week24:HC:FD	0.22	(-0.05,0.48)	0.18	-	-	-
Week24:HC:GS	-0.1	(-0.37,0.17)	0.54	-	-	-
Week24:CS:GS:FD	0.17	(-0.1,0.43)	0.31	-	-	-
Week24:HC:CS:FD	0.15	(-0.12,0.41)	0.37	-	-	-
Week24:HC:CS:GS	-0.08	(-0.35,0.18)	0.62	-	-	-
Week24:HC:GS:FD	0.15	(-0.11,0.42)	0.36	-	-	-
Week24:HC:CS:GS:FD	-0.12	(-0.39,0.14)	0.46	-	-	-

Main effects at baseline (time zero) do not test the hypotheses of interest and have been omitted from the table for brevity. All models used effect coding. Reported coefficients represent half the difference between component levels; multiply by 2 for the full effect size in kg. The completers analysis included main effects only in the model due to limited data for estimating higher order interactions. Significant effects (p<.10) are highlighted in bold. Abbreviations: CS = coaching drop-in webchat sessions; FD = food diary review plus feedback; GS = goal setting statements; HC = health coach introductory video call.

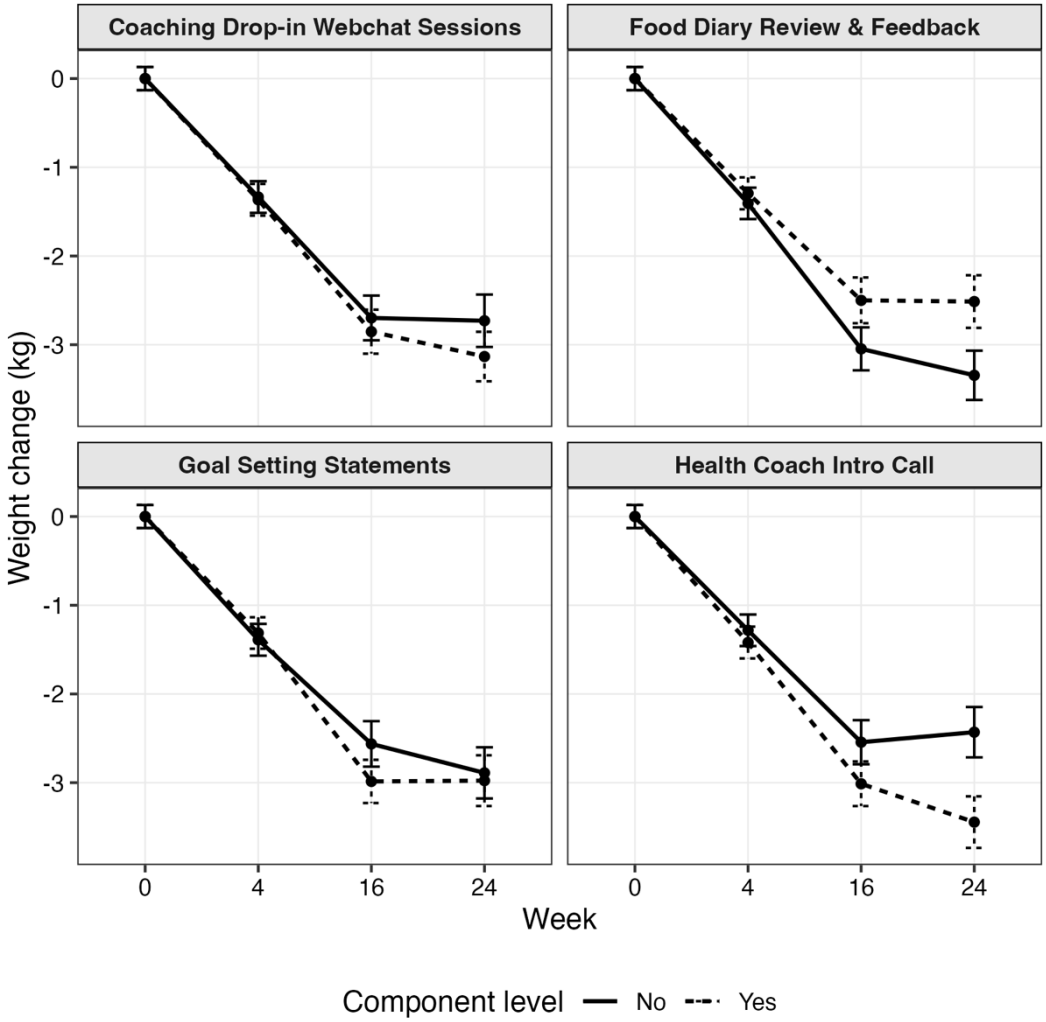

Figure 5.3: Predicted mean weight change (kg) over time by component level (No vs. Yes) using all available data (N=1,335). The dotted "Yes" line denotes that a participant received the intervention component, whereas the solid "No" line denotes that a participant did not receive the intervention component. Values represent predicted marginal means estimated from the linear mixed effects model. Error bars represent 90% confidence intervals.

Next, I examined any interactions, from lower to higher order (e.g., week x component 1 x component 2), that included components which had shown significant main effects. There was one significant synergistic two-way interaction at 24 weeks: food diary review × coaching drop-in webchat sessions (β = -0.50; 90% CI [-0.77, -0.24]; p = 0.002), in which

the negative effect of the food diary was buffered when coaching drop-in webchat sessions was set to 'Yes' (***Figure 5.4***).

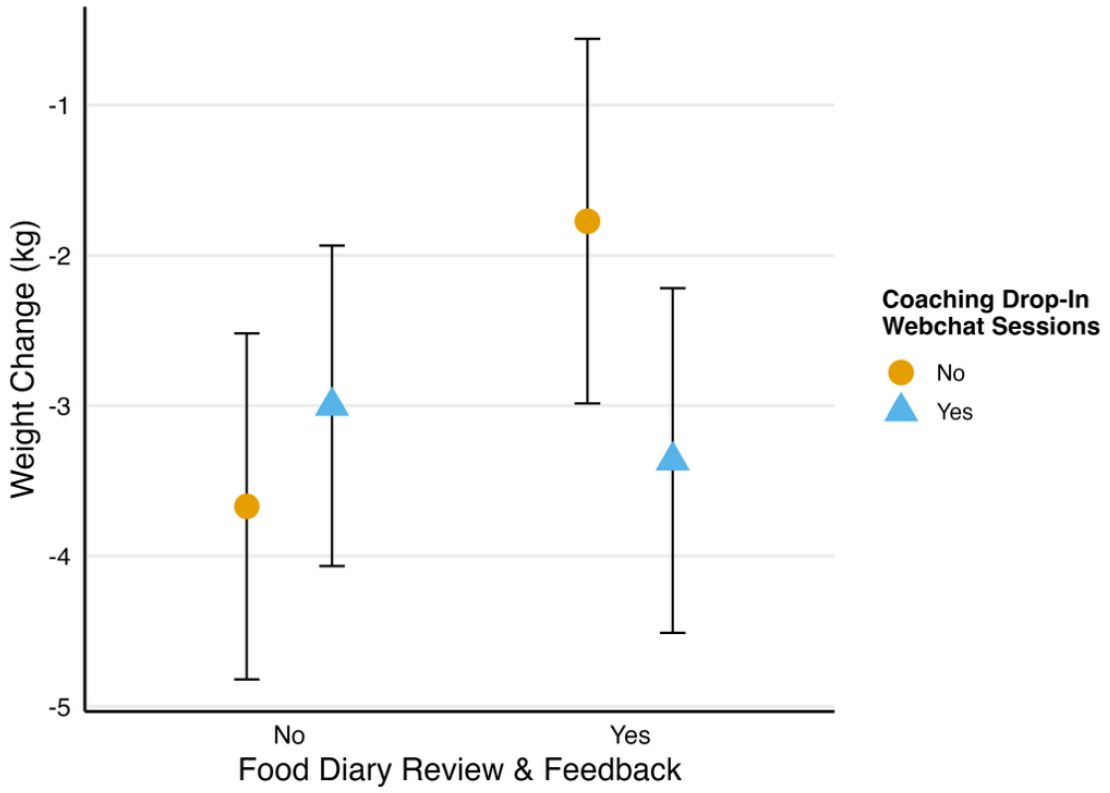

Figure 5.4: Effect of food diary review × coaching drop-in webchat sessions interaction on weight change (kg) at 24 weeks. Values represent estimated marginal means and error bars depict the 90% confidence intervals.

Table 5.5 lists the model-predicted mean weight loss for all 16 versions of the intervention, reflecting all combinations of the four candidate intervention components, computed using separate regression models at 16- and 24-weeks. The intervention with the greatest effect on weight loss at both 16- and 24 weeks included *health coach introductory video call, coaching drop-in webchat sessions,* and *goal setting statements*, but did not include the *food diary review plus feedback*.

Table 5.5: Predicted weight change at 16- and 24-weeks for each condition

Components				Predicted weight change (kg)				Rank	
Health coach intro call	Coaching drop-in sessions	Food diary review & feedback	Goal setting statements	16 weeks Mean [90% CI]		24 weeks Mean [90% CI]		16 weeks	24 weeks
Yes	Yes	No	Yes	-3.83	[-4.98, -2.68]	-4.84	[-6.60, -3.08]	1	1
No	No	No	No	-3.66	[-4.86, -2.46]	-3.96	[-6.09, -1.84]	2	4
Yes	No	Yes	Yes	-3.53	[-4.82, -2.24]	-1.76	[-4.06, 0.55]	3	15
Yes	Yes	Yes	No	-3.43	[-4.56, -2.31]	-3.61	[-5.35, -1.72]	4	6
Yes	Yes	Yes	Yes	-3.24	[-4.60, -1.88]	-4.19	[-6.40, -1.98]	5	3
Yes	Yes	No	No	-3.21	[-4.44, -1.99]	-3.81	[-5.78, -1.83]	6	5
Yes	No	No	No	-3.20	[-4.29, -2.12]	-4.48	[-6.19, -2.77]	7	2
Yes	No	No	Yes	-3.00	[-4.19, -1.82]	-3.53	[-5.41, -1.81]	8	7
No	Yes	Yes	Yes	-2.95	[-4.15, -1.75]	-3.07	[-4.87, -1.26]	9	9
No	Yes	No	Yes	-2.94	[-4.01, -1.88]	-1.87	[-3.51, -0.24]	10	14
No	No	No	Yes	-2.92	[-4.07, -1.78]	-3.19	[-5.16, -1.22]	11	8
No	No	Yes	Yes	-2.90	[-3.99, -1.82]	-2.38	[-4.09, -0.67]	12	11
No	Yes	No	No	-2.58	[-3.94, -1.22]	-2.00	[-3.80, -0.20]	13	13
No	Yes	Yes	No	-2.27	[-3.41, -1.12]	-3.05	[-4.90, -1.20]	14	10
No	No	Yes	No	-1.95	[-3.41, -0.50]	-1.11	[-3.34, 1.12]	15	16
Yes	No	Yes	No	-1.48	[-2.84, -0.11]	-2.28	[-4.13, -0.43]	16	12

Predicted values are estimated marginal means from separate linear regression models at each time point.

5.4.3 Programme Drop-Out

Figure 5.5 shows the cumulative drop-out (programme cancellation) by intervention component. Logistic regression models were fitted separately at each time point to assess main and interaction effects. There was only one significant main effect at 4 weeks, in which the coaching drop-in webchat sessions increased the odds of early programme cancellation (OR = 1.13; 90% CI [1.02, 1.26]; p = 0.04) (***Table 5.6***).

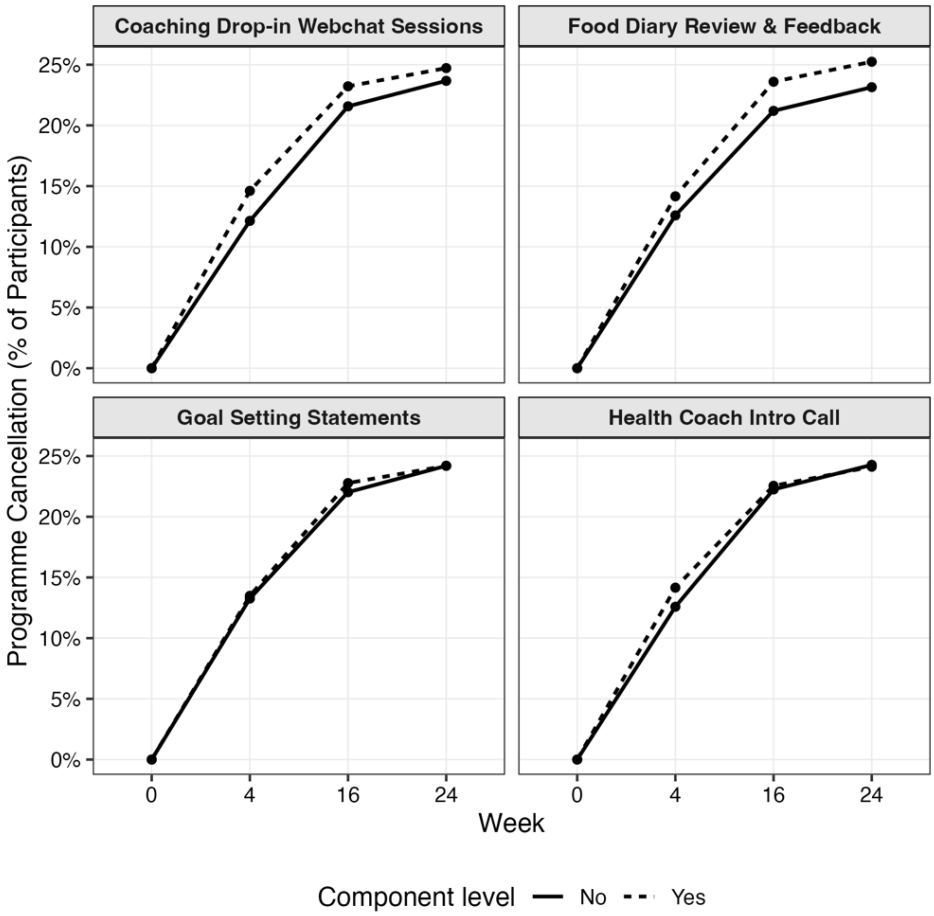

Figure 5.5: Cumulative percentage of participants who cancelled the programme by component level (No vs. Yes). The dotted "Yes" line denotes that a participant received the intervention component, whereas the solid "No" line denotes that a participant did not receive the intervention component.

Next, interaction effects were assessed for those components that showed significant main effects, in this case the coaching drop-in webchat sessions. A significant two-way interaction was observed between coaching drop-in webchat sessions and the health coach intro call (OR = 0.86; 90% CI [0.77, 0.95]; p = 0.01). This interaction suggests that when the health coach introductory call is 'On', it buffers the higher risk of programme cancellation associated with the coaching drop-in webchat sessions (***Figure 5.6***).

Table 5.6: Association between candidate components and likelihood of programme cancellation at 4, 16, and 24 weeks.

	Programme cancellation at 4 weeks			**Programme cancellation at 16 weeks**			**Programme cancellation at 24 weeks**		
Term	OR	90% CI	P-val	OR	90% CI	P-val	OR	90% CI	P-val
CS	1.29	(1.05,1.58)	***0.05***	1.10	(0.92,1.32)	0.38	1.05	(0.87,1.26)	0.68
FD	1.13	(0.92,1.39)	0.33	1.17	(0.97,1.4)	0.16	1.13	(0.94,1.36)	0.26
GS	1.03	(0.83,1.26)	0.84	1.08	(0.9,1.3)	0.48	1.02	(0.85,1.22)	0.88
HC	1.21	(0.99,1.49)	0.12	1.04	(0.86,1.24)	0.74	1.00	(0.83,1.2)	0.99
CS:FD	0.93	(0.76,1.15)	0.59	0.99	(0.83,1.19)	0.94	1.00	(0.83,1.19)	0.97
CS:GS	1.14	(0.93,1.41)	0.29	1.01	(0.84,1.21)	0.95	1.05	(0.87,1.26)	0.67
GS:FD	0.97	(0.79,1.2)	0.83	1.08	(0.9,1.3)	0.47	1.08	(0.9,1.29)	0.51
HC:CS	0.74	(0.6,0.9)	***0.01***	0.87	(0.73,1.05)	0.22	0.96	(0.8,1.15)	0.69
HC:FD	1.13	(0.92,1.4)	0.32	1.09	(0.91,1.31)	0.43	1.13	(0.95,1.36)	0.25
HC:GS	1.12	(0.91,1.37)	0.38	1.17	(0.97,1.4)	0.16	1.22	(1.02,1.47)	***0.07***
CS:GS: FD	1.16	(0.94,1.42)	0.25	1.12	(0.93,1.35)	0.3	1.07	(0.9,1.29)	0.51
HC:CS: FD	0.98	(0.8,1.21)	0.88	0.94	(0.79,1.13)	0.61	0.93	(0.78,1.12)	0.52
HC:CS: GS	1.05	(0.86,1.3)	0.68	1.26	(1.05,1.51)	***0.04***	1.29	(1.07,1.54)	***0.02***
HC:GS: FD	1.05	(0.86,1.3)	0.68	0.96	(0.8,1.15)	0.69	0.95	(0.79,1.14)	0.66
HC:CS: GS:FD	0.89	(0.72,1.09)	0.35	0.92	(0.77,1.1)	0.44	0.92	(0.77,1.1)	0.46

Odds ratios (OR) were calculated using independent logistic regression models at each timepoint (4, 16, and 24 weeks). Significant effects (p<.10) are highlighted in bold. Abbreviations: CS = coaching drop-in webchat sessions; FD = food diary review plus feedback; GS = goal setting statements; HC = health coach introductory video call; OR: odds ratio.

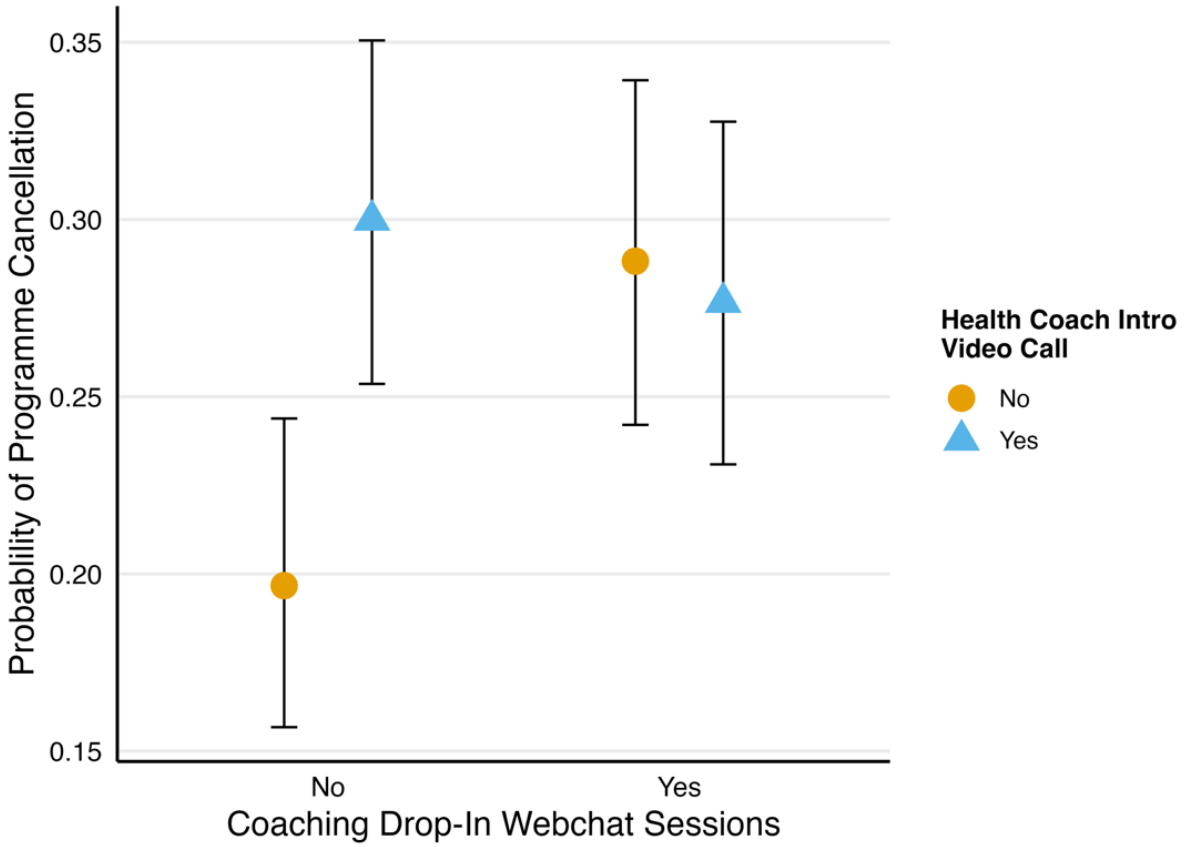

Figure 5.6: Effect of health coach intro video call × coaching drop-in webchat sessions interaction on probability of programme cancellation at 4 weeks. Values represent predicted probabilities and error bars depict the 90% confidence intervals.

5.4.4 Engagement

Table 5.7 shows the results of the full model testing all main effects and interactions of the candidate intervention components on engagement over the 24-week period. At 24 weeks, the food diary review plus feedback had a significant negative main effect on engagement (β = -15.61; 90% CI [-28.99, -2.23]; p = 0.06) (***Figure 5.7***).

Table 5.7: Results of mixed effects models examining effects of candidate components on engagement over a 24-week period, using all available data (n = 1,335).

Term	All Data (n = 1,335)		
	Coef	90% CI	P-value
Week (ref = 0)			
4	132.73	(119.35,146.11)	***<0.001***
16	264.51	(251.13,277.9)	***<0.001***
24	305.21	(291.83,318.59)	***<0.001***
Week4:CS	1.82	(-11.56,15.2)	0.82
Week4:FD	-2.88	(-16.26,10.5)	0.72
Week4:GS	-3.82	(-17.2,9.56)	0.64
Week4:HC	0.64	(-12.74,14.02)	0.94
Week4:CS:FD	1.97	(-11.41,15.35)	0.81
Week4:CS:GS	-1.95	(-15.33,11.43)	0.81
Week4:GS:FD	-0.23	(-13.61,13.15)	0.98
Week4:HC:CS	3.76	(-9.62,17.14)	0.65
Week4:HC:FD	-4.33	(-17.71,9.05)	0.60
Week4:HC:GS	-2.68	(-16.06,10.7)	0.74
Week4:CS:GS:FD	-5.4	(-18.78,7.98)	0.51
Week4:HC:CS:FD	-1.89	(-15.27,11.49)	0.82
Week4:HC:CS:GS	-3.74	(-17.12,9.64)	0.65
Week4:HC:GS:FD	3.51	(-9.87,16.89)	0.67
Week4:HC:CS:GS:FD	-2.51	(-15.89,10.87)	0.76
Week16:CS	8.31	(-5.07,21.69)	0.31
Week16:FD	-12.07	(-25.45,1.31)	0.14
Week16:GS	-7.28	(-20.66,6.1)	0.37
Week16:HC	6.72	(-6.66,20.1)	0.41
Week16:CS:FD	3.89	(-9.49,17.27)	0.63
Week16:CS:GS	-9.27	(-22.65,4.11)	0.26
Week16:GS:FD	-2.36	(-15.74,11.02)	0.77
Week16:HC:CS	4.64	(-8.74,18.02)	0.57
Week16:HC:FD	-7.94	(-21.32,5.44)	0.33
Week16:HC:GS	-13.66	(-27.04,-0.28)	0.10
Week16:CS:GS:FD	-18.85	(-32.23,-5.47)	***0.02***
Week16:HC:CS:FD	0.08	(-13.3,13.46)	0.99
Week16:HC:CS:GS	-8.71	(-22.1,4.67)	0.29
Week16:HC:GS:FD	-0.44	(-13.82,12.94)	0.96

Week16:HC:CS:GS:FD	-10.5	(-23.88,2.88)	0.20
Week24:CS	13.13	(-0.25,26.51)	0.11
Week24:FD	-15.61	(-28.99,-2.23)	***0.06***
Week24:GS	-8.22	(-21.6,5.16)	0.32
Week24:HC	8.64	(-4.74,22.02)	0.29
Week24:CS:FD	2.67	(-10.71,16.05)	0.74
Week24:CS:GS	-10.2	(-23.58,3.18)	0.21
Week24:GS:FD	-3.52	(-16.9,9.86)	0.67
Week24:HC:CS	2.81	(-10.57,16.19)	0.73
Week24:HC:FD	-8.46	(-21.84,4.92)	0.30
Week24:HC:GS	-15.75	(-29.13,-2.37)	***0.06***
Week24:CS:GS:FD	-22.57	(-35.95,-9.19)	***0.01***
Week24:HC:CS:FD	3.45	(-9.93,16.83)	0.67
Week24:HC:CS:GS	-10.94	(-24.33,2.44)	0.18
Week24:HC:GS:FD	-3.62	(-17.0,9.76)	0.66
Week24:HC:CS:GS:FD	-16.37	(-29.75,-2.99)	***0.05***

Main effects at baseline (time zero) do not test the hypotheses of interest and have been omitted from the table for brevity. All models used effect coding. Reported coefficients represent half the difference between component levels; multiply by 2 for the full effect size. Significant effects (p<.10) are highlighted in bold. Abbreviations: CS = coaching drop-in webchat sessions; FD = food diary review plus feedback; GS = goal setting statements; HC = health coach introductory video call.

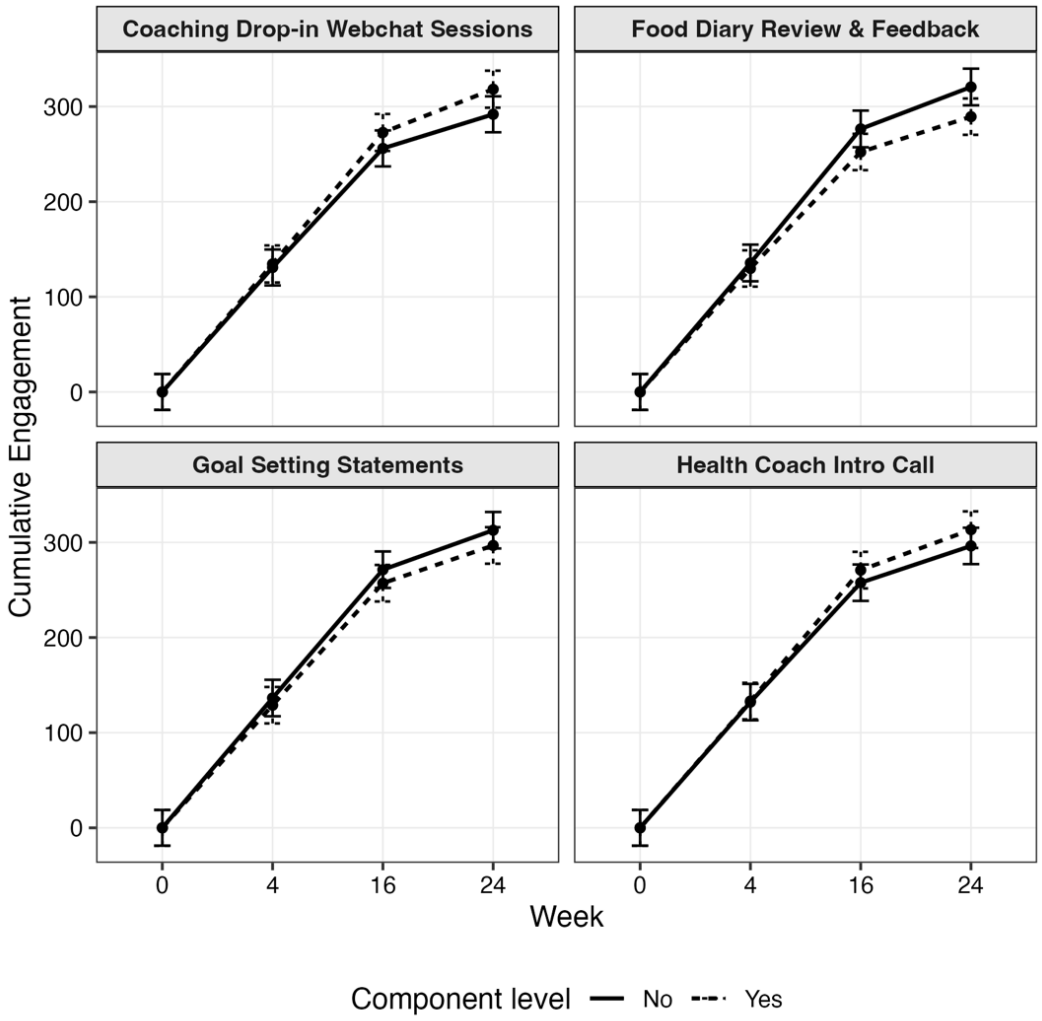

Figure 5.7: Predicted cumulative engagement over time by component level (No vs. Yes) using all available data (N=1,335). The dotted "Yes" line denotes that a participant received the intervention component, whereas the solid "No" line denotes that a participant did not receive the intervention component. Values represent predicted marginal means estimated from the linear mixed effects model. Error bars represent 90% confidence intervals.

To aid with decision making, I examined any important significant interactions with food diary review plus feedback at 24 weeks, to determine whether any of these components boosted or reduced the effect of food diary review plus feedback on engagement. There was a significant three-way interaction involving coaching drop-in sessions, goal setting

statements, and food diary review (β = -22.57; 90% CI [-35.95, -9.19]; p = 0.006), indicating that the effect of food diary feedback on engagement depended on the combination of other components (***Figure 5.8***). Specifically, the negative effect of food diary review plus feedback on engagement was buffered by pairing with either goal setting statements or coaching drop-in sessions alone but had a negative effect on engagement when all three components were included together.

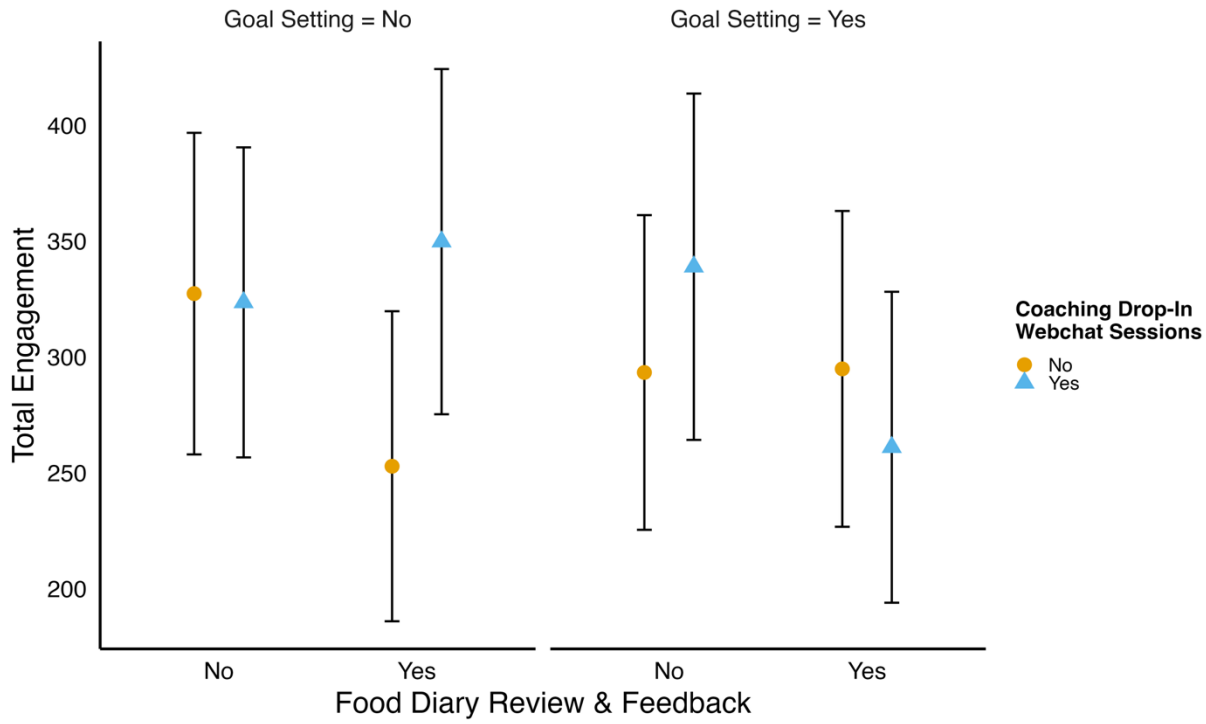

Figure 5.8: Three-way interaction between coaching drop-in sessions, goal setting statements, and food diary review on total engagement at 24 weeks. Values represent estimated marginal means and error bars depict the 90% confidence intervals.

There was also a significant four-way interaction involving health coach intro call, coaching drop-in sessions, goal setting statements, and food diary review (β = -16.37; 90% CI [-29.75,-2.99]; p = 0.05) (***Figure 5.9***). This indicated that the effect of the food diary

review plus feedback component on engagement was dependent on the presence of the other three components. When food diary feedback was excluded, engagement remained relatively stable across conditions. When it was included, in the absence of goal setting, pairing the food diary with coaching drop-ins and the health coach call appeared to buffer its negative effect. However, when all four components were active, engagement was lowest. These findings suggest that while individual components may be beneficial in isolation or in simple combinations, combining multiple effortful components may ultimately reduce user engagement.

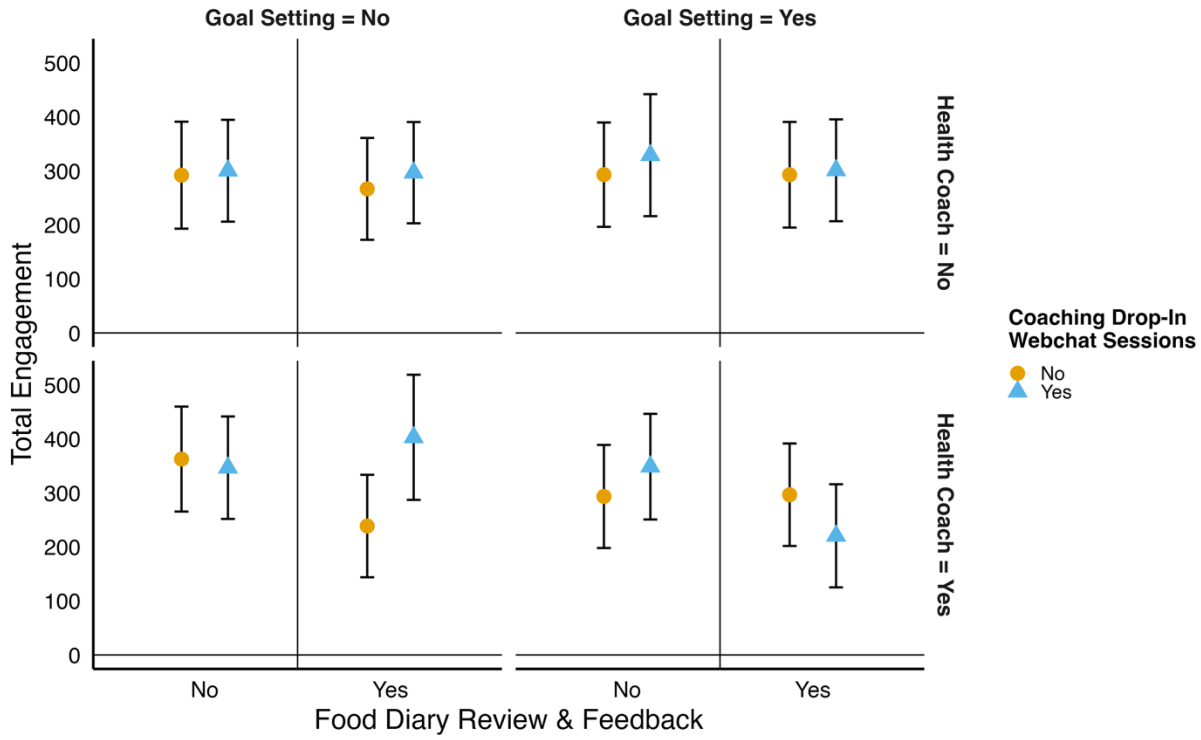

Figure 5.9: Four-way interaction between health coach intro call, coaching drop-in sessions, goal setting statements, and food diary review on total engagement at 24 weeks. Values represent estimated marginal means and error bars depict the 90% confidence intervals.

5.4.5 Acceptability

A total of 135 (10%) participants completed the acceptability questionnaire. Due to the low response rate caution is warranted in interpreting these findings. The views captured may reflect those of more engaged or motivated individuals and may not generalise to the wider sample. As such, conclusions about acceptability should be treated as indicative rather than definitive.

The Second Nature programme was rated positively overall, with varying levels of acceptability across intervention components (***Table 5.8***). Participants who were allocated the health coach introductory video call reported the highest perceived helpfulness of the overall programme, with 65.7% rating it as "helpful" or "very helpful," compared to 62.1% for coaching drop-in sessions, 59.2% for goal setting statements, and 62.6% for food diary feedback. Participants' likelihood to recommend the programme was high across all groups, with the proportion of participants reporting they were "likely" or "very likely" to recommend the programme ranging between 70 – 77.3% for all components.

Perceived helpfulness of the health coach was consistently high across all components, though slightly higher among those who were allocated to the health coach intro call (80.8% rated "helpful" or "very helpful") and coaching sessions (80.3%), compared to goal setting (77.7%) and food diary feedback (74.6%).

The coaching drop-in sessions and health coach intro call were rated as the most helpful intervention components, with 63.2% and 61.7%, respectively, rating these either

"helpful" or "very helpful." In contrast, 51.8% rated goal setting as helpful and 52.3% rated the food diary feedback as helpful.

Participants allocated to the goal setting statements reported the highest levels of effort, with 29.6% rating it as "a lot of effort" or a "huge effort," compared to 25.3% for food diary feedback, 6.8% for the health coach video call, and 3% for drop-in coaching sessions.

Table 5.8: Acceptability questionnaire scores by intervention component

Acceptability construct	Intervention components			
	Health coach intro video call (n = 73)	Coaching drop-in webchat sessions (n= 66)	Goal setting statements (n= 54)	Food diary review plus feedback (n= 67)
Perceived helpfulness of overall Second Nature programme, *N* (%)				
Very helpful	32 (43.8)	26 (39.4)	18 (33.3)	21 (31.3)
Helpful	16 (21.9)	15 (22.7)	14 (25.9)	21 (31.3)
Neutral	20 (27.4)	18 (27.3)	17 (31.5)	19 (28.4)
Unhelpful	4 (5.5)	6 (9.1)	4 (7.4)	5 (7.5)
Very unhelpful	1 (1.4)	1 (1.5)	1 (1.9)	1 (1.5)
How likely are you to recommend the Second Nature programme, N (%)				
Very likely	33 (42.5)	31 (47)	22 (40.7)	30 (44.8)
Likely	20 (27.5)	20 (30.3)	19 (35.2)	20 (29.9)

Acceptability construct	Intervention components			
	Health coach intro video call (n = 73)	Coaching drop-in webchat sessions (n= 66)	Goal setting statements (n= 54)	Food diary review plus feedback (n= 67)
Neutral	14 (19.2)	9 (13.6)	7 (13)	12 (17.9)
Unlikely	5 (6.8)	5 (7.6)	5 (9.3)	4 (6)
Very unlikely	1 (1.4)	1 (1.5)	1 (1.9)	1 (1.5)
Perceived helpfulness of health coach, *N* (%)				
Very helpful	34 (46.6)	31 (47)	22 (40.7)	25 (37.3)
Helpful	25 (34.2)	22 (33.3)	20 (37)	25 (37.3)
Neutral	10 (13.7)	9 (13.6)	8 (14.8)	13 (19.4)
Unhelpful	3 (4.1)	3 (4.5)	3 (5.6)	3 (4.5)
Very unhelpful	1 (1.4)	1 (1.5)	1 (1.9)	1 (1.5)
Perceived helpfulness of intervention component, *N* (%)				
Very helpful	31 (42.5)	29 (43.9)	10 (18.5)	19 (28.4)
Helpful	14 (19.2)	13 (19.7)	18 (33.3)	16 (23.9)
Neutral	14 (19.2)	13 (19.7)	17 (31.5)	24 (35.8)
Unhelpful	0 (0)	4 (6.1)	6 (11.1)	3 (4.5)
Very unhelpful	4 (5.5)	0 (0)	2 (3.7)	2 (3)

Acceptability construct	Intervention components			
	Health coach intro video call (n = 73)	Coaching drop-in webchat sessions (n= 66)	Goal setting statements (n= 54)	Food diary review plus feedback (n= 67)
Did not know this was a feature	10 (13.7)	7 (10.6)	1 (1.9)	3 (4.5)
Perceived burden of intervention component, *N* (%)				
No effort at all	22 (30.1)	18 (27.3)	3 (5.6)	8 (11.9)
A little effort	21 (28.8)	25 (37.9)	15 (27.8)	17 (25.4)
Neutral	16 (21.9)	15 (22.7)	18 (33.3)	21 (31.3)
A lot of effort	5 (6.8)	2 (3)	14 (25.9)	15 (22.4)
Huge effort	0 (0)	0 (0)	2 (3.7)	3 (4.5)
Did not know this was a feature	9 (12.3)	6 (9.1)	2 (3.7)	3 (4.5)

5.4.6 Fidelity

5.4.6.1 Health Coach Introductory Call

Of the 666 participants randomised to receive the health coach introductory call, 221 (33%) scheduled the call, and 185 (28%) attended the call. The mean duration of the attended health coach introductory calls was 24.4 (SD = 5.1) minutes.

5.4.6.2 Coaching Drop-In Webchat Sessions

Table 5.9 shows the number of participants who attended the sessions at each week in the programme. Of the 674 participants randomised to receive the coaching drop-in sessions, 228 (34%) attended at least one session. The number of coaching sessions attended per participant ranged from 0 to 15, and the mean number attended per participant was 0.67 (SD = 1.53).

Table 5.9: Number of participants attending the coaching drop-in webchat session in each week of the programme (N = 674)

Session Week	N (%) participants attending coaching drop-in session
1	215 (32)
2	81 (12)
3	45 (7)
4	26 (4)
5	22 (3)
6	18 (3)
7	13 (2)
8	13 (2)
9	12 (2)
10	10 (1.5)
11	6 (1)
12	4 (0.6)
13	3 (0.4)
14	2 (0.3)

15	2 (0.1)
16	1 (0.1)
17	0 (0)

5.4.6.3 Goal Setting Statements

Of the 665 participants randomised to receive the goal setting statements, 115 (17%) completed at least one goal setting statement, and 95 (14%) completed at least one reflection statement. The number of goal setting statements completed per participant ranged from 0 to 5, and the mean (SD) number completed per participant was 0.25 (0.60). The number of reflection statements completed per participant ranged from 0 to 9, and the mean number completed per participant was 0.25 (SD = 0.84).

5.4.6.4 Food Diary Review Plus Feedback

Of the 675 participants randomised to receive the food diary review plus feedback, the mean (SD) number of food diary entries completed over the 17-week programme was 24 (68), compared to 15 (66) among those who did not receive the food diary review plus feedback. At the three timepoints where the food diary review plus feedback was offered, a total of 64 (9%) participants had their food diaries reviewed at 4 weeks, 25 (4%) at 7 weeks, and 19 (3%) at 11 weeks. A total of 87 (13%) participants completed at least one food diary.

5.4.7 Decision Making

The decision about which components to include in the optimised intervention was primarily guided by the objective of identifying components that contributed to at least a minimal improvement in weight loss, defined as ≥ 0.75 kg at 16 weeks.

Decision making began with an evaluation of main effects. The health coach introductory call did not show a significant effect at 16 weeks; however, it demonstrated a statistically significant positive main effect on weight loss at 24 weeks, corresponding to an average 1 kg greater weight loss (***Table 5.4***). This component was also present in most of the top-performing conditions at 16- and 24- weeks (***Table 5.5***). I inferred that there was evidence for including the health coach introductory video call. In contrast, there was strong evidence for excluding food diary review plus feedback, which showed a significant negative main effect on weight loss at both 16- and 24- weeks (***Table 5.4***).

Interaction effects were then considered to refine decisions. The negative effects of the food diary were partially buffered by the inclusion of coaching drop-in webchat sessions (***Figure 5.4***). As shown in ***Table 5.5***, the combination of the health coach intro call, coaching drop-in sessions, and goal setting statements produced the greatest predicted weight loss at both 16- and 24- weeks. Therefore, the overall evidence supported the exclusion of the food diary review component.

Secondary outcomes, programme cancellation and engagement, were used to contextualise the preliminary component set. Coaching drop-in sessions were associated with higher likelihood of early programme cancellation at four weeks (***Table***

5.6), although this was mitigated when paired with the health coach call (***Figure 5.6***) and was not observed at later time points. The case for excluding food diary feedback was further supported by its negative impact on engagement (***Table 5.7***), particularly when combined with coaching drop-ins and goal setting (***Figure 5.8***). Engagement was lowest when all four components were active, suggesting that too many components may overburden participants (***Figure 5.9***).

Overall, although no component or combination exceeded the optimisation threshold at 16 weeks, the health coach introductory video call led to 1 kg greater weight loss at 24 weeks and consistently performed well across all outcomes. In contrast, the food diary review plus feedback component showed negative effects on weight loss and engagement. The combination of the health coach call, coaching drop-ins, and goal setting yielded the highest predicted weight loss, and the health coach call buffered potential downsides of the coaching drop-ins on early dropout. Nevertheless, differences among top-performing combinations were modest, and even the base programme (i.e. with no added components) performed well. This is unsurprising, given that Second Nature is already a well-established intervention, and the components tested represented modest adaptations.

5.5 Discussion

5.5.1 Principal Results

This chapter presents the results of a factorial optimisation experiment to test the individual and combined effects of four candidate intervention components as adjuncts to an existing digital weight loss programme. The components were: a health coach introductory video call, coaching drop-in webchat sessions, goal setting statements, and food diary review plus feedback, which were developed during the preparation phase (***Chapter 4***). The aim was to identify an optimised combination of components that meaningfully improved weight loss, whilst also considering participant engagement and programme drop-out. Overall, the results offer guidance for future intervention development, by identifying components that may be further refined and tested in subsequent studies.

The findings provide preliminary evidence in support of including the health coach introductory call and excluding the food diary review plus feedback component from the optimised package. While the combination of the health coach call, coaching drop-ins, and goal setting yielded the highest predicted weight loss, it is important to also consider pragmatic factors in the decision-making process. In contexts where scalability and resource efficiency are key priorities, a more streamlined version of the intervention, such as one including only the health coach introductory call, may represent the most practical and scalable option. This is supported by both the engagement data, where combining more components had a negative effect on engagement,

and the acceptability results. The health coach call and coaching drop-in sessions were consistently rated as both helpful and low effort. In contrast, goal setting was perceived as more demanding, and food diary feedback received the lowest ratings in terms of both helpfulness and effort. These findings reinforce the importance of balancing intervention effectiveness with user experience and burden.

5.5.2 Comparison with Prior Work

To date, relatively few digital weight loss interventions have been optimised using factorial designs, but the small number of existing studies have demonstrated the potential of this approach (149, 293, 294). This study builds on this previous work by applying a similar optimisation strategy in a commercial setting, where other considerations like feasibility, user burden, and implementation are especially important. As the largest factorial trial of its kind, and the first conducted within an industry setting, this study provides new insights into how human-supported and automated components perform when tested together in a real-world digital programme.

Here, I found that only the health coach introductory call showed a main effect on weight loss at 24 weeks. This reflects previous research which strongly supports the role of human support in improving engagement and weight loss outcomes in digital health interventions (128, 259, 298). In the Opt-IN factorial experiment, human support components, such as coaching calls and peer support via a buddy, significantly improved 6-month weight loss, whereas purely digital features like automated text messages provided no additional benefit (149). Further, a systematic review and network

meta-analysis of 15 studies found that web-based interventions that included tailored feedback from a professional were the most effective interventions for weight loss in people living with obesity (299). These findings align with the intervention theory which is grounded in the supportive accountability model, and posits that human support can enhance adherence to digital interventions by fostering a sense of accountability and connection to another person (286).

However, in this trial, the mean duration of the attended health coach introductory calls was 24.4 minutes, suggesting this could be a relatively time-intensive and potentially costly component to implement at scale. Moreover, uptake of the introductory call was low, with only around one-third of participants scheduling and attending the call. This suggests that some individuals who sign up for digital programmes don't especially want personal contact, and that other delivery formats - such as asynchronous or automated support - may be more acceptable.

Perhaps then surprisingly, the coaching drop-in webchat sessions had no main effect on weight loss. However, several previous digital weight loss trials have shown that providing more intensive support does not necessarily improve engagement or outcomes (300-302). A meta-analysis of 13 studies found that light-touch coaching layered onto an automated programme led to greater weight loss than more intensive formats (303), and in the Opt-IN study, doubling the number of coaching calls offered no additional benefit (149). Another study that randomly assigned participants to either low, moderate, or high doses of behavioural treatment found that moderate-intensity treatment achieved weight loss comparable to higher-intensity options (86). In my study,

early, brief support in the form of the health coach introductory call appeared to be the most effective, suggesting that minimal, but well-timed, human support may be key. Supporting this, a recent adaptive weight loss trial found that participants who received brief coaching from the outset lost significantly more weight at six months (-4.8 kg) than those who began with automated tools alone (-2.8 kg) (304). Notably, this early gap was not fully closed even when human support was added later for non-responders. Therefore, starting treatment with automated self-help alone may result in a sustained shortfall in outcomes, underscoring the value of early human support. The evidence suggests that it is not the frequency of contact that is most important, but rather its timing and personal nature. Brief but strategically timed human input may be sufficient to enhance weight loss outcomes in ways that technology alone cannot.

The food diary review plus feedback component showed negative effects on both weight loss and engagement, and was the only feature conclusively excluded from the optimised package. This was somewhat unexpected, given evidence that dietary self-monitoring is a key behaviour change strategy associated with greater weight loss (206, 305), and that dietary self-monitoring combined with feedback leads to greater weight loss than self-monitoring alone (265).

However, in most successful interventions, food diaries are paired with regular, tailored feedback or embedded within a coaching context to support consistency, accuracy, and sustained engagement, which is critical for their success (206, 306). One study found that only participants who logged food for more than 228 days achieved significantly greater weight loss, but participants who tracked between 114-228 days did not lose a

significant amount of weight, which highlights the importance of frequent and consistent tracking to see a benefit (307). These findings underscore that the food diary component is difficult to operationalise effectively. In this trial, participants were encouraged to log their food weekly but received only three rounds of feedback from a health coach, an approach that was designed to maintain scalability, but likely fell short of the support needed to maintain engagement. Notably, the negative effect of the food diary on weight loss was buffered when combined with the coaching drop-in webchat sessions, suggesting that the absence of accompanying human support may have limited its effectiveness.

When delivered in this form, the food diary component may have introduced more burden than benefit, which is supported by the low acceptability ratings for this component. Prior research has shown that poorly framed automated feedback can increase cognitive load and elicit negative emotional responses such as guilt or frustration (308, 309). Moreover, food logging is often perceived as tedious and time-consuming, contributing to adherence challenges and possibly explaining the reduced engagement observed in this study (206, 310). These findings highlight that the success of an intervention component also depends on how it is delivered. Even theoretically sound, well-intentioned strategies can have unintended negative effects if they are overly effortful.

This study offers important insights into how combining intervention components influences engagement. The food diary feedback component reduced engagement, particularly when delivered alongside multiple other active components. In contrast,

greater engagement was observed in conditions with fewer, more targeted components, especially when combined with some form of human support. These findings align with prior research indicating that too many features can diminish user engagement in digital interventions (311, 312), and that tasks requiring manual input or uploading data are often perceived as burdensome, undermining long-term adherence (147). Although reviews of health behaviour change interventions often advocate combining multiple strategies to promote sustained change (78, 235), doing so without attention to user burden could be counterproductive. Evidence from optimisation trials, further suggests that simply adding more components does not necessarily improve outcomes (149, 304). Optimising digital interventions for burden and effort from the very outset has therefore been strongly recommended (313). These findings underscore the importance of evaluating not only the individual effectiveness of each component but also how components interact within a multi-component programme, to achieve meaningful outcomes without compromising user engagement.

In light of these findings, an approach which is automated where possible, but supported by brief and well-timed human contact, may strike the right balance between effectiveness and scalability. The health coach introductory call stood out as a low-burden component with meaningful impact, reinforcing that early, targeted human input can improve outcomes. In contrast, the food diary review plus feedback component, despite its theoretical grounding, added participant burden without clear benefit. Its exclusion highlights the importance of delivering components in ways that feel useful and manageable to participants. More broadly, the findings underscore a key challenge

in digital intervention design, identifying the minimal level of support needed to improve outcomes without overwhelming participants and implementing this effectively at scale.

5.5.3 Strengths & Limitations

To my knowledge, this is the largest factorial optimisation trial conducted within a real-world digital health programme. A key strength of this study was the application of a factorial design, which provides an efficient method for optimising multicomponent digital interventions. Unlike a traditional RCT that evaluates an intervention as a full package, this approach provides valuable information about the contributions of individual components, both in isolation and in combination. This provides empirical evidence to guide decisions about which components to include and offers greater insight into which parts of the intervention may be driving outcomes.

The collaboration with Second Nature enabled this study to be delivered at scale and allowed for testing components under real-world conditions. Using their established intervention allowed me to complete a large and complex trial within the scope of a DPhil, something that would not have been possible without access to an existing digital health programme. Their user base made recruitment quick and efficient, resulting a large sample size of 1,355 participants. However, conducting research within a commercial context limited the data I was able to collect and meant I had less control over how participants used the intervention outside the core experimental components. For example, although Second Nature were asked not to move participants between groups, this did occasionally happen. To reduce the risk of contamination between components, participants who changed groups were removed from the analysis, but

there is a small risk that some contamination remains. Applying the MOST framework in a commercial context also came with challenges. The time required to design, implement, and analyse a fully powered factorial trial was considerable. In this case, some components were developed nearly two years before results were available, by which time the programme had evolved, and technology had advanced considerably.

Other limitations should be acknowledged. The intervention components were tested in a specific context, adults enrolled in a self-paid, remotely delivered commercial weight loss programme. The sample was predominantly female and from more affluent areas, which limits generalisability to other populations but reflects the real-world user base of the Second Nature programme and of most other commercial programmes (124, 199, 233). Although this was one of the largest factorial trials of its kind, there was a large amount of missing data which is not uncommon for these types of digital trials (234), but limited power, especially for detecting higher-order interactions remains a consideration. Therefore, to test different assumptions for missing data, I also employed sensitivity analyses with which did not lead to different conclusions. In addition, weight was self-reported by the participants, which may not have been accurate. Exploratory subgroup analyses were also limited by small subgroup sizes, particularly the low proportion of male participants, which means there is only weak evidence for any observed subgroup differences. Fidelity to the intervention components was low, meaning many participants assigned to a component did not actually use it. It is common in digital interventions that participants make suboptimal use of the intervention features (233, 314), but this makes it hard to determine whether a component wasn't efficacious, or whether people just didn't engage with it enough to have an effect. Lastly, although

this study provides guidance for optimisation, this was a screening experiment. A definitive evaluation of any selected component combination would still require a randomised controlled trial comparing the optimised package to a suitable comparator.

5.5.4 Implications & Further Research

This study demonstrates the feasibility and value of optimising a commercial digital intervention using a factorial experimental design. It contributes to our understanding of which strategies improve weight loss, engagement, and retention, which are key outcomes for realising the full potential of digital health interventions. Crucially, it highlights the need to empirically test candidate components before implementing them at scale. For example, while Second Nature were in favour of introducing the food diary feedback component, this feature did not enhance outcomes and may in fact be counterproductive. Even promising strategies can have unintended effects, reinforcing the importance of structured, evidence-based testing prior to implementation using frameworks such as MOST.

This study also involved a considered decision-making strategy. Although current best practice supports the use of Bayesian decision tools such as decision analysis for intervention value efficiency (DAIVE) to evaluate multiple outcomes simultaneously (315, 316), I opted for the Component Screening Approach (246, 250). This was due to the nature of the outcomes in this trial, weight loss, engagement, and programme cancellation, which represent distinct domains with different implications for intervention development. Unlike some previous studies, it did not make conceptual sense to combine these into a single composite measure of health (317). Weight loss

was prioritised as the primary outcome, while engagement and programme cancellation were examined separately for components showing potential. Although integrated tools like DAIVE are useful in many contexts, they are challenging to apply in trials involving complex interventions, higher-order interactions, and repeated measures. In practice, optimisation decisions required careful judgement to balance effectiveness, user experience, and feasibility, which can inherently be a subjective process that may benefit from improved methodological tools.

Although optimisation trials offer valuable insights into which components work best and how they can be effectively combined, they are often too slow to meet commercial timelines. Product teams typically need to make quick, responsive decisions, whereas academic research processes can take years. This disconnect highlights the need for more agile approaches to optimisation, and I'm not convinced MOST is the right fit in this context. Embedding shorter experiments or A/B tests into regular product cycles, while retaining some of the structured decision-making principles from MOST, may offer a better balance. Overall, more agile methods are needed to ensure digital health optimisation remains both academically rigorous but also responsive for industry-based intervention development.

No component or combination met the pre-specified optimisation criterion of ≥ 0.75 kg additional weight loss at 16 weeks, but the findings provide useful guidance for future intervention development by identifying components - such as the health coach introductory call - that may benefit from refinement and further testing. In line with the MOST framework, the next step would be to return to the preparation phase to adapt the

content and delivery of promising components, or to develop new ones. The evidence generated in this optimisation trial, including main and interaction effects, can be used to refine the underlying conceptual model and improve understanding of how components influence outcomes. A follow-up optimisation trial could then be conducted, and once a candidate package meets the optimisation criterion, a definitive randomised trial should be undertaken to compare the optimised intervention against the standard Second Nature programme.

Given the findings that light-touch but timely support can be beneficial, future research should explore key points in the participant journey where brief input might help prevent disengagement. For example, around known drop-off points in the programme, such as membership renewal at Week 16. A targeted coaching call at Week 14, for example, could help sustain engagement during this period.

Subgroup findings also highlight the importance of personalisation. Goal setting appeared more effective for men and participants from less deprived areas, while drop-in coaching sessions were more beneficial for older users. In contrast, the food diary review and feedback was more effective among participants in higher deprivation tertiles, suggesting these groups may benefit from more structured or intensive support. Future optimisation efforts should focus on tailoring both content and delivery to identify who benefits most from which components, when support is most needed, and what level of input is sufficient to drive meaningful outcomes whilst still maintaining the benefit of scalability. More adaptive trial designs like Sequential Multiple Assignment Randomised Trial (SMART) could offer a valuable framework for testing the timing,

tailoring, and intensity of support (318). However, operationalising these insights in real-world digital programmes, particularly in a way that is feasible at scale, remains an ongoing challenge.

5.5.5 Conclusions

This study represents the largest factorial optimisation trial of a commercial digital weight loss programme to date and offers important insights into how individual components influence effectiveness and engagement. The health coach introductory call proved beneficial, highlighting that even brief, well-timed human support can meaningfully enhance outcomes. In contrast, the food diary review plus feedback component was excluded due to negative effects on both weight loss and engagement, as well as low acceptability, demonstrating that even theoretically well-supported strategies can have unintended consequences if not delivered appropriately. More broadly, the findings highlight the importance of avoiding unnecessary burden in digital interventions and instead prioritising well-timed human support that promotes connection and accountability. Brief, early human contact can meaningfully enhance the effectiveness, which warrants further research, yet delivering it at scale continues to pose a challenge for digital interventions.

Chapter 6 : Effect of planned pauses versus continuous energy restriction on weight loss and attrition: a systematic review of randomised controlled trials

6.1 SUMMARY

This chapter reports a systematic review which aimed to investigate whether pausing a weight loss programme for a defined period of time could enhance weight loss and reduce attrition. The rationale was that scheduled breaks or pauses in a weight loss programme might offer greater flexibility, improve dietary adherence, and ultimately enable individuals to sustain a period of active weight management for longer.

The MEDLINE, Embase, PsycINFO, Web of Science, and Cochrane databases along with two trial registries were searched from inception to July 2023. Randomised controlled trials of adults with overweight and/or obesity were included if they compared planned pause interventions with a comparator of either continuous energy restriction, usual care, or a minimal intervention. To be included, the weight loss intervention must have incorporated a pause of at least one week. Pooled mean differences for weight change, and odds ratios for attrition, were calculated using random-effects meta-analyses.

Eight trials (nine intervention arms), representing 796 participants (77% female) were included. Pooled results did not detect a significant difference in weight change between

planned pauses and CER interventions at the end of the active intervention at a median 26 weeks (planned pauses vs. CER mean: −7.09 vs. −7.0 kg; mean difference: −0.09 kg; 95% CI: −1.10 to 0.93) or at final follow-up at a median 52 weeks (planned pauses vs. CER mean: −6.91 vs. −6.19 kg; mean difference: −0.72 kg; 95% CI: −2.92 to 1.48). There was also no difference in attrition between planned pauses and CER interventions at the end of the active intervention (risk ratio: 1.20, 95% CI: 0.82 to 1.75) or at final follow-up (risk ratio: 1.04, 95% CI: 0.89 to 1.22).

Overall, planned pauses produced similar outcomes to continuous energy restriction in both weight loss and attrition. Planned pauses could be incorporated into weight loss programmes without reducing effectiveness, although there was no evidence that they improved attrition.

Note: this chapter has been published in a peer-reviewed journal article.

- **Wren GM** et al. Effect of planned pauses versus continuous energy restriction on weight loss and attrition: a systematic review. Obesity. 2024. 32(3):454-65. https://doi.org/10.1002/oby.23976

6.2 INTRODUCTION

Although this thesis set out to identify and test possible strategies to improve engagement in digital programmes, sustaining engagement and retention was a recurring challenge throughout Chapters 2-5. This prompted me to explore a new approach, 'planned pauses', as a potential strategy to improve retention in this final chapter.

The conventional approach to weight loss involves continuous energy restriction (CER), where energy intake is restricted to below weight maintenance requirements over a single, continuous period of active weight loss. Such regimens typically consist of decreasing daily energy intake by 15–60% (319). Although CER is an effective weight loss strategy on average, there is significant inter-individual variability, which likely reflects individual challenges in adhering to the prescribed energy restriction (320-322).

As an alternative, intermittent energy restriction (IER) regimens involve alternating periods of energy restriction with periods of normal eating. IER has been proposed to increase dietary adherence due to its more flexible nature, which may lead to improved weight loss outcomes (323-325). Previous systematic reviews comparing IER to CER regimens, have reported comparable weight loss (326-331) and similar attrition rates (326, 330). However, in these reviews, the IER regimens varied considerably across studies, making it difficult to compare the effectiveness of different dietary regimens. The two most common and widely studied intermittent regimens - alternate day fasting and the 5:2 diet - have both been found to lead to similar weight loss compared to CER (319, 328, 332).

This review focuses on a less commonly studied approach involving intermittent intervals of greater than one week, or prescribed energy 'pauses'. For the purposes of this review, I consider planned pauses to be distinct from intermittent dieting. Planned pauses are defined as intermittent intervals lasting at least one week, in contrast to regimens within a one-week period (e.g., the 5:2 diet), which have been considered in previous reviews.

Evidence from individual randomised controlled trials comparing interventions that meet my definition of a 'planned pause', and CER interventions shows mixed results. Some studies have shown that energy restriction applied intermittently leads to greater weight loss than CER (333, 334), whilst most other studies have reported no advantage on weight loss (324, 335-337) or weight loss maintenance (338). It has been suggested that a key factor in explaining these differences may be whether participants successfully maintained their weight during pause phases, or the duration of each restriction cycle (339). Attrition findings are similarly inconsistent. Some studies report a higher dropout rate in CER compared to planned pauses (324, 335, 336, 340), whilst other studies report the opposite (333, 337). Other studies report a similar dropout rate in both interventions (334, 335, 338, 341).

It is uncertain whether longer-term periods of IER, or structured pauses within a weight loss programme, could improve weight loss. Together, these findings raise questions about the potential for planned pauses to improve both adherence and outcomes. Such 'planned pauses' may offer greater flexibility, enhancing dietary adherence, and in turn, improve weight loss. As attrition could be an indicator of non-adherence to an

intervention, lower attrition could also be indicative of a programme that is easier to sustain, potentially resulting in better long-term outcomes. Conversely, extended pauses within a weight loss programme may inadvertently lead to a decline in motivation and focus among participants, posing a risk of hindering overall weight loss progress. Therefore, identifying the optimal pause duration that balances both flexibility and sustained dietary adherence could be fundamental to the success of incorporating planned pauses within a weight loss regimen.

In light of the mixed evidence, a systematic review is warranted to evaluate whether planned pauses are a viable strategy for improving retention and supporting weight loss. This systematic review and meta-analysis of randomised controlled trials aimed to synthesise available evidence comparing planned pauses with CER, usual care, or minimal intervention. It also explored whether outcomes differed according to pause duration or the dietary approach used during pause intervals.

6.3 METHODS

A protocol for this systematic review was registered prospectively on International Prospective Register of Systematic Reviews (PROSPERO) (342). This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines (343).

6.3.1 SEARCH STRATEGY

MEDLINE, Embase, PsycINFO, Web of Science, and the Cochrane Central Register of Controlled Trials, were searched from database inception to July 2023, using terms for the following concepts: "planned pauses", "weight loss", and "randomised controlled trials". A sample search strategy for MEDLINE can be found in (***Appendix 6.1***).

I also screened references from systematic reviews identified through the search and requested full-text papers from authors for those I was unable to obtain. The searches were not restricted by country or language. The trial registries, ClinicalTrials.gov and the WHO International Clinical Trials Registry, were also searched. The reference lists of included studies were hand-searched to identify any additional relevant studies.

Studies were included if they recruited adults (≥18 years) with a BMI ≥25 kg/m^2 and had a randomised controlled design investigating a planned pause intervention during a weight loss programme. The intervention needed to explicitly state that the aim was to reduce weight or maintain lost weight, otherwise it was excluded. A planned pause was defined as intermittent intervals of no less than one-week long. To be considered a planned pause, the intervention must have included at least one pause accompanied by

a return to broadly the same programme. The initial intervention must have been at least one week, and the pause interval could not be longer than the preceding intervention interval. I included trials of interventions without restriction on the total length of the trial or the length of follow-up of participants. Studies were required to report at least one measure of weight loss (e.g. body weight, BMI, percentage body weight) and to include a comparator arm of either continuous (daily) energy restriction, usual care, or a minimal intervention.

6.3.2 Data Collection

The Covidence systematic review software was used for abstract and full-text screening and data extraction (344). Titles and abstracts were assessed for inclusion by two independent reviewers. Full-text papers of the included studies were obtained and independently assessed for inclusion by two reviewers. A second reviewer and I independently conducted data extraction using a pre-determined data extraction form, with data collected on the population, intervention, control groups, and outcomes. Any conflicts in screening or extraction were resolved by discussion, or where needed, by referral to a third reviewer. Study authors were contacted where further detail and clarification was required.

The primary outcome was the mean weight change at the end of the intervention and at final follow-up. Where outcome data were missing, I contacted authors for further information. Weight change data was extracted as reported. Where multiple methods were reported for participants lost to follow-up, the most conservative estimate was extracted (i.e., intention-to-treat analysis). The secondary outcome was attrition at the

end of the intervention and at final follow-up, so the numbers of participants at each time point were also extracted.

6.3.3 Risk of Bias and Overall Quality of the Evidence

Risk of bias was assessed using the Cochrane risk of bias tool (345). Risk of bias was assessed based on generation of the randomisation sequence, concealment of allocation, blinding of outcome assessment, and attrition bias. It is not possible to blind participants or study personnel in behavioural intervention trials; therefore, this domain was omitted. The selective outcome reporting domain was also omitted because I was only interested in extracting measures of weight loss, as specified in the eligibility criteria. Studies were judged at high risk of attrition bias if less than 80% of participants were followed up at the end of the intervention, if less than 60% were followed up at the final follow-up, or if the percentage followed up was different across trial arms (≥20% difference). Blinding of outcome assessment was judged as high risk if weight was self-reported by the participant.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment was conducted to assess the overall quality of evidence, based on the following domains: 1) risk of bias, 2) inconsistency of results across studies, 3) indirectness, 4) imprecision, and 5) other factors (e.g., publication bias) (346). The overall quality of the evidence was then categorised as high, moderate, low, or very low. GRADE assessments were conducted for the primary outcome included in the meta-analysis.

6.3.4 Statistical Analysis

Meta-analyses were conducted in Review Manager 5.2 (Cochrane) (347).The primary analysis aimed to examine the difference in weight change between the planned pause intervention and CER comparator groups at the end of the active intervention and at final follow-up. Pooled results were calculated as mean differences in kilograms (kg) with 95% confidence intervals.

The secondary analysis aimed to compare the attrition rate between the planned pause intervention and CER comparator groups. For each study, the proportion of participants that dropped out in the intervention arm (*pI*) and the comparator arm (*pC*) were used to calculate a risk ratio (*pI/pC*) using the Mantel–Haenszel method. A risk ratio greater than one indicates greater attrition in the planned-pause intervention arm compared with the comparator, and a risk ratio less than one indicates a lower attrition in the planned-pause intervention arm compared with the comparator. Each risk ratio was weighted by the inverse variance and pooled to create a summary effect.

Subgroup analyses were used to test for differences in the effectiveness and the attrition rate of the planned-pause intervention by calculating the mean difference in weight loss or risk ratio of attrition, and the χ^2 test was used for subgroup differences. Subgroups of studies were pooled by pause duration (short pauses of one-week, medium pauses of 2 weeks, or long pauses of >4 weeks) and by the regimen used in the pause interval (maintain weight, “usual” diet, or energy restriction).

All meta-analyses used a random effects model to account for variation in the intervention programmes and populations being tested. Statistical heterogeneity was assessed using the I^2 statistic (348). Where a study contributed more than one intervention arm to the analysis, the control group was divided equally between arms to avoid double counting in the pooled result.

Planned sensitivity analyses excluded studies at high risk of bias in any domain. I also assessed the consistency and precision of the evidence. Consistency was based on the direction of the effect estimates. Analyses were judged as consistent if the direction of the effect was the same for each of the studies included in the analysis. Precision was based on the width of the confidence intervals around the estimate of the effect. Visual assessment of funnel plots was used to determine the influence of publication bias.

6.4 RESULTS

The literature search identified a total of 4,484 records, 3,097 identified from database searches and 1,387 from other sources (***Figure 6.1***). After title and abstract screening, 2,756 references were excluded, and full texts were retrieved for 49 references. 31 references were excluded after full-text screening. The main reason for exclusion was that the intervention did not meet the definition of a planned pause.

Two studies that otherwise met my definition of a planned pause intervention were excluded due to being conducted in an ineligible population (i.e., BMI <25 kg/m^2) (340, 349). Two studies that met all other inclusion criteria were excluded as the duration of the pause interval was longer than the preceding energy restriction interval (341, 350). Ultimately, 18 references met the inclusion criteria which represented 8 individual studies (including one study abstract).

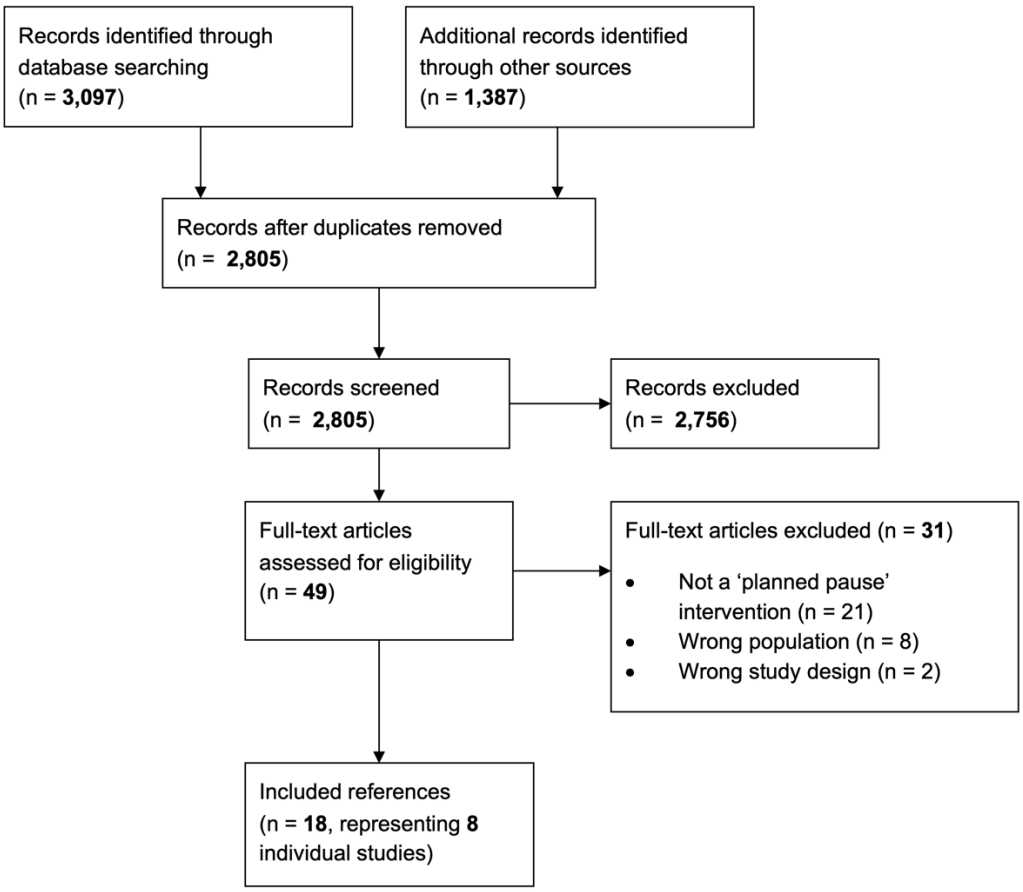

Figure 6.1: PRISMA flow diagram of review process.

6.4.1 Characteristics of Included Studies

The eight included studies included 796 participants. The number of participants in each study ranged from 25 to 214, with an average of 100 participants per study. Four studies were conducted in Australia (336, 351-353), two studies in the United States (324, 334), one study in Canada (335), and one study in Turkey (354). Four studies were conducted with people living with overweight or obesity (324, 336, 351, 354), three studies in people

living with obesity (335, 352, 353), and one study in people who were overweight and had type 2 diabetes (334).

Overall, 77% of participants were female; the mean age ranged from 36.0 to 60.5 years; and the mean BMI (reported in seven studies) ranged from 30.5 to 37.9 kg/m^2. Wing et al. had two intervention arms which qualified as a planned pause intervention and so were compared to the CER control separately; these are referred to hereafter as the short break (SB) and long break (LB) arms (324). For planned pause interventions, attrition rate ranged from 8% to 60% at the end of the active intervention and from 15% to 66% at the final follow-up. For CER interventions, attrition rate ranged from 3% to 49% at the end of the active intervention and from 25% to 62% at the final follow-up.

6.4.2 Intervention and Comparators

The median duration of the total intervention period in the nine included intervention arms was 26 weeks (range: 8 to 52 weeks). Six studies (seven intervention arms) reported weight change at a further time point after the end of the active intervention, with a median final follow-up of 52 weeks (range: 24 to 104 weeks) (324, 334-336, 351, 352).

Three interventions included short pause intervals of one-week (336, 351, 354), three interventions included medium pauses intervals of two weeks (324, 352, 353), and three interventions included long pause intervals of 5-12 weeks (324, 334, 335).

Three interventions used maintenance energy requirements in the pause intervals, where participants were advised to maintain their weight stable or provided with 100% of their energy requirements (335, 352, 353); five interventions guided participants to follow

their 'usual' diet during the pause interval (324, 336, 351, 354); and in one intervention participants followed moderate energy restriction during the pause interval (334). Two studies included food provision in both the intervention and control arms for the duration of the trial (352, 353).

In all eight included studies, the comparator arm included a CER intervention (324, 334-336, 351-354). None of the eligible studies included usual care or a minimal intervention as the comparator. The total intervention duration in the CER comparator arms ranged from 8 to 52 weeks. In all studies, the prescribed energy restriction during the restriction phase of the planned pause intervention was the same as the energy restriction in the CER arm.

Further details of the PP and CER arms for each included study can be found in ***Table 6.1***.

Table 6.1: Characteristics of included studies

Author, year (ref)	Country	Population	Control Regimen	Planned Pause Regimen	Pause Interval	Data collection time points	Attrition
Arguin, 2012 (335)	Canada	Postmenopausal women with obesity, n = 25 Mean age: 60.5 ± 6.0 years 100% female	n = 12, 15 weeks of CER. Energy restriction prescribed to reduce body weight by 1% of initial body weight per week.	n = 13, 3 x 5-week blocks of energy restriction alternating with 2 x 5-week blocks of weight maintenance. The same energy restriction requirements as CER.	Daily weighing Instructed to maintain stable body weight (± 2 kg)	End of intervention: 20/30 weeks Follow-up: 12 months	End of intervention: 8% PP; 17% CER Follow-up: 15% PP; 25% CER
Byrne, 2018 (352)	Australia	Men with obesity, n = 51 Mean BMI: 34.5 ± 3.7 kg/m^2 Mean age: 39.6 ± 8.0 years 0% female	n = 25, 16 weeks of CER. Food provided with 67% of weight maintenance energy requirements.	n = 26, 8 x 2-week blocks of energy restriction alternating with 7 x 2-week blocks of energy balance. The same energy restriction requirements as CER.	Daily weighing Food provided with 100% of weight maintenance energy requirements.	End of intervention: 16/30 weeks Follow-up: 48/62 weeks	End of intervention: 27% PP; 12% CER Follow-up: 42% PP; 48% CER
Byrne, 2020 (353)	Australia	Women with obesity, n = 52 Mean BMI: 35.0 ± 3.6 kg/m^2 Mean age: 40.0 ±	n = 24, 12 weeks of CER. Food provided with 67% of weight	n = 28, 6 x 2-week blocks of energy restriction alternating with 5 x 2-week blocks of energy balance.	Daily weighing Food provided with 100% of weight maintenance	End of intervention: 12/22 weeks	End of intervention: 43% PP; 29% CER

Author, year (ref)	Country	Population	Control Regimen	Planned Pause Regimen	Pause Interval	Data collection time points	Attrition
		7.0 years 100% female	maintenance energy requirements.	The same energy restriction requirements as CER.	energy requirements.	Follow-up: 6 months	Follow-up: 64% PP; 42% CER
Erdem, 2022 (354)	Turkey	Men and women with overweight or obesity, n = 144 Mean BMI: 30.5 ± 2.6 kg/m^2 Mean age: 36.0 ± 12.1 years 69% female	n = 72, 13 weeks of CER. Daily energy requirements calculated using the Schofield equation to calculate basal metabolic rate. A Mediterranean diet which met 70% of energy requirements was prescribed.	n = 72, 1-week Mediterranean energy restriction diet alternating with 1-week 'normal' diet for 13 weeks.	Participants instructed to return to their usual diet.	End of intervention: 13 weeks	End of intervention: 24% PP; 3% CER
Headland, 2019 (351)	Australia	Men and women with overweight or obesity, n = 214 Mean BMI: 33.9 ± 5.3 kg/m^2	n = 104, 52 weeks of CER. Prescribed energy intake of 4200 kJ/day for women and 5040 kJ/day for men.	n = 110, 1-week habitual diet alternating with 1-week energy restriction for 52 weeks. The same energy restriction requirements as CER.	Participants instructed to return to their usual diet.	End of intervention: 52 weeks Follow-up: 24 months	End of intervention: 60% PP; 49% CER Follow-up:

Author, year (ref)	Country	Population	Control Regimen	Planned Pause Regimen	Pause Interval	Data collection time points	Attrition
		Mean age: 50.3 ± 13.2 years 83.6% female					66% PP; 62% CER
Keogh, 2014 (336)	Australia	Women with overweight or obesity, n = 75 Mean BMI: 33.1 ± 5.8 kg/m^2 Mean age: 60.1 ± 10.5 years 100% female	n = 36, 52 weeks of CER. Research centre visits for first 8 weeks. Prescribed energy intake of 5500 kJ/day less than weight maintenance requirements.	n = 39, 1-week habitual diet alternating with 1-week energy restriction for 52 weeks. Research centre visits for first 8 weeks. The same energy restriction requirements as CER.	Participants instructed to return to their usual diet.	End of intervention: 8 weeks Follow-up: 12 months	8 weeks: 36% PP; 44% CER Follow-up: 51% PP; 53% CER
Wing, 1994 (334)	USA	Men and women with overweight and type II diabetes, n = 93 Mean BMI: 37.9 ± 6.3 kg/m^2 Mean age: 51.8 ± 9.7 years 64.5% female	n = 48, 50 weeks of moderate energy restriction. Prescribed energy intake of 4187-5024 kJ/day per day.	n = 45, severe energy restriction (1675- 2093 kJ/day) for 2 x 12-week blocks alternating with 2 x 12-week blocks of moderate energy restriction (same energy requirements as CER).	Prescribed intake increased over a 4-week period until participants consumed 4187- 5024 kJ/day (same as CER).	End of intervention: 50 weeks Follow-up: 24 months	End of intervention: 16% PP; 15% CER Follow-up: 20% PP; 23% CER

Author, year (ref)	Country	Population	Control Regimen	Planned Pause Regimen	Pause Interval	Data collection time points	Attrition
Wing & Jeffery, 2003 (324)	USA	Men and women with overweight or obesity, n = 142 Mean BMI: 33.1 ± 3.3 kg/m^2 Mean age: 42.6 ± 9.3 years 84.5% female	n = 48, 14 weeks of a behavioural weight loss programme including CER. Prescribed energy intake of 4200–6300 kJ/day depending on initial body weight.	Long break (LB), n = 47: 7 weeks of energy restriction, 6-week break, 7 weeks of energy restriction. Short break (SB), n = 47: 3 x 3-week blocks of energy restriction alternating with 3 x 2-week break, then 5 weeks of energy restriction. The same behavioural weight loss programme and energy restriction requirements as CER.	Participants instructed to stop all weight loss efforts and eat and exercise as before the programme. Participants instructed to not monitor their behaviours or weight.	End of intervention: 20 weeks Follow-up: 11 months	End of intervention: 6% LB; 23% SB; 21% CER Follow-up: 32% LB; 30% SB; 36% CER

Abbreviations: BMI: body mass index; CER: continuous energy restriction; LB: long break; PP: planned pause; SB: short break

6.4.3 Risk of Bias

A summary of the risk of bias assessment for the included studies can be found in ***Figure 6.2***. I was unable to formally test for publication bias due to the small number of included studies.

Five interventions were judged to be at high risk of bias in at least one domain (336, 351-354), with all others judged to be at unclear risk of bias in at least one domain. Four interventions were judged at unclear risk of random sequence generation bias, due to insufficient reporting (324, 334, 354). Three interventions were judged as high risk of allocation concealment bias as allocation was not concealed (351-353), and five interventions were judged as unclear risk because they did not report whether allocation was concealed or not (324, 334, 335, 354). Four studies were judged as high risk of attrition bias as <80% of participants were followed up at the end of the intervention, <60% were followed up at the final follow-up, or the percentage followed up was different across trial arms (≥20% difference) (336, 351, 353, 354).

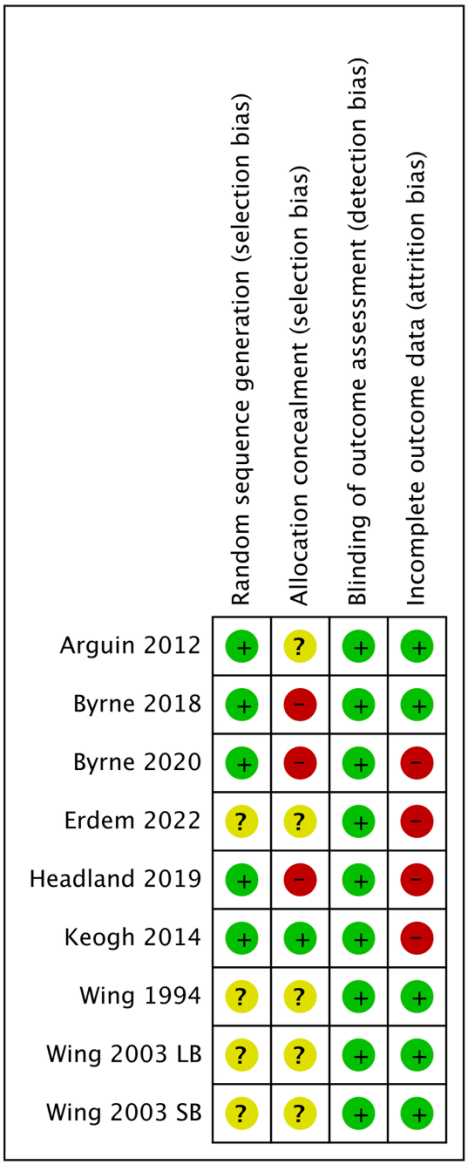

Figure 6.2: Risk of bias assessment for included studies.

Results from the GRADE assessment indicated that overall, the evidence comparing planned pauses to CER for overweight and obesity in adults was of low quality (***Table 6.2*** & ***Table 6.3***).

Table 6.2: GRADE assessment for weight change at end of active intervention

Certainty assessment							Summary of findings			
No. of arms	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other factors (publication bias)	Number of participants		Effect estimate (MD, 95% CI)	Certainty
Outcome: Weight change										
9	RCT	Serious [a]	No serious concerns	No serious concerns	Serious [b]	No serious concerns	PP: 361	CER: 325	-0.09 (-1.10,0.93)	LOW

a. Four out of eight included intervention arms present high risk of bias in at least one domain; all others have unclear risk of bias in at least one domain.
b. There was serious imprecision considering the small number of included intervention arms and wide confidence interval.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

Abbreviations: CER: continuous energy restriction; CI: Confidence interval; MD: Mean difference; PP: planned pause; RCT: randomised controlled trial.

Table 6.3: GRADE assessment for weight change at final follow-up

Certainty assessment							Summary of findings			
No. of arms	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Other factors (publication bias)	Number of participants		Effect estimate (MD, 95% CI)	Certainty
Outcome: Weight change										
7	RCT	Serious [a]	No serious concerns	No serious concerns	Serious [b]	No serious concerns	PP: 184	CER: 147	-0.72 (-2.92,1.48)	LOW

a. Three out of seven included intervention arms present high risk of bias in at least one domain; all others have unclear risk of bias in at least one domain.
b. There was serious imprecision considering the small number of included intervention arms and wide confidence interval.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

Abbreviations: CER: continuous energy restriction; CI: Confidence interval; MD: Mean difference; PP: planned pause; RCT: randomised controlled trial.

6.4.4 Weight Change

Eight studies (nine intervention arms) were included in the analysis examining weight change at the end of intervention (***Figure 6.3***), and six studies (seven intervention arms) in the analysis at final follow-up (***Figure 6.4***).

One study found a significantly greater weight loss in the planned pause intervention compared to CER at the end of the active intervention and at final-follow up (352). However, pooled results revealed no difference in weight change between the planned pause intervention group and the CER control group at the end of the intervention or at final follow-up. At the end of the active intervention mean weight change among participants in planned pause intervention group (n = 361) was -7.09 kg, compared to the CER group (n = 325) who had a weight change of -7.0 kg (mean difference: -0.09 kg, 95% CI: -1.10 to 0.93).

At the final follow-up, mean weight change among participants in the planned pause intervention group (n = 184) was -6.91 kg, compared to the CER group (n = 147) who had a weight change of -6.19 kg (mean difference: -0.72 kg, 95% CI: -2.92 to 1.48). In planned sensitivity analyses, removing studies with high risk of bias in at least one category, did not meaningfully affect the results (***Figure 6.5*** & ***Figure 6.6***).

Overall, the evidence was mostly consistent but imprecise for weight change at both time points. Statistical heterogeneity was moderately high with an I^2 of 58% and a Tau^2 of 1.22 for the end of intervention, and an I^2 of 67% and a Tau^2 of 5.89 for the final follow-up.

This was not unexpected due to the variability in the planned pause regimen between studies and this was explored further in subgroup analyses.

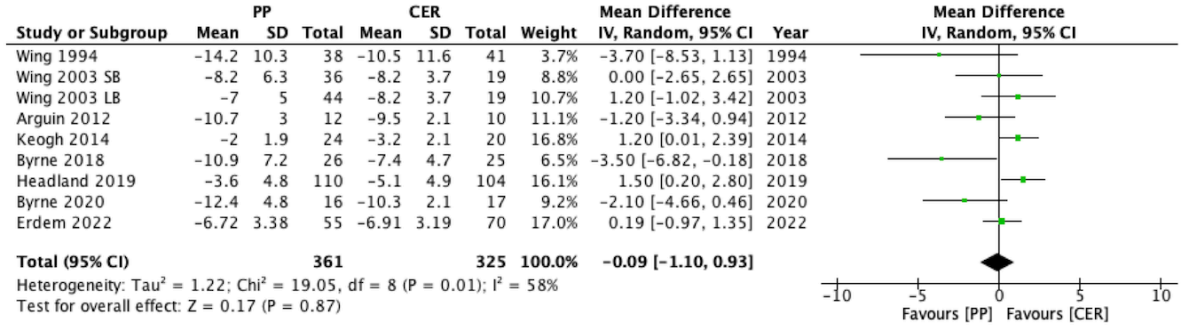

Figure 6.3: Forest plot showing mean difference in weight change (kg) from baseline to the end of the active intervention in planned pause (PP) interventions versus continuous energy restriction (CER).

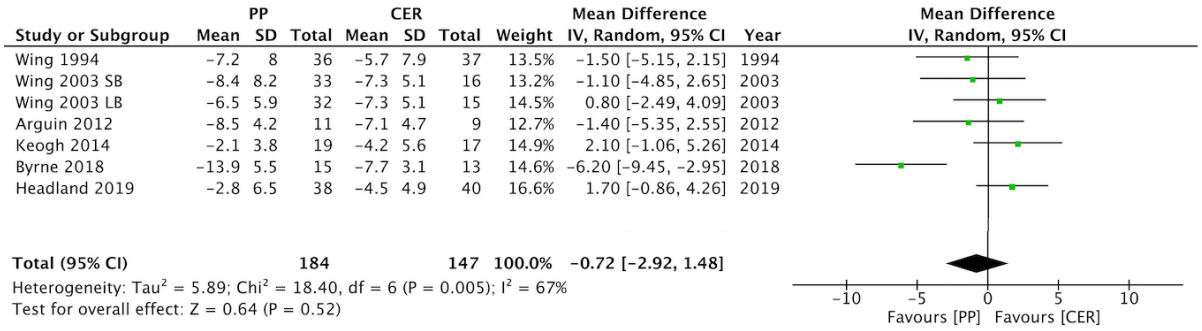

Figure 6.4: Forest plot showing mean difference in weight change (kg) from baseline to final follow-up in planned pause (PP) interventions versus continuous energy restriction (CER).

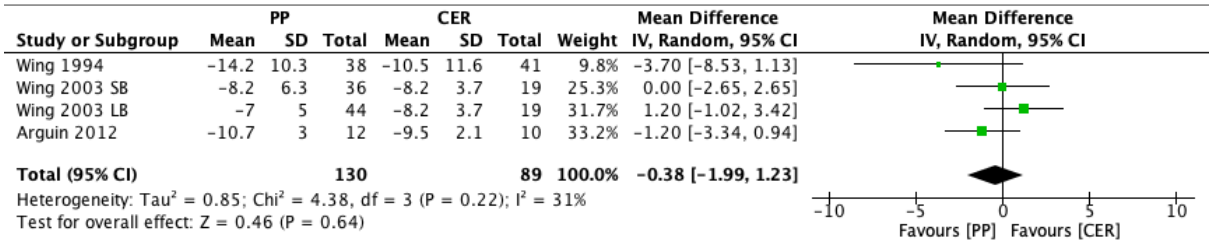

Figure 6.5: Sensitivity analysis, removing studies with high risk of bias in at least one category. Forest plot showing mean difference in weight change (kg) from baseline to the end of the active intervention in planned pause (PP) interventions versus continuous energy restriction (CER).

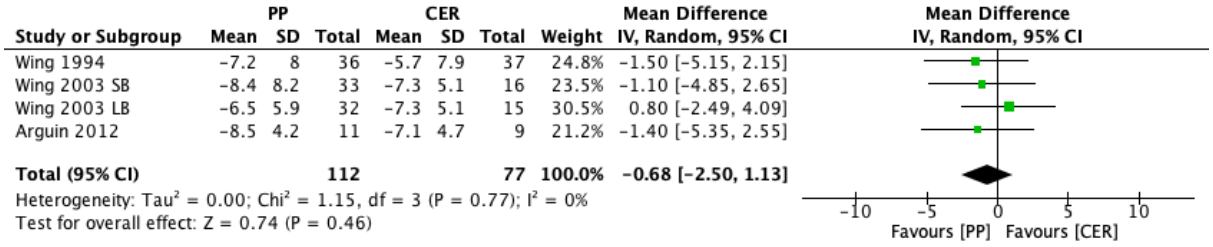

Figure 6.6: Sensitivity analysis, removing studies with high risk of bias in at least one category. Forest plot showing mean difference in weight change (kg) from baseline to final follow-up in planned pause (PP) interventions versus continuous energy restriction (CER).

6.4.5 Pause Interval Duration

Interventions with similar pause interval duration were grouped for analysis. There were significant between-group differences overall at the end of the active intervention (***Figure 6.7***), but not at final follow-up (***Figure 6.8***).

There was consistent and precise evidence from three studies that short pause intervals of one-week led to less weight loss in the planned pause intervention compared to control at the end of the active intervention (mean difference: 0.93 kg, 95% CI: 0.15 to

1.71, I^2 = 20%). Two of these studies also reported weight change at a further follow-up time where no difference in weight change was detected between the planned pause intervention or control (mean difference: 1.86 kg, 95% CI: -0.13 to 3.85, I^2 = 0%).

Based on consistent but imprecise evidence, there was no difference in weight change between the planned pause intervention and control for medium pause intervals of two weeks or longer pause intervals of >4 weeks at either the end of the active intervention or at final follow-up (n = 3 studies for each interval). Significant subgroup differences at the end of the active intervention were not maintained at final follow-up.

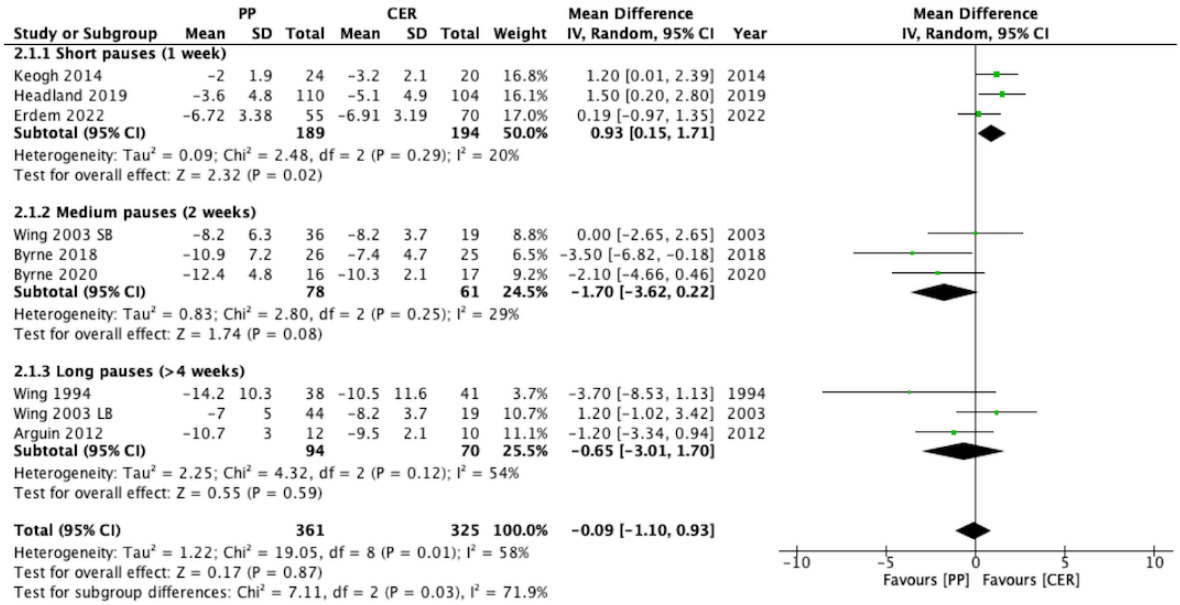

Figure 6.7 : Forest plot showing mean difference in weight change (kg) from baseline to the end of the active intervention in planned pause (PP) interventions versus continuous energy restriction (CER) by pause interval duration.

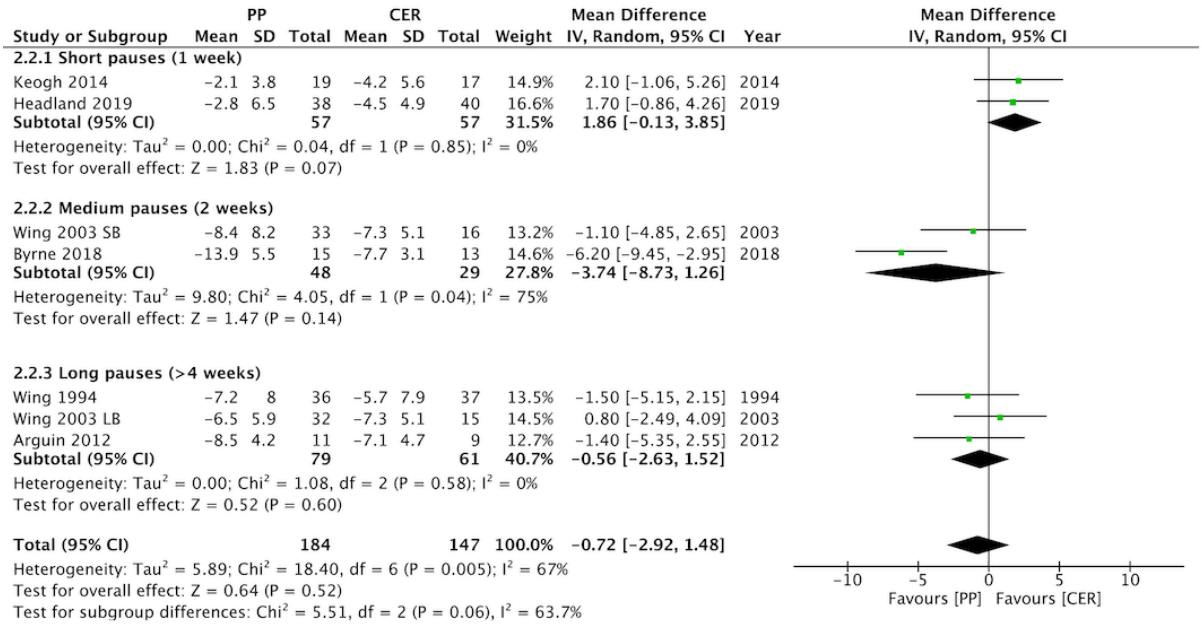

Figure 6.8 : Forest plot showing mean difference in weight change (kg) from baseline to final follow-up in planned pause (PP) interventions versus continuous energy restriction (CER) by pause interval duration.

6.4.6 Dietary Regimen in Pause Interval

Different dietary regimens used in the pause interval were grouped for analysis. There were significant between-group differences overall at the end of the active intervention (***Figure 6.9***), but not at final follow-up (***Figure 6.10***). There was consistent but imprecise evidence that intervention arms which advised patients to maintain their weight stable during the pause interval led to greater weight loss in the planned pause intervention compared to CER (mean difference: -1.95 kg, 95% CI: -3.42 to -0.48, I^2 = 0%, n = 3 studies). Two of these studies also reported weight change at a further follow-up time where no difference in weight change was detected between the planned pause intervention or control (mean difference: -3.94 kg, 95% CI: -8.63 to 0.76, I^2 = 70%).

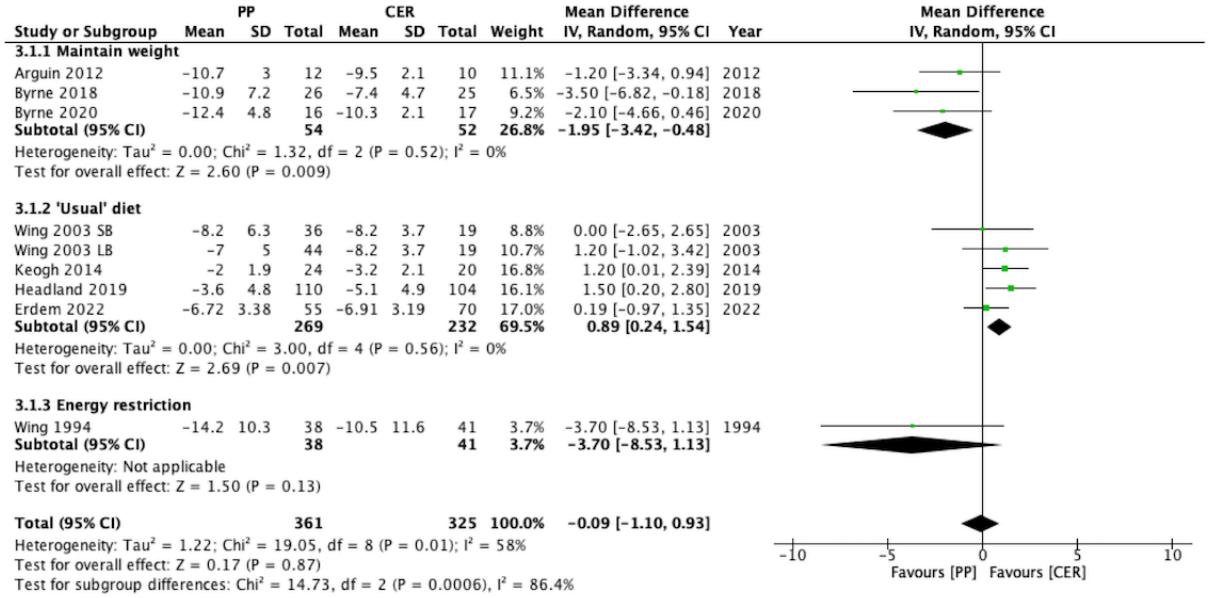

Figure 6.9 : Forest plot showing mean difference in weight change (kg) from baseline to the end of the active intervention in planned pause (PP) interventions versus continuous energy restriction (CER) by dietary regimen in pause interval.

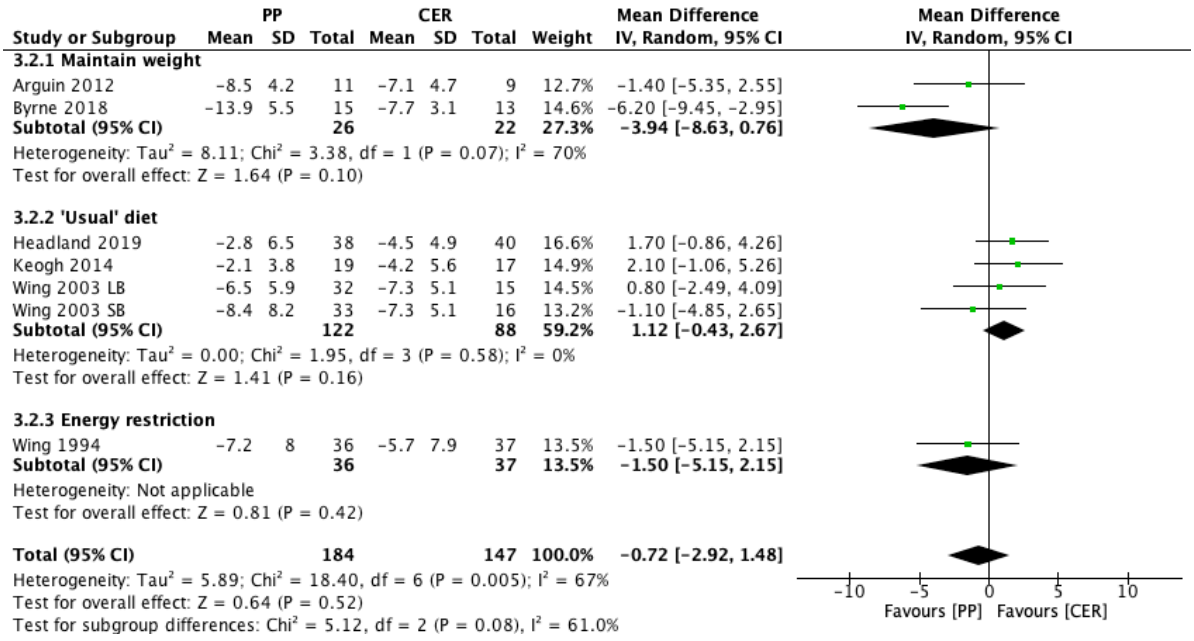

Figure 6.10 : Forest plot showing mean difference in weight change (kg) from baseline to final follow-up in planned pause (PP) interventions versus continuous energy restriction (CER) by dietary regimen in pause interval.

Based on consistent and precise evidence, arms which instructed participants to follow their 'usual' diet during the pause interval, led to less weight loss in the planned pause intervention compared to control (mean difference: 0.89 kg, 95% CI: 0.24 to 1.54, $I^2 = 0\%$, n = 5 studies). Four of these studies also reported weight change at a further follow-up time where no difference in weight change was detected between the planned pause intervention or control (mean difference: 1.12 kg, 95% CI: -0.43 to 2.67, $I^2 = 0\%$). Although there were significant differences between subgroups at the end of the active intervention, these were not maintained at the final follow-up.

No difference in weight change between the planned pause intervention and the CER control was found at either the end of the active intervention or at final follow-up for the one study arm where participants followed a moderate energy restriction during the pause interval.

6.4.7 Attrition

Nine intervention arms reported the proportion of participants that dropped out at the end of the active intervention and eight intervention arms at a further follow-up. Greater attrition in the planned pause group compared to CER was found in one study at the end of the active intervention (354), and in one study at the final follow-up (353). However overall, the pooled risk ratio showed no difference in attrition rate in the planned pause intervention arms versus the CER arms at the end of the active intervention (risk ratio: 1.20, 95% CI: 0.82 to 1.75, $I^2 = 47\%$; ***Figure 6.11***) or at final follow-up (risk ratio: 1.04, 95% CI: 0.89 to 1.22, $I^2 = 0\%$; ***Figure 6.12***).

Overall, the evidence was mostly consistent but imprecise for attrition at both time points. In subgroup analyses, there were also no significant between-group differences in attrition rate when studies were categorised by pause duration or the dietary regimen used in the pause interval (***Appendix 6.2***).

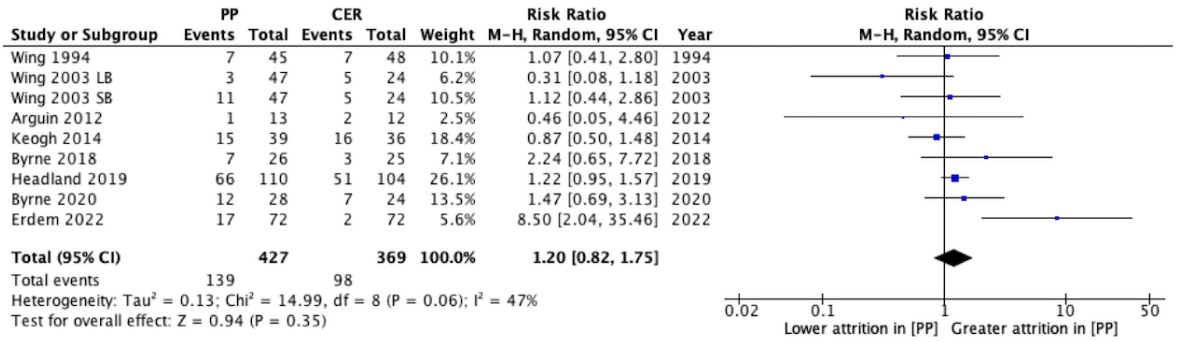

Figure 6.11 : Forest plot showing mean risk ratio of attrition at the end of the active intervention in planned pause (PP) interventions versus continuous energy restriction (CER). A risk ratio > 1 indicates greater attrition in the PP arm compared to CER, and a risk ratio < 1 indicates lower attrition in the PP arm compared to CER.

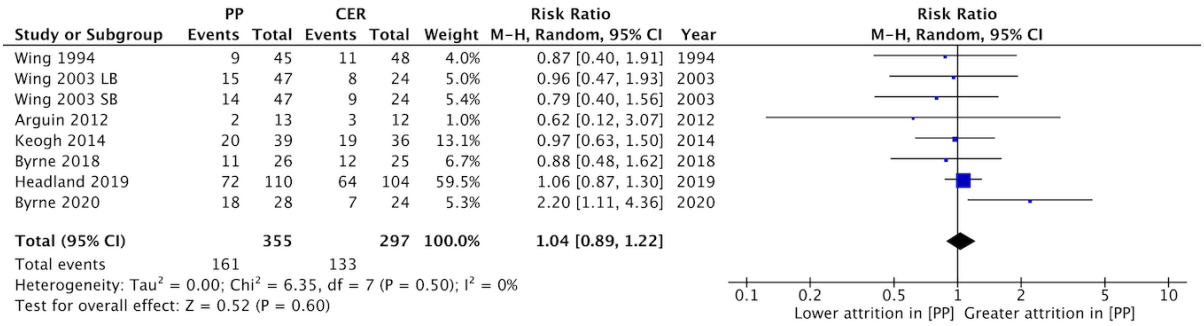

Figure 6.12 : Forest plot showing mean risk ratio of attrition at the final follow-up in planned pause (PP) interventions versus continuous energy restriction (CER). A risk ratio > 1 indicates greater attrition in the PP arm compared to CER, and a risk ratio < 1 indicates lower attrition in the PP arm compared to CER.

6.5 Discussion

6.5.1 Principal Results

This systematic review and meta-analysis illustrated that weight loss programmes incorporating planned pauses led to clinically significant weight loss, but outcomes were not significantly different from CER interventions. There was also no evidence that planned pauses reduced attrition. There was some evidence that when participants were guided to maintain their weight stable during the pause intervals weight loss was improved. Short pauses (< one-week) were less effective than both continuous dieting and longer pauses during the active intervention, but this difference was not observed at final follow-up.

6.5.2 Comparison with Prior Work

Most previous systematic reviews and meta-analyses have reported comparable weight losses for IER compared to CER regimens (326-331). The results presented here are broadly consistent with previous conclusions, despite differences in the definition of the IER intervention. Here, I defined a planned pause as intermittent intervals of no less than one-week long, where the pause interval could not be longer than the preceding intervention interval. This choice was derived from the aim of studying interventions that simulated as much as possible a planned pause or a break in a weight loss programme. Although this definition was chosen to be specifically different than intermittent dieting within a one-week period (e.g., the 5:2 diet) the overall conclusions are largely similar (319, 327, 328). Another systematic review investigated similar intermittent intervals of ≥7 days but

operationalised this differently - with no limitations on the energy restriction period relative to the pause period - and also found comparable weight loss to CER (355). Absolute mean weight losses in both the planned pause and CER groups were greater than 5 kg at the end of the active intervention and at final follow-up, suggesting that both interventions could be effective strategies for weight loss.

Given the scope of the review, there was a large degree of variability in the planned pause regimen in the included studies, reflected by high statistical heterogeneity observed in the meta-analyses. To address this, I conducted subgroup analyses to investigate potential explanations for this variation in weight losses. Short pauses of one-week resulted in less weight loss compared to CER and longer pauses at the end of the intervention. This possibly indicates that short intervals may not provide sufficient time to recharge motivation or improve adherence. At the end of the active intervention, interventions guiding participants to maintain their weight stable during the pause interval led to greater weight loss, whilst interventions advising participants to follow their 'usual' diet in the pause interval resulted in lower weight loss, compared to CER. These findings are in accord with a previous review, which suggested that the key differentiator between studies that reported greater weight losses in IER interventions compared to CER was the nature of the weight maintenance phase (339).

However, subgroup differences were small, only apparent at the end of the active intervention, and not maintained over longer periods of time. One study reported a much larger mean weight loss of -13.9 kg in the planned pause group compared to -7.7 kg in the CER group at their final follow-up time point (352), but this study supplied all food to

participants and it is uncertain whether the same results could be achieved in routine practice without food provision. Overall, there was little evidence to suggest that planned pauses provide a more effective long-term strategy for weight control compared to CER.

It was hypothesised that planned pauses could be a strategy to reduce attrition and achieve longer-term engagement, thus improving weight loss. However, attrition was comparable between planned pause interventions and CER at each time point. These results are in agreement with other reviews comparing CER and IER interventions (326, 330), as well as other weight loss programmes which show attrition rates of 30-60% (326, 356, 357). Given that attrition could be an indicator of non-adherence to an intervention, these results provide no clear evidence that planned pauses are easier to adhere to than CER. However, there was also no clear indication that planned pauses were inferior, suggesting that they may still be an effective option for some people.

Whilst I did not formally assess adherence in the current review, Wing et al. reported that participants followed the prescribed breaks (either multiple 2-week breaks or one longer 6-week break) with interruption to self-monitoring, dietary adherence, and self-weighing. Importantly, they then quickly resumed their adherence to these behaviours after the prescribed breaks ended (324). This suggests that planned pauses may represent a manageable disruption to a weight loss attempt, allowing individuals to successfully return to the programme without evidence of hindering overall weight loss progress.

6.5.3 STRENGTHS & LIMITATIONS

This review has several strengths. The scope of this review differs from previous reviews investigating the effect of shorter periods of IER, thus providing novel insights into the effectiveness of implementing planned pauses into a weight loss programme. To minimise bias and confounding, this review included only randomised controlled trials and had no restrictions on year, language, or intervention duration. I only included trials that compared planned pauses to a fixed dietary regimen of CER, which allowed the estimation of effect sizes through the inclusion of meta-analyses. I was also able to conduct exploratory subgroup analyses to assess whether the planned pause regimen impacted the effectiveness of the intervention.

However, this review also has some limitations. As a specific definition of planned pauses was used, only nine intervention arms met the inclusion criteria, each with moderate sample sizes and subsequent small numbers in each subgroup meaning one group couldn't be pooled for meta-analysis. Additional studies identified during the systematic review search, included pause intervals which were longer than the preceding intervention interval, these were not considered a planned pause by my definition and therefore excluded. Although I attempted to group similar planned pause dietary regimens in the subgroup analyses, pooled interventions were still highly variable in prescribed energy restriction, intervention duration, and timing of the intermittent periods, reflected by the heterogeneity within some subgroups.

Inadequate reporting prevented clear assessment of the quality of included studies, particularly random sequence generation and allocation concealment methods,

meaning the possibility of selection bias cannot be ruled out. Studies in the review also had considerable attrition and only two out of the nine intervention arms reported intention-to-treat analyses at the end of the active intervention, and one at the final follow-up. Due to the relatively small number of studies, I was unable to formally test for publication bias. Finally, the majority of participants included in this review were female, limiting the generalisability of the findings to males.

6.5.4 Implications & Further Research

Although planned pauses do not appear to offer a universal benefit, they also do not seem to have an adverse effect on either weight loss or retention. This review reported pooled average effect sizes, but considerable variability was observed even within individual studies. Taken together, these findings suggest that planned pauses may be more effective for some individuals, although such differences could not be detected in this analysis. Given the variation in preferences and responses to dietary strategies, offering planned pauses as an option may help prolong engagement for those who benefit from more flexible approaches. This may be particularly useful during common high-risk periods such as holidays, special occasions, or in response to treatment fatigue. Future research should aim to identify which individuals are most likely to benefit from structured pauses. Trials examining individual-level characteristics, such as baseline motivation, self-regulation, or previous dieting history, may help clarify who is best suited to this approach.

It is also important to consider how dietary guidance is delivered during pause intervals. There was some indication that advising participants to maintain their weight during the

pause interval improved weight loss outcomes. Future studies should investigate how different types of dietary guidance during these periods influence adherence and effectiveness.

Pause duration also appears to be an important factor. Evidence from this review suggests that longer pauses (greater than one week) were more promising, while shorter pauses appeared less effective. However, extended pauses may carry a risk of reduced motivation or disengagement, potentially hindering progress. This suggest that there may be an optimal pause duration, which is long enough to restore motivation, but not so long that it disrupts behavioural momentum. Future work could aim to identify this optimal length and explore how best to structure pause timing and guidance to support long-term adherence.

The studies included in this review were conducted in controlled research settings, with a median follow-up of 52 weeks. It remains unclear whether planned pauses would be more beneficial in self-directed or pragmatic settings, where dietary fatigue and motivational decline may be more common. In these contexts, planned pauses may offer greater flexibility, supporting sustained adherence and helping individuals to maintain active weight management over a longer timeframe. This could be especially relevant when managing obesity as a chronic, relapsing condition. However, longer-term and real-world trials are needed to draw more definitive conclusions.

6.5.5 Conclusions

For people living with overweight or obesity, planned pauses were found to be consistently no more effective than CER to achieve weight loss, and there was also no evidence that they were beneficial for attrition. Planned pauses could be incorporated into weight loss programmes without reducing effectiveness. There is some indication that longer pauses and advice to maintain weight stable during the pause may improve the effectiveness of the planned pause.

Chapter 7 : Discussion

7.1 SUMMARY

This final chapter provides an overview of the key findings and contributions from the studies presented in this thesis and situates them within the broader context of the literature. I begin by highlighting the main strengths of this DPhil project, notably its multi-method design, theory-informed approach, and focus on conducting research in a real-world setting. I then outline the general limitations, including the low follow-up rates and the reliance on self-reported data. Key considerations and challenges encountered during the research are also discussed, with particular attention to the industry collaboration with Second Nature, which offered significant advantages but also introduced practical constraints. In the final section, I discuss the clinical and research implications of this work and outline the priority areas for future research.

7.2 FINDINGS AND CONTRIBUTIONS OF THIS THESIS

In the introduction of this thesis (***Chapter 1***), I presented evidence that behavioural support programmes are an effective treatment option for risk reduction in people living with overweight or obesity, but the high costs and labour-intensive nature of such programmes can make them unsustainable for implementation at the population level. There is a clear need for effective, accessible weight loss interventions that can be delivered at scale. I introduced digitally delivered programmes as a promising solution, potentially offering convenient, cost-effective, and scalable alternatives to traditional

approaches. However, their effectiveness is often hindered by difficulties in sustaining user engagement and high attrition rates. Designing interventions that maintain participants' engagement over time is therefore fundamental to maximising the effectiveness of digital programmes. In this thesis, I aimed to identify and test intervention components that could promote sustained participant engagement and enhanced weight loss. My collaboration with the commercial partner, Second Nature, provided valuable industry insights into the practical design and implementation of digital interventions. This partnership enabled me to conduct experiments and empirically test intervention strategies within real-world settings. Collectively, the research presented in this thesis contributes to a growing evidence base on the development and evaluation of effective interventions and, when paired with the scalability of digital interventions, this has the potential to provide considerable public health impact.

The first study was conducted to allow me to familiarise myself with the Second Nature data and programme by conducting an observational prospective longitudinal analysis using their existing programme data (***Chapter 2***). I found that the Second Nature programme was broadly successful for weight loss irrespective of demographic characteristics but, as is common in digital programmes, data availability was limited, participant engagement was relatively low, and attrition rates were high. My analysis specifically focused on one BCT, goal setting, to understand its association with weight loss, engagement, and attrition. I explored whether three aspects of goals - overall goal preference, percentage weight loss goal, and primary motivation for weight loss - were associated with both weight loss outcomes and programme dropout rates over a 24-

week period. The results showed that setting weight loss goals of >10% and being motivated by health or fitness reasons were associated with greater weight loss and lower likelihood of drop out. Engagement with programme components decreased over time and higher engagement was a significant independent predictor of weight loss but did not mediate the association between goals and weight loss. These findings emphasised the importance of sustained engagement and suggested that encouraging individuals to set larger goals may support better outcomes and retention. However, due to the observational nature of the study, further trials would be needed to confirm these results.

Alongside this, an unexpected opportunity arose during my DPhil that enabled me to develop and evaluate a fully automated digital intervention, which provided a useful point of comparison with the Second Nature programme which includes human-based coaching (***Chapter 3***). In this project, I developed a purpose-built mobile application grounded in self-regulation theory (ARTEMIS: Adults Regulating Their weight Everyday with Mobile Internet Support), building on a previous pilot study (209). The app was designed to be fully self-managed, requiring no human support. It was evaluated using a two-arm randomised controlled trial with 1,607 participants to assess the effectiveness of this intervention compared to a control, where participants were given simple advice to lose weight. The results showed that participants randomised to the intervention group lost an average of 1.85 kg more than controls at 26 weeks and were more than twice as likely to achieve ≥5% weight loss. Additionally, participants in the intervention group reported reductions in symptoms associated with disordered eating, indicating that the app is a safe and effective self-management tool. The findings offer evidence for

the viability of a self-managed digital intervention that requires no in-person coaching or professional input. The intervention's broad reach and minimal resource demands suggest it could have meaningful population-level impact if offered at scale. Whilst the sample was skewed towards more affluent and White participants, the absence of subgroup differences in outcomes is encouraging, as it suggests the intervention may not exacerbate existing disparities. However, these analyses were likely underpowered due to the low representation of minority ethnic and socioeconomically disadvantaged groups, and the findings should therefore be interpreted with caution.

The modest engagement levels and effect sizes from a self-managed intervention like ARTEMIS prompted me to explore whether adding support components could improve outcomes. In ***Chapter 4***, I outlined the preparatory work I undertook to develop candidate components that were hypothesised to increase engagement and, in turn, weight loss in the Second Nature programme. As part of my iCASE studentship, I completed a 3-month internship with Second Nature, working in the product and user research team. I conducted interviews with current programme participants to better understand their experiences and identify small changes that might improve effectiveness. While none of these changes alone warranted a standalone trial, they each had potential to make a small difference. Rather than rely on Second Nature's usual iterative approach to testing, I took a more research-led route, using the MOST framework. Drawing on insights from user interviews and existing literature, I developed four candidate components: health coach introductory video call, coaching drop-in webchat sessions, goal setting statements, and food diary review plus feedback. These were grounded in the supportive accountability model, which suggests that added

human support can improve adherence to digital interventions by fostering a sense of accountability to another person.

These components were then tested systematically using an optimisation trial. ***Chapter 5*** outlines the results of the trial which used a 2^4 factorial design, allowing me to test each component individually and in combination, as adjuncts to the Second Nature programme. The results showed that the health coach intro video call was the only component that had a significant positive effect on weight loss at 24 weeks, resulting in an average additional loss of 1.0 kg compared to those who did not receive the call. In contrast, the food diary review plus feedback component had significant negative effects on weight loss at both 16- and 24- weeks and was associated with lower engagement. Engagement also tended to be lower in conditions that included multiple components, particularly when the food diary was present. Although no component or combination met the pre-defined optimisation objective of ≥ 0.75 kg additional weight loss at 16 weeks, the findings offer insight to inform future intervention development by identifying useful components – like the health coach intro call - that could be refined and tested in subsequent studies. It also reinforces the value of empirically testing components before implementing them in a commercial programme. Overall, brief, early human contact can meaningfully enhance the effectiveness of digital interventions, while effortful components that lack adequate support may reduce engagement.

Although this thesis set out to identify strategies to improve engagement in digital programmes, maintaining consistent engagement and retention remained a recurring challenge throughout Chapters 2-5. This prompted me to explore a novel approach, ‘planned pauses’, as a potential strategy to improve retention. The rationale was that

scheduled breaks or pauses in a weight loss programme might offer greater flexibility, improve dietary adherence, and ultimately enable individuals to sustain active weight management over a longer period. I conducted a systematic review and meta-analysis comparing the effectiveness and attrition rates of continuous energy restriction versus planned pauses, defined as intermittent intervals of at least one week within a weight loss programme (***Chapter 6***). The results showed that planned pauses produced weight loss outcomes comparable to continuous energy restriction, but with no clear evidence that they improved retention. Subgroup analyses suggested that longer pauses with structured dietary guidance were more promising, while shorter pauses appeared less effective. Taken together, these findings suggest that in a controlled research setting, planned pauses were not more effective than continuous dieting but importantly, they were no less effective either. In a more pragmatic, self-directed context with longer follow-up, this approach could promote sustained engagement by allowing greater flexibility, reducing burnout, and helping individuals maintain dieting efforts for longer.

7.3 Strengths & Limitations

In the following section, I will discuss the general strengths and limitations of the work presented in this thesis. Strengths and limitations of individual studies were discussed in their respective chapters.

7.3.1 Strengths

This thesis took a multimethodological approach, including a systematic review, observational analysis, and the rigorous evaluation of digital interventions through two trials using different experimental designs. Managing both a factorial optimisation trial

and a definitive randomised controlled trial within the timeframe of a DPhil was a significant undertaking and reflects the scale and ambition of this work. Both trials were delivered in real-world, fully remote settings, which brought their own set of practical and methodological challenges (discussed below). However, including these two trials strengthened the rigour and external validity of the evidence generated in this thesis.

A notable strength of this work is the theory-informed approach. There is an abundance of mobile applications available on the market claiming to promote weight loss, but many lack a solid theoretical grounding or rigorous evaluation of their effectiveness beyond anecdotal reports or observational studies (202, 203). Several researchers have called for intervention development to be more theory-based (236, 252). In this thesis, I consistently applied behavioural science theories and principles to inform the development and refinement of digital interventions. For example, the ARTEMIS intervention (***Chapter 3***) was grounded in self-regulation theory, and the intervention components developed during the MOST preparation phase (***Chapter 4***) were guided by the supportive accountability model. The benefits of incorporating theory into the intervention development process extend beyond potentially increasing intervention effectiveness. Theory can also help explain why an intervention does or does not work during subsequent evaluations and provides a useful framework for exploring the determinants of behaviour. This was evident in the ARTEMIS study (***Chapter 3***), where the process evaluation demonstrated that guiding participants through the self-regulation process and engagement with each element of the self-regulation process was positively associated with weight loss, providing further evidence to support the efficacy of self-regulation theory in promoting weight loss.

Rapid recruitment of large samples was another strength of this thesis. Industry partnerships and social media advertising enabled efficient, wide-reaching recruitment. In some instances, recruitment was also strategically timed to coincide with the January peak in interest in weight loss programmes, which helped to maximise sign-up. These recruitment strategies made it possible to reach large numbers of participants very efficiently, something that is often a major barrier in research. Without these partnerships, it would have taken significantly more time and resource to recruit a similar sample, making it harder to run large-scale studies within a reasonable timeframe.

This partnership also supported the development and delivery of more robust interventions. In the context of mobile health development, it has been argued that rigorous research requires partnerships that integrate commercial expertise with behaviour change science (154). This thesis exemplifies this principle in practice, enabling co-development of interventions that were both technically evidence-based and feasible for implementation in a real-world setting.

The real-world setting of this thesis represents both a strength and a limitation. A key aim was to collect data through mobile health technologies and evaluate interventions under naturalistic environments, to better reflect how people use digital weight loss programmes in an everyday environment. Many studies on digital weight loss interventions are carried out in highly controlled research environments, which can limit their relevance to real-world implementation. In contrast, the approach taken here enhanced the ecological validity of the findings providing a more accurate sense of actual user behaviour and how these interventions might work when implemented at scale.

7.3.2 LIMITATIONS

Conducting research in real-world settings also presented several limitations. While the remote nature of data collection offered convenience for participants and enabled the inclusion of a large sample, a key challenge was the considerable amount of missing data due to reliance on self-report. Low follow-up rates are common in digital intervention trials ranging from 9–86% across digital health studies (16), and 9–89% specifically in digital weight loss interventions (234). Here, low data availability complicated both the analysis and interpretation of results. There is also evidence that individuals are less likely to continue weighing themselves once their weight begins to increase, which may introduce self-selection bias into who chooses to submit weight readings and could lead to an overestimation of treatment effects (196). To address these challenges, I used mixed models for repeated measures, assuming data were missing at random, and conducted sensitivity analyses under alternative assumptions to test the robustness of the findings across all studies. While these approaches helped to strengthen confidence in the results, a more complete dataset would have further enhanced their reliability. In hindsight, introducing higher barriers to entry, such as requiring more onboarding forms or delaying access to the app, may have helped ensure that participants enrolling in the trials were more motivated, potentially resulting in more sustained engagement over time. However, this may have created bias in recruitment.

The reliance on self-reported weight data, with no external validation, meant there is a risk that the outcome measures were not accurately reported. This risk was partially mitigated in the ARTEMIS study by asking participants to upload a photograph of their scales displaying their weight at the time of reporting. In the Second Nature studies, any

implausible weight readings were checked against weight entries recorded directly in the app, allowing for some cross-verification. These checks helped to improve confidence in the data but given that self-reporting is still subject to error or misreporting, I cannot rule out that some of the data may have been inaccurate. Importantly, both were randomised controlled trials, which helps mitigate this limitation, as any reporting errors are likely to have been balanced across arms.

Another limitation across the studies was the demographic profile of the samples, which were predominantly white, middle-aged, and more affluent women. Although this aligns with the typical users of digital weight loss programmes, it doesn't fully reflect the broader population living with obesity and so limits the generalisability of these findings to other populations (124, 199). The studies conducted with Second Nature included only paying users. These were individuals who could afford the programme and were likely to be more self-motivated to lose weight. Payment may have contributed to higher levels of commitment and engagement than would be expected in non-paying populations. As such, it is uncertain how well these findings apply to groups who face financial constraints or structural barriers, which can affect their ability to engage with digital health interventions.

Although digital interventions offer advantages in scalability and reach, they also risk exacerbating existing health inequalities. Access to digital technologies and digital literacy levels vary considerably, particularly across socioeconomically disadvantaged groups. This is especially important given that obesity prevalence is higher among people from lower socioeconomic backgrounds, who are also less likely to access weight loss support in the first place (358, 359). Although I aimed to explore subgroup differences in

my studies, the small proportion of participants from minority ethnic or disadvantaged backgrounds meant these analyses were likely underpowered to detect differences. As such, it's not possible to say whether these interventions would work equally well across more diverse groups. If effects do vary by group, this could further compound existing inequalities, so ensuring equitable access and effectiveness remains a key priority for future research.

7.4 Key Reflections

This section outlines some of the practical challenges encountered during this thesis that were not included in the chapters or associated publications. While not central to the primary findings, these experiences offer important context on the logistical and operational aspects of the work, as well as personal reflections on the research process during my DPhil.

The iCASE studentship provided a unique opportunity to collaborate with a commercial partner, Second Nature, allowing me to work directly at the interface between academic research and industry practice. I began leveraging this collaboration from the outset of my DPhil, during my goal setting project (***Chapter 2***). This collaboration offered several advantages. I had access to their large pre-existing datasets, which allowed me to conduct larger and more impactful studies than would have been feasible if working independently on my DPhil. These datasets included thousands of users across the UK, enabling analyses with high statistical power and enhancing the generalisability of findings to typical users of a commercial weight loss programme. However, the reliance on data routinely collected by Second Nature limited the scope of my research

questions. I was constrained by the specific items included in their health questionnaire, which was designed for user onboarding rather than research purposes, and meant I had to adapt my research questions to fit what was available. There were also several practical and logistical barriers. Data sharing agreements meant that it took much longer than expected to receive data. In addition, the way the data was stored at Second Nature required considerable work to accurately define the variables of interest, with a substantial amount of time spent on data cleaning and validation before analysis could begin. Although time-consuming, these steps were essential and gave me experience in managing complex real-world datasets and collaborating with non-academic teams.

A related challenge was the evolving nature of the Second Nature platform over the course of my DPhil. By the time I carried out the optimisation trial (***Chapter 5***), the platform had changed considerably from when I first analysed data from the goal-setting project (***Chapter 2***). New features had been introduced, the programme content had evolved, and the onboarding and payment structures had changed. These changes made it difficult to maintain consistency across projects and meant I had to adapt my study procedures between studies.

A key challenge throughout was defining and measuring engagement in a way that was both meaningful and practical. The digital health literature is inconsistent in how engagement is conceptualised, making it difficult to compare findings across studies (131, 132). This issue was particularly evident when working with Second Nature's dataset, as identifying which behaviours reflected 'meaningful' engagement was complex. During the development of the goal-setting paper, I invested significant time in establishing a definition of engagement that focused on meaningful use of the app's

three core features. This approach avoided metrics like number of logins or home screen views, which are often reported in other studies but are unlikely to reflect engagement that promotes behaviour change (131, 132). While this definition ensured relevance to the context of the Second Nature programme, it may not have been optimal and limits comparability with studies using more standardised engagement metrics.

As my DPhil progressed, balancing academic research priorities with the practical constraints of a commercial setting became increasingly important. This was particularly evident during the development of the optimisation trial (***Chapter 4***). Selecting candidate intervention components using the MOST framework was not straightforward. Decisions had to reflect both theoretical rationale and what was operationally feasible and commercially interesting for Second Nature. These considerations are not well accounted for within the MOST framework, meaning certain processes were impractical to implement in a commercial setting. While MOST offers a structured approach to intervention development and evaluation, one that many commercial partners may lack, its rigidity and resource demands limited its application in this context. The three-stage framework assumes a stable context in which interventions can be refined over long timelines. In reality, products evolve quickly, teams iterate based on live data, and new features are often deployed within weeks. By the time all phases of MOST are completed, the programme or technology itself may have evolved significantly, making the 'optimised' intervention less relevant or already outdated.

Throughout this DPhil, I gained experience in both project and trial management. Conducting two trials during this period was not only a significant undertaking within the

timeframe, but also provided hands-on experience managing teams, timelines, and operational challenges. The ARTEMIS trial (***Chapter 3***) provided experience of managing a definitive RCT within a traditional academic setting, supported by a dedicated trials team. I used social media recruitment strategies, which allowed me to rapidly recruit a large sample, and all follow-up procedures were conducted entirely remotely. This demonstrated that remote trials are feasible and capable of achieving large-scale reach within a short timeframe. However, the low barrier to entry may have contributed to lower follow-up rates, as some participants likely enrolled with limited commitment to the trial. Despite the dedicated trials support from the Clinical Trials Unit, I still faced challenges. A REDCap system outage disrupted access for all participants shortly after our first follow-up opened, and due to the speed of recruitment, this affected most of the sample and significantly impacted follow-up rates. Due to difficulties with follow-up, incentives were raised twice, and a considerable amount of effort went into follow-up calls from the team. Ultimately, this led the trial steering committee to make the decision to cut the trial short to conserve effort for relatively limited additional data.

In contrast, the optimisation trial (***Chapter 5***) was embedded within a commercial setting, which brought a different set of challenges and required a high level of preparation and self-direction. Without access to dedicated trial management software, I developed all trial documentation myself, including data monitoring plans, intervention materials, and training resources. I also trained and managed a small research team of research assistants and health coaches. The collaboration with Second Nature once again made it possible to deliver something I wouldn't have been able to otherwise, as it

provided access to an established digital intervention, a trained team of health coaches, and a large, readily available participant pool.

Embedding the trial within a commercial structure also introduced limitations. Trial processes had to align with existing company systems and workflows. This sometimes restricted research autonomy and created challenges in setting up certain processes such as participant identification, group allocation, and randomisation. The way groups are assigned at Second Nature necessitated a cluster design trial, which reduced statistical power and wouldn't have been my choice in a more controlled research setting. Additional challenges included providing adequate training for team members who were unfamiliar with the trial design, managing competing priorities within a company running multiple concurrent projects, and operating with limited technical support. Notably, I was not allocated any engineering resource from Second Nature, which meant adapting the intervention components to delivery formats that did not require modifications to the app. In retrospect, a pilot trial could have helped to surface some of these operational issues earlier, as typically recommended during the preparation phase of the MOST framework. However, given the timing of my DPhil and the opportunity to partner with an industry collaborator, this felt like a valuable opportunity to explore whether a factorial optimisation trial could be successfully applied in a real-world commercial context.

Taken together, these two trials provided complementary experiences that gave me a well-rounded understanding of what it takes to design and deliver digital trials in both academic and commercial environments, and the practical trade-offs involved in each.

More broadly, the question of how we define programme 'success' remains a challenge and was a recurring consideration throughout this thesis. In this work, weight was used as the primary outcome measure. While this is standard practice in weight loss interventions and offers a clear, objective metric, it does not fully reflect the broader benefits that behavioural interventions may produce. Other studies increasingly collect measures of metabolic health, psychological well-being, behaviour change, and quality of life. These reflect the recognition that meaningful health improvements can occur even without substantial weight loss (40, 360). Although I was limited in what I could collect due to the constraints of working with Second Nature's routinely collected data, broader outcome measurement will be important for future research to evaluate the overall impact of digital interventions.

Finally, this research was conducted with an awareness of the wider commercial landscape in digital health. From the outset, I was conscious that any intervention developed through this work would need to be feasible for real-world implementation, and I actively sought opportunities to gain experience in industry-led environments. During my DPhil, I undertook internships with Second Nature, Google, and Stanford University, each offering a different perspective on how research operates in more commercially driven settings. These experiences reinforced the importance of academic research keeping pace with evolving technologies, shifting user expectations, and the speed at which industry iterates. Whilst at Second Nature, for example, the licensing of weight loss medications in the UK required the company to rapidly pivot its projects. This was a situation that required quick decision-making and flexibility that academic frameworks often struggle to accommodate. During my time at Google, generative

artificial intelligence (Gen-AI) became a major focus, and I saw how quickly priorities and resources were redirected in response. Both experiences highlighted how responsive industry can be to emerging technologies, often reshaping products and strategies on timelines that are difficult to align with traditional academic research.

7.5 Implications of this Research and Future Directions

7.5.1 Clinical Implications

The findings from this thesis support the role of digital weight loss interventions in managing overweight and obesity at scale. As health systems face growing pressures and resource constraints, there is a need for scalable, cost-effective solutions to complement traditional care. Theory-driven, evidence-based digital interventions offer a promising route to extend behavioural support to wider populations. However, a one-size-fits-all approach is unlikely to meet the needs of all users. Some individuals may prefer fully self-managed interventions, while others may benefit from more structured guidance. A blended approach, which offers interventions tailored to user preference, readiness, or clinical risk, may help maximise both effectiveness and resource efficiency.

ARTEMIS demonstrated that a fully automated intervention can produce clinically meaningful weight loss without requiring human support, highlighting its potential as a low-cost, accessible option. This is particularly relevant in primary care and community settings, where time and professional input are limited. It offers an opportunity for real-world implementation at scale, and I have been in discussions with the Digital Prevention

Strategy team at the Department of Health and Social Care, who have expressed interest in ARTEMIS as a scalable treatment option.

However, ARTEMIS is likely to attract individuals who were relatively motivated and digitally enabled, with the sample skewed towards more affluent, White participants. While ARTEMIS may reduce access barriers for some, it did not reach underserved populations and is unlikely in its current form to reduce health inequalities. Its potential for promoting equitable access would depend on targeted implementation strategies to engage and support more diverse populations.

ARTEMIS also requires a high level of individual agency which may not be suitable for everyone, but it could serve as a low-burden first step in a stepped-care model, linking with more intensive or personalised support for those who need it. For individuals less likely to succeed with a self-managed approach, early, low-intensity human support may enhance effectiveness. For example, the health coach introductory call evaluated in the factorial trial produced a meaningful improvement in weight loss and helped mitigate negative effects from other components. These findings suggest that even minimal contact, when delivered early and purposefully, can significantly improve outcomes.

In contrast, more burdensome components, such as personalised feedback on food diaries, were associated with poorer outcomes, and adding multiple features simultaneously reduced programme effectiveness. This highlights the importance of evaluating both the effectiveness and burden of individual components before implementation. Future digital programmes should integrate systematic evaluation

methods to ensure that added features are evidence-based, acceptable, and appropriate for their users.

Findings from ***Chapter 6*** suggest that incorporating greater flexibility, such as planned pauses within a programme, may help support long-term adherence, particularly in more intensive interventions. Although planned pauses did not clearly improve outcomes in controlled trials, they produced comparable weight loss and retention to continuous dieting. In more pragmatic, self-directed settings, this approach could promote sustained engagement by allowing greater flexibility, reducing burnout, and helping individuals maintain dieting efforts over longer periods.

Observational findings from this thesis also suggest that encouraging users to set more ambitious weight loss goals (e.g. >10% initial body weight) and to identify intrinsic motivations such as health or fitness may improve both retention and outcomes. These strategies are straightforward to implement and could be incorporated early in intervention delivery.

Importantly, digital interventions should not be seen as replacements for traditional care, but as complementary tools to enhance reach and continuity of support. This is particularly relevant in the context of newly licensed pharmacological treatments for obesity in the UK. While these medications offer important clinical benefits, sustained weight loss and long-term behaviour change still require ongoing behavioural support. Digital tools could fill this gap by providing structured, consistent behavioural input between appointments or after treatment ends, helping to prevent relapse and promote weight loss maintenance.

Many companies are beginning to develop digital support specifically for individuals using weight loss medications, though much of this work is in its early stages. Outside of my DPhil, I was involved in preliminary service evaluations of Second Nature's medication-assisted weight loss programme (361, 362). However, there remains a notable lack of long-term evaluations of these digital support programmes. Robust evidence from high-quality randomised controlled trials is needed to assess the sustained effectiveness, safety, and user engagement of these digital medication-assisted programmes over longer periods of time. The learnings from this thesis, particularly around engagement, tailoring, low-intensity support, and methods for evaluating of digital interventions, are highly relevant to the development of effective digital interventions to support pharmacotherapy.

7.5.2 Research Implications

7.5.2.1 Improving our Understanding of Engagement

This thesis contributes to a growing body of work focused on maintaining long-term engagement in digital weight loss interventions, which remains one of the biggest challenges in the field. Findings from both the observational and experimental studies presented here, confirm that higher engagement is associated with better outcomes, but it is difficult to sustain over time. Understanding how, when, and why users engage or disengage continues to be central to improving intervention effectiveness. Future research should aim to capture engagement as a dynamic, non-linear process by drawing on in-app behavioural data and usage patterns, rather than relying on static or retrospective measures. In particular, better understanding how and when users re-

engage after periods of inactivity could provide valuable insights for designing interventions that support longer-term engagement. There is also an opportunity to use real-time engagement data to guide adaptive intervention strategies, for example, by triggering timely support at times when people are at risk of disengaging. This kind of personalisation may help mitigate attrition and improve outcomes in real-world settings.

While this thesis has contributed to efforts to define and measure engagement, there is still no widely accepted definition of meaningful engagement in digital health. This lack of consistency limits comparability across studies and makes it difficult to establish clear benchmarks for success. Building on work from my time visiting Stanford University, I am currently conducting a scoping review to identify the most commonly reported engagement metrics in digital weight loss interventions, with the aim of supporting the collection of more standardised engagement measures. In the future, this work could help researchers determine how engagement should be measured and reported, while also opening up opportunities to investigate which aspects of engagement are most strongly associated with outcomes.

7.5.2.2 Improving the Development of Future Weight Management Interventions

The findings from this thesis suggest that both human-supported and automated interventions can be effective for weight loss, though each involves trade-offs in terms of scalability, effectiveness, and engagement.

Early, low-intensity human support appears to enhance the effectiveness of digital interventions, but delivering this support at scale remains a significant challenge. One

approach would be to automate labour-intensive components, such as coaching, or to reduce the level of training and expertise required for intervention delivery. However, trials adopting these strategies have typically produced only modest outcomes, with average weight losses of 1–3% (130). Instead, emerging technologies, such as Gen-AI, may offer promising opportunities to deliver this support in a resource-efficient way. These tools have the potential to simulate coaching interactions, provide real-time feedback, and tailor content based on user data, potentially replicating aspects of human support without the associated resource demands. Early studies of AI-powered chatbots suggest they can deliver weight loss outcomes comparable to in-person interventions (363, 364). They also have potential to integrate wearable device data and messaging platforms to deliver more personalised, responsive interventions (365). However, most existing evidence comes from feasibility or uncontrolled studies, with few high-quality randomised controlled trials assessing their long-term effectiveness, safety, or acceptability (364). There remains a need for rigorous, large-scale evaluations of these technologies before they can be reliably integrated into clinical or commercial practice.

An alternative approach to managing intervention scalability and costs without compromising outcomes, is to tailor intervention intensity to individual response. Studies have shown that 30–50% of individuals in lower-intensity behavioural programmes achieve ≥10% weight loss (271, 366), suggesting that higher-intensity support may not be necessary for everyone. Delivering lower intensity interventions to those who respond well, while reserving more intensive approaches for those with suboptimal early outcomes, could allow more efficient allocation of resources without

compromising effectiveness. This kind of triaged care model may be particularly relevant in healthcare systems and commercial platforms where capacity is limited. This is already exemplified in the NHS Digital Weight Management Programme, which offers support at three different intensity levels based on individual need (112), but there may be potential to go further by dynamically tailoring support as people progress.

Building on this, future research should continue to examine which components work best, for whom, and under what conditions. Interventions could be more responsive to changes in users' needs and behaviours, offering the right level of support at the right time. This points to the value of more adaptive trial designs like just-in-time adaptive interventions (JITAIs) and Sequential Multiple Assignment Randomised Trial (SMART) (318, 367), which allow researchers to systematically test how timing, tailoring, and intensity of support influence outcomes. SMART designs, for example, involve multiple stages of randomisation at key decision points based on participant response to earlier treatment, which could offer a framework for optimising more personalised interventions (368). Future studies may wish to apply these designs to test different thresholds or decision rules for adjusting support. For example, triggering a timely coaching call at known times of disengagement, or reducing input for users who demonstrate early success.

7.5.2.3 Improving the Evaluation of Digital Interventions

Here, I have shown that remote trials using digital platforms are both feasible and valuable for rapidly generating large-scale evidence. However, these methods face well-recognised challenges in the digital health field, particularly high attrition, missing data,

and difficulties sustaining engagement. Improving data completeness and retention will be essential for future studies and may be supported by embedding follow-up assessments more seamlessly within the programme itself, or by incorporating passive data collection methods that minimise participant burden.

The findings also support the value of using structured frameworks for intervention optimisation. The MOST framework provided a useful approach for identifying active components and testing their combinations before integrating them into a treatment package. A logical next step would be to return to the preparation phase of MOST to refine the conceptual model and further develop the content of promising components like the health coach introductory call. Once an optimised intervention is determined, future studies could include a fully powered randomised controlled trial testing the health coach introductory call against the core Second Nature programme.

That said, traditional RCTs may not be the best fit for evaluating digital interventions in fast-moving, real-world settings. RCTs remain important for assessing effectiveness and cost-effectiveness, but they are most appropriate when the intervention and delivery model are stable, can be implemented with high fidelity, and are expected to produce clinically meaningful outcomes (369). In digital health research, this is often not the case, and interventions are updated rapidly, shaped by commercial priorities, and influenced by evolving user needs. In such contexts, more flexible methods are needed.

One approach could be a more dynamic version of MOST that includes decision points throughout the process to guide transitions between phases. Rather than progressing through discrete stages, this would treat optimisation as a continuous, iterative process.

Choices about whether to continue data collection, revisit earlier phases, or move to evaluation would be guided by the data emerging at each point (370). These adaptations could improve efficiency and make the framework more compatible with the pace of digital product development. However, further work is needed to make this approach practically usable, including developing new methods for real-time decision-making.

Another approach is to draw on implementation science, which offers useful frameworks for evaluating digital interventions in applied settings (371). Hybrid effectiveness-implementation designs assess both clinical impact and real-world implementation, helping accelerate the translation of evidence into practice (372). Frameworks such as EPIS (Exploration, Preparation, Implementation, Sustainment) (373) and RE-AIM (374, 375), could help researchers consider contextual factors and mechanisms of implementation throughout intervention development, which are areas where MOST may be less well aligned. MOST, while not explicitly designed for implementation science, could be viewed as complementary, and future research may wish to explore how these frameworks can be integrated.

No single framework currently addresses all the needs of industry-academic collaboration. Evaluating digital interventions requires a shift in mindset, moving away from viewing interventions as fixed packages and towards seeing them as evolving systems shaped by user needs, technological advances, and contextual factors. Drawing inspiration from iterative development models in engineering and software design, there is a need for evaluation frameworks that are faster and flexible to be better aligned with the realities of digital product development, while still upholding academic rigour.

In my view, a more appropriate evaluation framework for digital interventions would need to follow a set of 10 key principles:

1) **Iterative -** Support continuous learning through repeated cycles of development, testing, and refinement.
2) **Modular -** Evaluate at the feature or component level to support ongoing optimisation.
3) **Adaptive -** Include flexible components and remain responsive to diverse users, differing needs, and varying contexts.
4) **Context-sensitive -** Account for delivery constraints like technical infrastructure, workflows, and staffing.
5) **User-centred -** Assess what matters to users, including perceived usefulness, ease of use, and burden.
6) **Outcome-appropriate -** Use proxy or intermediate measures in early stages, progressing to clinical outcomes for later-stage or definitive evaluation.
7) **Time-sensitive -** Fast and responsive enough to match the pace of product development.
8) **Data-enabled -** Make strategic use of routinely collected digital data to understand user interaction and optimise effectiveness.
9) **Theory-guided -** Grounded in behavioural theory and focused on mechanisms of action.
10) **Decision-informed -** Incorporate structured, data-driven decision-making at key points in the process.

7.6 CONCLUSIONS

Overall, this thesis addresses key evidence gaps in the development and evaluation of digital weight loss interventions. I explored strategies to improve engagement and retention, which remain major barriers to the long-term success of digital programmes. I examined how interventions perform in real-world conditions, moving beyond controlled trials to generate evidence that better reflects how people use these tools in practice. I tested whether the MOST framework could be applied to improve effectiveness within a commercial programme, offering a more efficient, evidence-based alternative to typical industry practices. Finally, I explored novel intervention strategies beyond current offerings, including a fully automated, self-regulation-based app and the potential value of planned pauses as a flexible way to support long-term adherence. The work was conducted in partnership with Second Nature, a provider of NHS digital weight management services, enabling close collaboration with industry throughout the research.

Together, these studies offer insights into how we can develop and evaluate digital interventions that are not only grounded in behavioural theory, but also feasible for real-world implementation. Both fully automated and supported interventions proved effective, but not universally so, and sustaining engagement remained a persistent challenge across studies. This highlights the need for more flexible, adaptive frameworks capable of identifying what works best for whom, and when, while also supporting faster, more responsive ways of working between academic and industry partners. Drawing on these learnings, I outlined a set of design principles that could underpin a more fit-for-purpose evaluation framework for digital health interventions.

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APPENDICES

CHAPTER 2: APPENDIX

APPENDIX 2.1: SECOND NATURE PRIVACY POLICY

Second Nature Healthy Habits Ltd, trading under the name Second Nature, ("we") are committed to protecting and respecting your privacy. We are registered with the UK Information Commissioner's Office as a Data Controller (Reg No. ZA148098) and have in place a comprehensive Company data protection policy and code of practice.

This Privacy Policy ("Policy") (together with our Terms, which can be accessed at https://www.secondnature.io/terms, and any other documents referred to on it) sets out the basis on which any personal information we collect from you, or that you provide to us, will be processed by us and how you can get access to this information. If you are located in the European Economic Area (“EEA”) or the United Kingdom (UK), “personal information” means any information relating to an identified or identifiable individual. Please review it carefully.

1. Purpose of this Policy

Second Nature provides you (the "User") with access to the online and mobile services including but not limited to, secondnature.io and all associated subdomains (the "Website"), the Second Nature mobile application (the "App"), and any provided healthcare tracking technology, collectively the "System". Our privacy policy is designed in accordance with numerous national and international regulation frameworks, including (but not limited to) the General Data Protection Regulation (“GDPR”), the UK Data Protection Act 2018 and the UK General Data Protection Regulation (“UK GDPR”).

2. What personal information do we hold and how we get it

We may collect and process personal information provided by filling in forms on the Website or App, including personal information provided during completion of surveys and other online tools, posting of comments in the Community or requesting further services, and when you report a problem with our System. If you contact us, we may also keep a record of that correspondence. Second Nature also collects and processes personal information with the health tracking technology provided as part of the System, such as wireless weighing scales (which track your weight) and activity trackers (which track your steps and sleep).

Throughout your use of the System we may collect personal information such as: personal demographics information (including but not limited to first and last names, date of birth or age, address, email, phone number); lifestyle or health data (referred as “special category data” and includes height, weight, body mass index, ethnicity, smoking status); other personal health profile information and details of your visits to the System and the resources that you access (including, but not limited to, traffic data, location data, weblogs, other communication data, and the resources that you access).

Your personal information (steps per day and weight) may also be collected via Apple HealthKit or Google Fit upon installing our iOS and Android apps. This consent will be explained and obtained from you within the app, and you may revoke this access at any point within your phone's operating system settings.

Your personal information, including your health data (referred as “special category data” and includes height, weight, HBA1C level, BP level, cholesterol level, PAM score) may also be provided to us by an electronic patient record, referral or through a secure online platform in order to refer you to the System, e.g. provided through your GP, local NHS service or our partner REED. If this is the case, the relevant party will ask for your explicit consent .

We collect as well technical information and analytics from you concerning your use of the System, including but not limited to pages visited, links clicked, non-sensitive text entered, mouse movements, system and operating system type and version, browser or app version, time zone setting and usage of our iPhone and Android apps.

3. IP addresses and cookies

We may collect personal information about your device, including where available your IP address, operating system, browser type and screen size for use in system administration, to tailor your experience of the System, provide you with customer support and to report aggregate information internally.

For the same reason, we may obtain personal information about your usage of the System by using a cookie file which is stored on the hard drive of your device. Cookies help us to give you a smooth user experience, improve the System and deliver a better and more personalized service. They enable us to: recognize you when you return to our site; maintain personal information you have entered (e.g. during completion of a survey); speed up your searches; estimate our audience size and usage pattern; store information about your preferences; and allow us to customize our site according to your individual interests.

Both Second Nature and our third-party vendors, including Google, may use first-party cookies (such as the Google Analytics cookie) to inform, optimize, and serve ads based

on your past visits to the Website on sites across the Internet (also known as 'remarketing'). If you would like to opt out of this, you can do so via your Google Ads Preferences Manager.

Below is an overview of the types of cookies we and third parties may use to collect information.

— Strictly necessary cookies. Some cookies are strictly necessary to make the services available to you. We cannot provide you with the services without this type of cookies.

— Functional cookies. These are used to recognize you when you return to the services. This enables us to adapt our content for you, and remember your preferences (for example, your choice of language or region).

— Analytical or Performance cookies. We also use cookies for website and app analytics purposes in order to operate, maintain and improve our services. We may use our own analytics cookies or use third party analytics providers such as Facebook, FOSPHA, HotJar, Metabase, Mixpanel, Twitter, Taboola and VWO to collect and process certain analytics data on our behalf. These providers may also collect information about your use of other websites, apps, and online resources. You can opt out of ... without affecting how you visit our services by going to ....

Where required by applicable law, we obtain your consent to use cookies.

You may refuse to accept cookies by changing the settings on your device to prevent cookies from being set. However, if you select this setting, you may be unable to access certain parts of the System. Unless you have adjusted your browser setting so that it will refuse cookies, our system will issue cookies when you visit the Website and App.

4. How we use your personal information

Second Nature is dedicated to maintaining the privacy and integrity of your personal information. As such, we have policies and procedures and other safeguards to help protect your personal information from improper use and disclosure.

We collect and use your personal information to deliver our contract to you. We may collect and use your personal information, including your special category data, only if you have given us your specific consent.

We may use and disclose your personal information and special category data for our internal operations, which include administration, planning and various activities that assess and improve the quality and cost effectiveness of the service that we deliver to you. Examples are using information about you to improve quality of the service,

satisfaction surveys, de-identifying personal information, customer services and internal training. We may use and disclose your personal information to contact you as a reminder to interact with, or complete tasks relating to your use of the System.

We use also automated decision-making to allocate you to a group of users before starting the use of our service.

We follow a Minimum Necessary Access Policy, so any required disclosure of your identifiable personal information is minimized. The following categories describe different ways that we use your personal information within Second Nature and disclose your personal information to persons and entities outside of Second Nature. We have not listed every use or disclosure within the categories below, but all permitted uses and disclosures will fall within one of the following categories. In addition, there are some uses and disclosures that may require your specific authorization.

How much personal information is used or disclosed without your written permission will vary depending, for example, on the intended purpose of the use or disclosure.

— Disclosure at your request: We may disclose personal information relating to your use of the System when requested by you. This disclosure at your request may require written authorization by you.

— Payment: We do not store your credit/debit card details; they are processed directly by a third-party processor (for example, Stripe or Braintree) that will store all payment information and transaction details. We will only retain details of transactions on secure servers, and we will not retain your credit or debit card information.

— Operations: We may use and disclose your personal information for our internal operations, which include administration, planning and various activities that assess and improve the quality and cost effectiveness of the service that we deliver to you. Examples are using information about you to improve quality of the service, satisfaction surveys, de-identifying personal information, customer services and internal training.

— Reminders and notifications: We may use and disclose your personal information to contact you as a reminder to interact with, or complete tasks relating to your use of the System.

— Third party service providers:

— We may share personal information with third-party service providers we have hired to provide services on our behalf, including those who act as data processors on our behalf. Those data processors are subject to privacy and security obligations consistent with our privacy policy and with the current data protection regulation and framework. They can only use and process the personal information in the ways specified

by us. These service providers include (but are not limited to) Amazon Web Services which provides the Second Nature app and website, analytics and search engine providers (including but not limited to Mixpanel, HotJar, Intercom) which assist us in improving Second Nature app or website and your user experience, help us to collect information on your use of the System, and to assist you in case of an issue.

— We may share anonymised information with third-party service providers who assist us in our marketing and advertising activities or in the improvement of Second Nature app or website. These are third party services that allow Second Nature to collect information from you concerning your use of the System, including but not limited to pages visited, links clicked, non-sensitive text entered, mouse movements, and usage of our iPhone and Android apps. These services are used to help Second Nature enhance or improve the user experience on this website and to perform any other function that Second Nature reasonably believe in good faith is required to protect and ensure the proper functionality and security of this website.

— Third party medical professionals: with additional permission that we will separately explain to you and request your consent for; we may disclose your personal information to a third-party medical professional nominated by you: e.g. your GP or local NHS service. This may be in the form of a discharge letter or an electronic disclosure to an electronic patient record.

— Threat to health or safety: We may use and disclose your personal information when necessary to prevent a serious threat to your health and safety or the health and safety of the public or another person. Any disclosure, however, would only be to someone able to help prevent the threat.

— As required by law: Certain laws permit or require certain uses and disclosures of personal information, for example, for public health activities, health oversight activities and law enforcement. We may be required to disclose personal information for these and other compliance purposes, including as may be required by applicable laws and regulations or requested by a judicial process or government agency. In these instances, Second Nature will only use or disclose your personal information to the extent the law requires.

— For research and publicity purposes: We may use personal information for internal and external research and publicity purposes. This may include publishing aggregate, anonymous information about our users in the context of providing public information and conducting academic research.

— Transfer of business assets: If Second Nature or substantially all of its assets are acquired by a third party, personal information held by it about its customers will be one of the transferred assets.

National personal information opt-out policy: as part as our contracts with the NHS, we collect, process and disclose confidential patient information. We always make sure that we do so for individual care purposes only; we only use and/or disclose anonymised personal information for research purposes, and we don't use or disclose confidential patient personal information for planning purposes. As such, we are compliant with the National data opt-out policy.

Except as described above, we will never share your personal information with any other party without your consent.

5. Legal Bases for Processing European Personal Information

If you are located in the European Economic Area or the United Kingdom, we only process your personal information when we have a valid "legal basis", including when:

— Consent. You have consented to the use of your personal information, for example to send you marketing communications or to use cookies.

— Contractual necessity. We need your personal information to provide you with the services, for example to respond to your inquiries.

— Compliance with a legal obligation. We have a legal obligation to use your personal information, for example to comply with tax and accounting obligations.

— Legitimate interests. We or a third party have a legitimate interest in using your personal information. In particular, we have a legitimate interest in using your personal information for product development and internal analytics purposes, and otherwise to improve the safety, security, and performance of our services. We only rely on our or a third party's legitimate interests to process your personal information when these interests are not overridden by your rights and interests.

6. Where we store your personal information

All personal information you provide to us is stored on secure servers with trusted 3rd party suppliers, Amazon Web Services ('AWS') within the European Economic Area ('EEA'). AWS complies with the GDPR and the UK GDPR, which set out several data protection requirements, which apply when personal information is being processed. AWS are industry leaders in the provision of hosting services and take security very seriously - you can find out more about their security policies and processes in their Security Whitepaper.

We may transfer personal information outside the EEA or the UK to countries deemed adequate by the European Commission; based on Standard Contractual Clauses; to perform the services that you have requested from us, or with your consent.

Unfortunately, despite these measures, the transmission of information via the internet is never completely secure. Although we will do our best to protect your personal information, we cannot guarantee the security of your information transmitted to the System, and any transmission is at your own risk. Once we have received your personal information, we will use strict procedures to try to prevent unauthorized access in accordance with our Company data protection policy and code of practice, and responsibilities as a registered Data Controller in the UK.

7. Your rights regarding your personal information

You have certain rights with respect to your personal information. If we do not agree to a request by you with respect to your personal information, please consult the Second Nature Privacy and Security Officer whose contact information is below.

If you are based in the UK or the European Economic Area and we do not comply with any of the below, you have the right to complain to the ICO or to your local Supervisory Authority, and to a judicial remedy.

— Restrictions: You have the right to request in writing that we do not disclose certain information about you. To request a restriction, please contact the Privacy and Security Officer whose contact information is below.

— Confidential Communications: You have the right to request in writing that we restrict the way in which we communicate information regarding your health and health care services, such as ceasing to send email or SMS messages to notify or remind you about aspects of the System or your progress through the Second Nature program. We will make every effort to accommodate your request.

— Access: You have the right to inspect and copy your personal information maintained by us. Normally, we will provide you with access within one month of your request. To request your personal information:

— Please download a subject access request form here, fill it in and return it to us using the contact details on the form, along with copies of information that confirms your identity (if applicable). Please do not send in any original copies of documents. More details of acceptable types of identification documents are included in the application form.

— You can email your completed form and electronic copies of your identification documents to: support@secondnature.io

— Or print the form, fill it in and post it with paper copies of your identification documents to:

— Second Nature

— Scale Space White City

— 58 Wood Ln

— London, W12 7RZ

— United Kingdom

— We will endeavour to respond promptly and in any event within one month. You can alternatively call us on +44 20 3488 0769

— Deletion: You have the right to ask that we delete all information that the System has collected on you via email to the Second Nature privacy and Security whose contact information is below.

— Amendment: You have the right to request that we amend your written personal information. For instance, you can request that we correct an incorrect date of birth in your records. We will amend your personal information within one month of your request and will notify you when we have amended your personal information. We can deny your request in certain circumstances, such as when we believe that your personal information is accurate and complete.

— Personal Information Portability: You have the right to obtain and reuse your personal information from Second Nature for your own purposes across different services. This can be freely downloaded in .csv format within the settings page of your Second Nature account.

— Objection: You have the right to object to processing based on legitimate interests or the performance of a task in the public interest, to direct marketing, and to processing for the purposes of scientific research & statistics. To request an objection, please contact the Privacy and Security Officer whose contact information is below.

— Automated Decision Making & Profiling: You have the right not to be subject to a decision based on automated processing and it produces a legal effect or a similarly significant effect on you. To request an opt-out of automated decision making & profiling, please contact the Privacy and Security Officer whose contact information is below.

Before meeting your request, we may ask you to provide reasonable information to verify your identity. Please note that there are exceptions and limitations to each of these rights, and that while any changes you make will be reflected in active user databases instantly or within a reasonable period of time, we may retain information for backups, archiving, prevention of fraud and abuse, analytics, satisfaction of legal obligations, or where we otherwise reasonably believe that we have a legitimate reason to do so.

8. Personal Information Retention

As per the ICO's 'Principal 5' and the article 5 of GDPR and the UK GDPR, we retain personal information no longer than is necessary for the purpose we obtained it for. With the context that your personal information may be used for research purposes (as covered in section 3), Second Nature will retain any information held on an individual for up to 10 years after that individual has ceased use of the System. At that point, the

individual's information will be deleted. As covered in section 5, you may request that we delete your personal information at any time.

9. EU Representative

If you are based in the EU Second Nature Healthy Habits Ltd has appointed DataRep as its Data Protection Representative for the purposes of GDPR, so that you can contact them directly in your home country. DataRep has locations in each of the 27 countries and Norway & Iceland in the European Economic Area (EEA). If you want to raise a question to Second Nature Healthy Habits Ltd, or exercise your rights (explained above) in respect of your personal information, you may do so by:

— Sending an email to DataRep at datarequest@datarep.com, quoting Second Nature Health Ltd in the subject line.

— Contacting DataRep using their online webform at www.datarep.com/data-request or mailing your enquiry to DataRep at the most convenient of the addresses that you can find below

— Austria: DataRep, City Tower, Brückenkopfgasse 1/6. Stock, Graz, 8020, Austria

— Belgium: DataRep, Place de L'Université 16, Louvain-La-Neuve, Waals Brabant, 1348, Belgium

— Bulgaria: DataRep, 132 Mimi Balkanska Str., Sofia, 1540, Bulgaria

— Croatia: DataRep, Ground & 9th Floor, Hoto Tower, Savska cesta 32, Zagreb, 10000, Croatia

— Cyprus: DataRep, Victory House, 205 Archbishop Makarios Avenue, Limassol, 3030, Cyprus

— Czech: Republic DataRep, IQ Ostrava Ground floor, 28. rijna 3346/91, Ostrava-mesto, Moravska, Ostrava, Czech Republic

— Denmark: DataRep, Lautruphøj 1-3, Ballerup, 2750, Denmark

— Estonia: DataRep, 2nd Floor, Tornimae 5, Tallinn, 10145, Estonia

— Finland: DataRep, Luna House, 5.krs, Mannerheimintie 12 B, Helsinki, 00100, Finland

— France: DataRep, 72 rue de Lessard, Rouen, 76100, France

— Germany: DataRep, 3rd and 4th floor, Altmarkt 10 B/D, Dresden, 01067, Germany

— Greece: DataRep, 24 Lagoumitzi str, Athens, 17671, Greece

— Hungary: DataRep, President Centre, Kálmán Imre utca 1, Budapest, 1054, Hungary

— Iceland: DataRep, Kalkofnsvegur 2, 101 Reykjavík, Iceland

— Ireland: DataRep, The Cube, Monahan Road, Cork, T12 H1XY, Republic of Ireland

— Italy: DataRep, BPM 335368, Via Roma 12, 10073 , Ciriè TO, Italy

— Latvia: DataRep, 4th & 5th floors, 14 Terbatas Street, Riga, LV-1011, Latvia

— Liechtenstein: DataRep, City Tower, Brückenkopfgasse 1/6. Stock, Graz, 8020, Austria

— Lithuania: DataRep, 44A Gedimino Avenue, 01110 Vilnius, Lithuania

— Luxembourg: DataRep, BPM 335368, Banzelt 4 A, 6921, Roodt-sur-Syre, Luxembourg

— Malta: DataRep, Tower Business Centre, 2nd floor, Tower Street, Swatar, BKR4013, Malta

— Netherlands: DataRep, Cuserstraat 93, Floor 2 and 3, Amsterdam, 1081 CN, Netherlands

— Norway: DataRep, C.J. Hambros Plass 2c, Oslo, 0164, Norway

— Poland: DataRep, Budynek Fronton ul Kamienna 21, Krakow, 31-403, Poland

— Portugal: DataRep, Torre de Monsanto, Rua Afonso Praça 30, 7th floor, Algès, Lisbon, 1495-061, Portugal

— Romania: "DataRep, 15 Piaţa Charles de Gaulle, nr. 1-T, Bucureşti, Sectorul 1, 011857,

— Slovakia: DataRep, Apollo Business Centre II, Block E / 9th floor, 4D Prievozska, Bratislava, 821 09, Slovakia

— Slovenia: DataRep, Trg. Republike 3, Floor 3, Ljubljana, 1000, Slovenia

— Spain: DataRep, BPM 335368, Avd. Castilla La Mancha Nº 70-1 (Nave A), 45270, Mocejon-Toledo, Spain

— Sweden: DataRep, S:t Johannesgatan 2, 4th floor, Malmo, SE - 211 46, Sweden

When mailing enquiries, please mark your letters for “DataRep” and not “Second Nature Healthy Habits Ltd”, otherwise the letter may not reach DataRep. Please refer clearly to Second Nature Healthy Habits Ltd in your correspondence. On receiving your correspondence, we are likely to request evidence of your identity, to ensure your personal data and information connected with it is not provided to anyone other than you.

If you have any concerns over how DataRep will handle the personal data they will require to undertake their services, please refer to their privacy policy at www.datarep.com/privacy-policy.

10. Children's Privacy

We do not knowingly collect, maintain, or use personal information from children under 13 years of age, and no part of our Service is directed to children. If you learn that a child

has provided us with personal information in violation of this Privacy Policy, then you may alert us at support@secondnature.io.

11. Data Security

We make reasonable efforts to protect your information by using physical and electronic safeguards designed to improve the security of the information we maintain. However, as no electronic transmission or storage of information can be entirely secure, we can make no guarantees as to the security or privacy of your information.

Second Nature provides the System to referrals provided through the NHS. As such, we are compliant with the Data Security and Protection Toolkit 2019 / 2020, our organisation code is 8JF17.

12. Concerns or complaints

If you believe that any of your rights with respect to your personal information has been violated by us, our employees or agents, please communicate with the Second Nature Privacy and Security Officer at: support@secondnature.io for UK users, or DataRep for EU-based users (contact details above)

13. Amending this Policy

We reserve the right to revise this Policy and to make the revised Policy effective for all personal information that we created or received prior to the effective date of the revised Policy. If you are a registered user, we will notify you of changes by the email address we have for you on file.

Questions relating to revisions to this Policy may be addressed to the Privacy and Security Officer whose contact information is above. This Policy will be promptly revised if there is a material change to a policy described herein.

Effective Date: This Policy is effective as of May 19th, 2021.

APPENDIX 2.2: RESULTS OF MIXED EFFECTS MODEL USING THE MISSING-INDICATOR METHOD

Table A : Results of mixed effects model for the association between weight loss motivation and weight using the missing-indicator method (N = 36,794)

Variables	All Data (N = 36,794)		
	Coef	95% CI	P-value
Motivations (ref = Appearance)			
Fitness	6.06	(5.49,6.63)	***<0.001***
Health	14.88	(14.42,15.34)	***<0.001***
Self-efficacy	9.88	(9.38,10.39)	***<0.001***
Week (ref = 0)			
4	-3.80	(-3.89,-3.71)	***<0.001***
12	-5.25	(-5.37,-5.13)	***<0.001***
24	-5.59	(-5.74,-5.45)	***<0.001***
Interaction terms			
Fitness*week4	-0.27	(-0.45,-0.09)	***<0.001***
Fitness*week12	-0.44	(-0.68,-0.2)	***<0.001***
Fitness*week24	-0.36	(-0.66,-0.07)	***0.01***
Health*week4	-0.73	(-0.87,-0.59)	***<0.001***
Health*week12	-1.10	(-1.29,-0.92)	***<0.001***
Health*week24	-1.42	(-1.64,-1.19)	***<0.001***
Self-efficacy*week4	-0.28	(-0.45,-0.12)	***<0.001***
Self-efficacy*week12	-0.08	(-0.3,0.14)	0.48
Self-efficacy*week24	-0.05	(-0.33,0.22)	0.70

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes.

Table B : Results of mixed effects model for the association between goal preference and weight using the missing-indicator method (N = 36,794)

Variables	All Data (N = 36,794)		
	Coef	95% CI	P-value
Goal Preference (ref = medium)			
High	-0.18	(-0.71,0.35)	0.51
Low	3.73	(3.19,4.28)	***<0.001***
Missing	-0.51	(-1.22,0.19)	0.15
Week (ref = 0)			
4	-4.04	(-4.11,-3.97)	***<0.001***
12	-5.65	(-5.75,-5.55)	***<0.001***
24	-6.08	(-6.2,-5.96)	***<0.001***
Interaction terms			
High*Week4	-0.29	(-0.46,-0.13)	***<0.001***
High*Week12	0.04	(-0.19,0.27)	0.72
High*Week24	0.28	(0.01,0.54)	***0.04***
Low*Week4	-0.01	(-0.17,0.16)	0.95
Low*Week12	0.15	(-0.08,0.37)	0.20
Low*Week24	0.07	(-0.2,0.34)	0.59
Missing*Week4	-0.10	(-0.31,0.12)	0.37
Missing*Week12	-0.25	(-0.52,0.03)	0.08
Missing*Week24	-0.42	(-0.75,-0.08)	***0.02***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes.

Table C : Results of mixed effects model for the association between percent weight loss goal and weight using the missing-indicator method (N = 36,794)

Variables	All Data (N = 36,794)		
	Coef	95% CI	P-value
Percent Category (ref = 5-10%)			
<5%	-7.78	(-8.56,-7)	***<0.001***
>10%	-1.12	(-1.54,-0.7)	***<0.001***
Week (ref = 0)			
4	-3.29	(-3.37,-3.22)	***<0.001***
12	-3.83	(-3.94,-3.73)	***<0.001***
24	-3.31	(-3.44,-3.17)	***<0.001***
Interaction terms			
<5*Week4	0.44	(0.1,0.78)	***0.01***
<5*Week12	0.48	(0.04,0.93)	***0.03***
<5*Week24	0.76	(0.23,1.28)	***0.01***
>10*Week4	-2.00	(-2.11,-1.89)	***<0.001***
>10*Week12	-3.72	(-3.86,-3.57)	***<0.001***
>10*Week24	-5.22	(-5.4,-5.05)	***<0.001***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes.

APPENDIX 2.3: RESULTS OF MIXED EFFECTS MODEL ADJUSTED FOR BASELINE WEIGHT

Table D : Results of mixed effects model for the association between weight loss motivation and weight with adjustment for baseline weight (n = 28,391)

Variables	All Data (n = 28,391)		
	Coef	95% CI	P-value
Motivations (ref = Appearance)			
Fitness	0.15	(0.05,0.24)	***<0.001***
Health	0.33	(0.25,0.4)	***<0.001***
Self-efficacy	0.20	(0.11,0.28)	***<0.001***
Week (ref = 0)			
4	-3.85	(-3.93,-3.78)	***<0.001***
12	-5.40	(-5.5,-5.29)	***<0.001***
24	-5.71	(-5.84,-5.59)	***<0.001***
Interaction terms			
Fitness*week4	-0.21	(-0.36,-0.06)	***0.01***
Fitness*week12	-0.42	(-0.63,-0.22)	***<0.001***
Fitness*week24	-0.35	(-0.6,-0.1)	***0.01***
Health*week4	-0.72	(-0.84,-0.6)	***<0.001***
Health*week12	-1.14	(-1.3,-0.98)	***<0.001***
Health*week24	-1.44	(-1.63,-1.25)	***<0.001***
Self-efficacy*week4	-0.24	(-0.38,-0.1)	***<0.001***
Self-efficacy*week12	-0.07	(-0.26,0.12)	***0.45***
Self-efficacy*week24	0.11	(-0.12,0.34)	0.35
Baseline Weight	0.98	(0.98,0.98)	***<0.001***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes. 8,403 participants had missing IMD values.

Table E : Results of mixed effects model for the association between goal preference and weight with adjustment for baseline weight (n = 26,158)

Variables	All Data (N = 26,158)		
	Coef	95% CI	P-value
Goal Preference (ref = medium)			
High	0.02	(-0.06,0.1)	0.56
Low	0.06	(-0.03,0.14)	0.20
Week (ref = 0)			
4	-4.07	(-4.13,-4.01)	***<0.001***
12	-5.81	(-5.89,-5.72)	***<0.001***
24	-6.17	(-6.27,-6.07)	***<0.001***
Interaction terms			
High*Week4	-0.31	(-0.45,-0.17)	***<0.001***
High*Week12	0.11	(-0.08,0.3)	0.26
High*Week24	0.38	(0.16,0.61)	***<0.001***
Low*Week4	-0.02	(-0.16,0.12)	0.76
Low*Week12	0.13	(-0.06,0.32)	0.17
Low*Week24	-0.03	(-0.25,0.2)	0.82
Baseline Weight	0.98	(0.98,0.98)	***<0.001***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes. 8,403 participants had missing IMD values. 3,054 participants had missing goal preference values.

Table F : Results of mixed effects model for the association between percent weight loss goal and weight with adjustment for baseline weight (n = 28,391)

Variables	All Data (n = 28,391)		
	Coef	95% CI	P-value
Percent Category (ref = 5-10%)			
<5%	-0.16	(-0.28,-0.05)	***<0.001***
>10%	-0.02	(-0.08,0.04)	0.58
Week (ref = 0)			
4	-3.31	(-3.37,-3.25)	***<0.001***
12	-3.91	(-4.00,-3.82)	***<0.001***
24	-3.34	(-3.45,-3.22)	***<0.001***
Interaction terms			
<5*Week4	0.28	(0.02,0.55)	***0.04***
<5*Week12	0.27	(-0.1,0.63)	0.16
<5*Week24	0.38	(-0.05,0.82)	0.09
>10*Week4	-2.02	(-2.11,-1.93)	***<0.001***
>10*Week12	-3.70	(-3.82,-3.57)	***<0.001***
>10*Week24	-5.17	(-5.32,-5.02)	***<0.001***
Baseline Weight	0.98	(0.98,0.98)	***<0.001***

Models were adjusted for gender, age, IMD decile, Type 2 and/or pre-diabetes. 8403 participants had missing IMD values

CHAPTER 3: APPENDIX

APPENDIX 3.1: ARTEMIS PARTICIPANT INFORMATION SHEET

Participant Information Sheet

We would like to invite you to take part in this research study, which may help you lose weight. Joining the study is entirely up to you. Before you decide we would like you to understand why this research is being done and what it would involve for you. Please take the time to read this information and discuss it with others if you wish. If anything is unclear, or if you would like more information, please contact the researchers on artemis@phc.ox.ac.uk. They will be more than happy to address any questions you may have.

Purpose of the Research

The aim of this study is to test whether an online weight loss intervention helps people to lose weight.

Who are we looking for?

We are looking for people living in the UK who are overweight and want to lose weight with the help of a mobile phone app.

Do I have to take part?

Taking part is entirely voluntary. You can ask questions about the study before deciding whether or not to participate by contacting the researchers on artemis@phc.ox.ac.uk. If you do agree to participate, you may withdraw yourself and your data from the study at any time during the study period, without giving a reason and without penalty, by advising the researchers of this decision.

What would taking part involve?

You will be invited to complete four assessments online over 12-months, for which you will be reimbursed for your time. The first assessment will occur when you have agreed to take part, then again after 12, 26, and 52 weeks. During each assessment you will be asked to weigh yourself on your own digital weighing scale and report your weight. You will also be asked to upload a photograph of your weight displayed on the scales for verification purposes, and to complete two short questionnaires. The first assessment will take approximately 20 minutes to complete. The subsequent assessments will take approximately 5 minutes.

Following the first assessment, you will be randomly assigned by a computer programme to an online weight loss programme, or a control group which will receive no treatment. We cannot predict which group you will be assigned, and it would not be a fair test of the benefits of the app if we took your preference into account. If you are randomised to the intervention group, you will be asked to

download the ARTEMIS app from the Apple or Android store on your mobile device, and access this using a unique code and password. This app will contain a guided weight loss programme, which will help you find weight loss strategies that work for you and fit with your lifestyle. It involves logging on every day for some weeks to allow you to try out the strategies. The app also gives you feedback on how you are doing and helps you build a collection of useful weight loss strategies personalised to you. Once you have found what works for you, you can move to weekly check-ins.

What are the possible benefits of taking part?

We know that this approach helps people lose more weight in the short-term than trying to lose weight without support. What we need to know is whether it works in the long-term. Half the people who take part will get access to the app. Regardless of whether this helps you personally, taking part in this research helps us learn more about the science of weight loss and this can help other people wanting to lose weight in the future.

Will I be reimbursed for taking part?

You will receive financial reimbursement for your time within the study, in the form of Amazon gift vouchers sent to your email address, on three occasions: when you complete the study assessments at the 12-week (£5), 26-week (£8), and 52-week (£12) follow up.

What are the potential disadvantages and risks of taking part?

There are no known risks from taking part. Some people worry that weighing oneself regularly may cause undue concern about weight and food. However, research suggests that there are no negative long-term consequences of regular weighing, but we will check this through the study.

What happens if I don't want to continue with the study after I consent?

If you change your mind, you can of course stop taking part in the study. At any time, you can request your account to be deleted on the study app, and for any data collected about you to be withdrawn.

How will my information be kept confidential?

When the study is finished, your responses will be anonymised. This means it won't be possible to know that the data came from you. Any information that is collected about you during the course of the research will be kept strictly confidential. The data will be stored on a secure University server and will only be accessible to the study team.

What will happen to my data?

All data will be collected through the study specific website and app, owned and managed by the University that have been developed by us in collaboration with a team of app developers. These developers been checked thoroughly by the University to make sure they follow all relevant data protection guidelines. All data will be kept confidential, accessible only to the research team, on University approved servers.

Once all follow-up assessments are completed, we will destroy information that could identify you. The de-identified research data and records will be stored securely for up to 30 years and then deleted. Relevant members of the University of Oxford may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations. At all times personal data collected from you will be held in compliance with the requirements of the GDPR and the Data Protection Act 2018.

The University of Oxford is the data controller with respect to your personal data, and as such will determine how your personal data is used in the study. The University will process your personal data for the purpose of the research outlined above. Research is a task that is performed in the public interest. Further information about your rights with respect to your personal data is available at https://compliance.admin.ox.ac.uk/individual-rights.

What will happen to the results of this study?

The results will be published in scientific journals or presented at research meetings. Your individual data will never be made publicly available. However, anonymised data may be shared through secure, private channels with other researchers in the interest of open and transparent science. We will also send you a summary of the study results at the end of the study.

Who is organising and funding the research?

This study has been funded by the National Institute for Health Research (NIHR) as part of the Oxford and Thames Valley Applied Research Collaboration (ARC).

Who has reviewed this study?

This project has received ethics approval from a subcommittee of the University of Oxford Central University Research Ethics Committee (Reference number: TBC).

Who do I contact if I have a concern about the study or I wish to complain?

If you have a concern about any aspect of this project, please contact the research team on artemis@phc.ox.ac.uk. The research team should acknowledge your concern within 10 working days and give you an indication of how they intend to deal with it. If you remain unhappy or wish to make a formal complaint, please contact the Chair of the Medical Sciences Interdivisional Research Ethics Committee at the University of Oxford: Email: ethics@medsci.ox.ac.uk; Address: Research Services, University of Oxford, Wellington Square, Oxford OX1 2JD.

Thank you for taking the time to read this information sheet. You can download a copy of this information here. If you are interested in participating in this study, please click here, where you will be taken to the consent form hosted on a secure University of Oxford website.

Appendix 3.2: Detailed overview of ARTEMIS actions and associated tips and tricks

Weight loss action category: regulate your sleep (turquoise)

No	Action	What to do	Why does it matter?	Tips (see next section)
1	Sleep for 8 hours	Plan what time you need to wake up in the morning and try to ensure you are asleep at least 8 hours before that time.	Evidence suggests that sleep plays a role in weight loss. Insufficient sleep can increase overeating unhealthy food choices. Losing sleep may also mean you have less energy for exercise, physical activity as well as overcoming temptations.	C, H7, H8
2	Go to bed 30 minutes earlier than usual	If you typically sleep less than 8 hours per night, try setting an alarm or other reminder to go to bed 30 minutes earlier than you normally would. If you typically get much less than 8 hours sleep, you may wish to increase this.	Evidence shows there is a link between fewer total hours of reported sleep and excess bodyweight. Among a range of possible factors contributing to this being tired can lead to increased hunger, reduces appetite control and feeling of fullness, and poorer food choices.	C, H7, H8
3	Avoid scrolling on your phone, using your computer, or watching TV, in your bedroom	Avoid using any electronic devices (e.g., phone, computer, or TV) in your bedroom before going to bed. Try to leave your devices in a separate room or away from your bedside.	Exposure to the blue light of electronic devices closely before sleep can make it harder to fall asleep and reduce the quality of your sleep. Poor sleep duration and quality can increase overeating and unhealthy food choices.	C, B11, B12, B13, H8

4	Sleep in a darker environment	Turn off all sources of light in your bedroom and close your blinds / curtains or wear a sleep mask to bed.	Sleeping in a darker environment will reduce sleep disturbance and should help you get a better-quality sleep. Poor sleep quality increases overeating and unhealthy food choices.	C, H8
5	Sleep in a cooler environment	A bedroom temperature between 15-20 degrees Celsius is optimal for most people's sleep. To reduce the temperature in your room try altering your thermostat, using a fan, a lighter duvet, or opening a window.	Sleeping in a cooler room can help you to fall asleep faster and will reduce sleep disturbance. Poor sleep quality increases overeating and unhealthy food choices.	C, H8
6	Do not drink alcohol in the evening	Do not drink any alcohol in the evening, especially not within several hours of going to bed.	Alcohol can affect the quality of your sleep and disrupts your sleep cycle. Some people may find alcohol helps them get to sleep initially, but this is outweighed by the negative effect on sleep quality through the night. Poor sleep quality increases overeating and unhealthy food choices.	A, C, D6
7	Avoid eating for three hours before going to bed	Do not eat or drink anything (except from water) three hours before going to bed. Make sure you plan your evening meal 3 hours before going to bed and ensure you don't have any evening snacks.	Eating or drinking too close to bedtime may impair sleep quality and is associated with increased risk of waking up. Not eating for 3 hours before bed will also help you reduce your overall calorie intake throughout the day.	A, C, D

8	Do not drink caffeine after 12pm	Stop drinking caffeinated beverages (e.g., coffee, some tea, energy drinks, or soft drinks such as coke) after 12 noon. You can swap these for decaffeinated versions in the afternoon.	Caffeine is a stimulant and can have a disruptive effect on your sleep. It will make it hard for you to fall asleep and reduce your total sleep time. It can take up to 10 hours to completely clear caffeine from your bloodstream. Evidence suggests that good quality plays a role in weight loss.	A, B1, B9, E1

Weight loss action category: eating in a structured way (red)

No	Action	What to do	Why does it matter?	Tips (see next section)
1	Plan what and when you will eat today in advance	Take the time to plan what you will eat over the next 24 hours. Make it quite detailed – when will you eat, what will you cook, will you take something prepared if you're going out? If you know you are eating out, look up their menu in advance and plan your order. Then make sure that you stick to your plan.	A lot of calories are added to our diet from impulsive snacks or poor food choices. Committing to a food plan in the morning, when you are mindful of your goals and not exposed to temptations, can help you eat healthily throughout the day.	A, B, C, D, H
2	Eat no more than three times in the day	Make sure that you have no more than three eating occasions throughout the day. You can have breakfast, lunch, and dinner, but no snacks in between or after.	Impulsive snacking between meals can add a lot of calories. Cutting out snacks will reduce your daily energy intake.	A, B, C, D

3	Skip a meal	Skip either breakfast, lunch, or dinner. Make sure you don't compensate for skipping the meal by snacking instead.	Skipping a meal is an easy way to reduce your overall calorie intake throughout the day.	A, B, C, D
4	No food or drink except water after 8pm	Do not eat any food after 8pm and ensure any drinks you consume after 8pm have zero or very few calories (e.g., water or black tea).	Food and drink consumed in the late evening are often unhealthy and high in calories (e.g. crisps, chocolate, alcohol). Cutting out all foods and calorie-rich drinks in the evening can help reduce your overall calorie consumption.	A, B, C, D
5	Check the calorie count of everything you want to eat or drink	Use nutrition labels, websites, or apps to check the calorie content of food before you eat it. Make sure you consider how the calories are presented as they sometimes refer to a portion size or per 100g. Compare the calorie content with that of similar items and see if there are lower calorie alternatives. Make a conscious decision about whether you want to consume the food or drink or go for a lower calorie alternative.	Many people don't know how many calories their foods and snacks contain. You might realise that a lower calorie alternative will be just as satisfying.	A, B, C, D, E
6	Set yourself a calorie goal and stick to it	Go to the following website to find out how many calories you need per day: https://www.bbc.com/food/diets/how_many_calories_do_you_need. Subtract 600 calories and set the resulting	Research shows that setting calorie goals can help you lose weight. It makes your goal for the	A, B, C, D, E

		figure as your goal for the day. Then keep track of the calorie content of everything you eat throughout the day. Ensure you do not exceed your target. You can use free calorie counting mobile phone apps, such as MyFitnessPal.	day more tangible and helps you think about how to spread your daily calorie intake.	
7	Have a "fasting" day by eating less than 800kcal	Have a day of "fasting" where you consume less than 800 calories (kcal). You can find some low calorie recipes to help you here: https://www.bbc.com/food/collections/intermittent_dieting_recipes https://www.bbc.com/food/diets/low-calorie_diet Make sure you drink at least 2 litres of low-calorie fluids to avoid dehydration. You can use free calorie counting apps, such as MyFitnessPal, to help you keep track.	Eating only 800 calories means cutting out more than half of the calories you would consume on a normal day.	A, B, C, D, E
8	Keep a diary of what you eat and how you feel	Keep a record of all the foods and drinks you consume throughout the day. Make a note of the time when you consume them, and also the reason e.g., whether you were craving this kind of food, wanted to reward yourself, or were hungry. Write down how you felt after consuming the food or drink. Go through your food diary in the evening and see which foods or drinks you could have avoided.	Keeping a diary will make you think more about how you use food not only to feed yourself but also to provide comfort or reduce boredom. You can then think of other strategies to handle these emotions that do not include food.	C, D3

9	Use a portion size measure	Weigh everything before you eat it and check your portion against the recommended serving size on the packet or by using this general guide: https://blog.myfitnesspal.com/essential-guide-portion-sizes/	Most people are unaware of recommended serving sizes. Checking portion sizes will help to prevent you eating over the recommended amount.	A, B, C
10	Only eat when sitting at a table	Only eat while you are sitting at a dining table. Don't eat while you're on the go or when working.	When you eat while doing other tasks, it is easy to overeat. Sitting down at a dining table will help you focus on your food and be more mindful of what and how much you're eating. By committing to only eating while sitting at the table, you will reduce snacking.	A, B, C, D
11	Eat only within an 8-hour time window (e.g., 10am - 6pm)	Plan to eat all your meals and snacks for the day within a pre-set 8-hour time frame, for example between 10am to 6pm. Do not eat or drink anything apart from water and other no-calorie beverages, like plain coffee or tea, in the remaining 16 hours of the day.	Restricting your eating window to 8 hours per day can cut your calorie intake over the course of the day, which in turn may contribute to weight loss.	A, B, C, D, H7

Weight loss action category: avoiding or swapping specific foods (orange)

No	Action	What to do	Why does it matter?	Tips (see next section)
1	Do not eat between meals	Do not eat any snacks between meals. Stick to your three main meals, breakfast, lunch and dinner.	Impulsive snacking between meals can add lots of calories to your overall daily intake. Cutting out snacks between meals will reduce the overall amount you consume in day.	A, B, C, D
2	Cut out crisps, biscuits, cakes, and sweets	Do not eat any crisps, biscuits, or highly processed baked goods (e.g., pastries and croissants), cakes, chocolates, and sweets throughout the day.	These foods are highly 'energy dense' and contain a lot of calories in each bite, without being nutritious. You would have to eat a lot to fill you up so it's easy to overeat them. Cutting them out will reduce your calorie intake.	A, B, C, D
3	Cut out fried foods	Do not consume any fried foods today. This includes for example fries or chips, onion rings, poppadoms, battered fish.	Fried foods are highly 'energy dense' and contain a lot of empty calories, without being nutritious. You would have to eat a lot to fill you up so it's easy to overeat them. Cutting them out will reduce your calorie intake.	A, B, C, D, E

4	Have only one course at mealtime	Do not consume any starters or desserts with your lunch and dinner. For breakfast, consume just one type of food (e.g., only toast or cereal).	Starters and desserts add to your calorie intake. Cutting them out will reduce your consumed calories.	A, B, C, D
5	Cut out carbohydrates	Avoid carbohydrates, including potatoes, rice, pasta, bread, breakfast cereals, beans, and sugary foods such as pastries, cakes, biscuits, confectionery and chocolates. Meat, fish, poultry, fruit / green vegetables, and dairy are allowed.	Carbohydrates account for around 40% of all the calories we eat. When you cut out carbohydrates, you will tend to reduce your overall energy intake.	A, B, C, D, E
6	Swap unhealthy snacks for fruits and vegetables	Swap unhealthy snacks with fruits and vegetables, such as apples, carrots, celery, or peppers.	Unhealthy snacks are high in calories, but usually low in calories. Swapping them with fruits and vegetables will reduce your calorie intake.	A, B, C, D
7	Swap rice, potatoes, and pasta for extra vegetables	Avoid rice, potatoes, and pasta as a side to your main course. Instead swap them with boiled or steamed vegetables, including broccoli, carrots, or cabbage.	Rice, potatoes and pasta contain far more calories than vegetables. Replacing starchy carbohydrates with vegetables will help you stay full while eating fewer calories.	C, D, E

8	Use meal replacement products	Try swapping breakfast, lunch and/or dinner for a meal replacement product such as a specially formulated meal bar, shake, or soup. You can buy these online or in your local pharmacy.	Specially formulated bars, shakes, or soup shakes contain all the nutrients you need and are usually much lower in calories than a typical meal.	A, B, C, D
9	Swap unhealthy snacks with 6-8 individual nuts	Replace all unhealthy snacks with 6-8 nuts.	Nuts are high in protein and fibre which will help you to feel fuller for longer.	A, B, C, D

Weight loss action category: changing what you drink (yellow)

No	**Action**	**What to do**	**Why does it matter?**	**Tips (see next section)**
1	Drink only water or unsweetened coffee or tea	Drink only water, coffee and tea today. Your tea or coffee may include a small amount of milk, but no sugar, honey, or syrups.	High calorie drinks can quickly increase your calorie intake without increasing your sense of fulness. Switching to low-calorie drinks will help you lose weight.	C, D4, E1

2	Swap sugary soft drinks with diet or no sugar versions	Swap your sugary soft drinks for the zero or low-sugar versions. This includes sodas, sport drinks, and energy drinks. You might have to experiment with different brands to discover your preferred taste.	A typical can of sugary drink contains about 100 calories. Switching to zero or low-sugar versions of soft drinks can help reduce your calorie intake.	C
3	Do not drink alcohol	Refrain from drinking any alcohol today.	Alcohol contains a lot of calories. A pint of beer contains about 250 calories, 150ml of red wine contain 125 calories. By avoiding drinking alcohol, you can reduce the calories you consume.	C, D6
4	Drink 500ml of water before each meal	Drink 500ml of water before you choose your meal and decide on the portion size.	Drinking 500ml of water can help fill up your stomach. That way you will feel less hungry when making meal decisions, helping you to make healthier choices and choose smaller portion sizes.	C, E1
5	Swap juices or smoothies for a portion of whole fruit and vegetables	Avoid juices or smoothies and eat a piece of whole fruit or vegetable instead.	Juices and smoothies tend to be highly processed with a high calorie and sugar content. Swapping juice with whole fruits and vegetables has the advantage that you benefit from the fibre they contain. Fibre is good for digestion, cholesterol, and helps you feel fuller for longer. Eating whole fruits and vegetables rather than drinking a smoothie slows down the rate of eating and increases feelings of fullness.	C

6	Swap coffee or tea containing milk, creamers, and sugar for a black coffee or tea	Swap high-calorie coffee or tea beverages containing milk, creamers, sugar or syrups for a black coffee or tea.	Switching to black coffee or tea without milk, creamers, sugar, or syrups will help you reduce your calorie intake.	A, C, D4
7	Drink at least 2 litres of water per day	Drink at least 2 litres of water today.	Drinking 2 litres of water per day can help fill up your stomach. That way you will feel less hungry when making meal decisions, helping you to make healthier choices, and choose smaller portion sizes.	C, E1

Weight loss action category: creating a healthier diet (green)

No	**Action**	**What to do**	**Why does it matter?**	**Tips (see next section)**
1	Eat at least 5 portions of fruit or vegetables each day	Eat at least five portions of different fruits and vegetables.	Fruits and vegetables typically contain few calories and are nutrient dense, so can help bulk out a meal. This will help you to feel fuller on fewer calories.	C, H

2	Snack only on vegetables	Tempted to snack outside of your three main meals? Then snack on vegetables, such as carrots, peppers, or cucumber.	Vegetables are low in calories and consuming them as a snack won't add too many calories to your daily intake.	A, B, C, D
3	Eat only foods with a green nutrition label for total fat	Only eat foods with low total fat (3g or less per 100g). This is often indicated by a green colour-coding for total fat on the nutrition label.	Fat contains a lot of calories. Eating low-fat foods will therefore reduce your calorie intake.	A, B, C, D, E
4	Eat only foods with a green nutrition label for sugar	Only eat foods with low sugar content (5g or less per 100g). This is often indicated by a green colour-coding for sugars on the nutrition label.	Sugary foods contain a lot of calories. Eating low-sugar foods will reduce your calorie intake.	A, B, C, D, E
5	Make sure half of your main meal for the day is a salad or vegetables	Make sure that half of your main meal of the day - lunch or dinner - consists of boiled or steamed vegetables, or a salad. Potatoes do not count as vegetables. Salad dressings should be low fat, such as lemon juice, balsamic vinegar, or yoghurt dressing.	Vegetables provide you with many important nutrients and are low in calories. Salads, and steamed or boiled vegetables, are a great side to your main meal. They add bulk to a meal, so you feel fuller and satisfied.	C, D, E
6	Swap rice, potatoes, and pasta with extra vegetables	Avoid rice, potatoes, and pasta. Instead swap for boiled or steamed vegetables, including greens, carrots, or parsnips.	Rice, potatoes and pasta contain far more calories than vegetables. Replacing starchy	C, D, E

			carbohydrates with vegetables will help you stay full while eating fewer calories.	
7	Swap fatty meats with lean meats or fish	Avoid fatty meats, including salamis, sausages, steaks, pork belly, or high fat minces. Swap them with lean cuts of meat which have a relatively low-fat content. Remove all visible fat from meat, including the skin from chicken. Choose extra lean mince or ask your butcher for a leaner cut. Or choose fish instead.	Fatty meats contain many calories. You can reduce your calorie intake by switching to lean meats.	B, C, D
8	Avoid high fat salad dressings and spreads	Avoid high fat salad dressings and spreads such as margarines, mayonnaise, butter and peanut butter.	High fat salad dressings and spreads contain many calories. One tablespoon of mayonnaise or butter contains about 100 calories. Avoiding eating high fat salad dressings and spreads will reduce your calorie intake.	A, B, E

Weight loss action category: meal-time tactics (blue)

No	Action	What to do	Why does it matter?	Tips (see next section)
1	Eat slowly (e.g., 20 chews per bite)	Slow down how quickly you eat. You can achieve this by chewing each bite twenty times, decreasing your chewing speed, or putting your cutlery down between bites.	Reducing your eating speed will help you notice feelings of fullness before you have overeaten.	C, H
2	Avoid distraction and focus on your food while eating	Eat your meals without distractions e.g., do not use your phone, watch TV, or read a book whilst eating. Be mindful about eating, and your feelings of satisfaction and fullness.	Being mindful can help you identify feelings of fullness and support you in avoiding overeating.	C, D
3	Stop eating before you feel full	Stop eating before you feel full. Instead look out for the moment when you stop feeling hungry and stop then. You can freeze leftovers or keep them in the fridge for another time.	It takes a while for feelings of fullness to set in. Stopping eating at the moment you don't feel hungry anymore, will prevent you overeating.	B, C, D
4	Use smaller plates and bowls	Use smaller plates or bowls and smaller serving spoons to help with your portion control.	Using smaller crockery and utensils will help you eat smaller portions and reduce your calorie intake.	C, D

5	Cut food into smaller pieces	Cut your food into smaller pieces when eating.	Reducing the bite size will increase the time you need to eat. This will provide your gut hormones more time to tell your brain you are full, meaning you can feel satisfied before you have overeaten. It will also give you the feeling of having had a larger meal.	C, H
6	Eat for less than 20 minutes at a time	Don't spend more than 20 minutes eating each meal. Eat at a normal pace. You can freeze your leftovers or keep them in the fridge.	Restricting the time, you spend consuming your food will automatically restrict your calorie consumption.	B, C

Weight loss action category: burn more calories (purple)

No	**Action**	**What to do**	**Why does it matter?**	**Tips (see next section)**
1	Walk up and down a flight of stairs for 30 minutes	Walk up and down a flight of stairs for approximately 30 minutes. If you can't manage 30 continuously you can take a short at the bottom of the stairs and then go again.	Engaging in exercise burns calories and helps you lose body fat. 30 minutes of moderate-to-vigorous physical activity is the daily recommendation for adults.	C, F

2	Go cycling for 30 minutes	Go cycling outdoors or at the gym for 30 minutes. Take breaks if necessary.	Engaging in exercise burns calories and helps you lose body fat. 30 minutes of moderate-to-vigorous physical activity is the daily recommendation for adults	C, F, G
3	Go swimming for 30 minutes	Go swimming for 30 minutes. If you can't manage 30 minutes continuously take a short break at the side of the pool and then go again.	Engaging in exercise burns calories and helps you lose body fat. 30 minutes of moderate-to-vigorous physical activity is the daily recommendation for adults.	C, F, G
4	Perform stretching exercises for 30 minutes (e.g., Pilates or yoga)	Do stretching exercises (e.g., Pilates or yoga) at home for 30 minutes. There are many online tutorials available, such as this one: https://www.youtube.com/watch?v=9jAyRP0bqKA	Stretching exercises help develop flexibility. This may enable you to engage in more physical activities. Any extra exercise helps to burn more calories.	C, F
5	Attend an exercise class	Attend a structured group exercise or sports class. This may be a class at a gym or sports club led by a trainer, e.g., a spin class, a dance class, or you could use online videos/exercise apps.	Engaging in exercise burns calories and helps you lose body fat. Doing exercise in a group can be especially motivating and fun.	C, F

6	Play a group sport or perform a solo activity	Play a group sport such as football, basketball, badminton or tennis, or a solo activity such as golf. This might either be formal training or a game between friends.	Engaging in exercise burns calories and helps you lose body fat. Doing exercise in a group can be especially motivating and fun.	C, F, G
7	Go to the gym	Go to the gym for a workout. A good way to structure your training is to start with a warm-up on a cardio machine, followed by strength training, and a light cardiovascular cool-down exercise to finish. Make sure to ask the trainers or someone else at the gym to explain any unfamiliar equipment. Most equipment will also have useful diagrams and instructions.	The suggested gym routine will help you strengthen several muscles in your body, which helps boost your long-term metabolic rate. The cardio routine will get your heart rate going and burn calories.	C, F, G, H6, H7
8	Exercise at home with the 21-minutes NHS Choices workout	Try one of the NHS Choices website 21-minute workouts that you can perform easily at home. They include: a 6-minute warm-up, 10-minute workout of your choice and 5-minute cool-down. You can find them here: https://www.nhs.uk/live-well/exercise/10-minute-workouts/	The NHS Choices workouts will strengthen several body muscles. Building muscle mass will help boost your long- term metabolic rate. Plus, engaging in exercise burns calories.	C, F
9	Go for a brisk walk or gentle hike	Go for a brisk walk or gentle hike until you are out of breath and can no longer sustain a conversation.	Engaging in exercise burns calories and helps you lose body fat.	C, F, G

Weight loss action category be more active as part of your daily life (pink)

No	Action	What to do	Why does it matter?	Tips (see next section)
1	Walk 10,000 steps	Set yourself the goal of walking at least 10,000 steps. You can count your steps using a pedometer or fitness tracker. There are many free apps that have pedometer functionality as well. They record the number of steps you made on your phone.	Walking 10,000 steps in one day burns around 500 calories, which helps you lose body fat.	C, F
2	Walk or cycle instead of taking the bus, train, or car	If you are going somewhere, cycle or walk some or all of the way.	Engaging in physical activity burns calories and helps you lose body fat.	C, F
3	Go for a 30-minute walk	Go for a 30-minute walk instead of sitting down, this can either be with others or alone.	You burn more calories while walking than sitting. Any extra physical activity helps to burn more calories.	C, F, G
4	Stand up while working	Stand up while you're working. If your workplace does not have a height adjustable desk, try to find a cupboard or cabinet that has a good height to work on. Alternatively, try to have standing or walking meetings with your colleagues if more practical.	You burn more calories standing than sitting.	C, F

5	Take the stairs whenever you can	Always choose the stairs over the lift.	Engaging in physical activity burns calories and helps you lose body fat.	C, F
6	Have an active day	Have an active day, for example go for a hike or play a sport such as football, golf, or tennis. This can either be with friends or family, or alone.	Engaging in physical activity burns calories and helps you lose body fat. Doing this together with family or friends can make it more enjoyable.	C, F, G
7	Stand up while watching TV	Stand up while watching TV.	You burn more calories standing than sitting. Any extra physical activity helps to burn more calories.	C, F
8	Walk when talking on the phone	Every time you are talking on the phone, get up and walk around. Do this for the full duration of the phone call.	You burn more calories while walking than sitting. Any extra physical activity helps to burn more calories.	C, F
9	Plan a walk-and-talk meeting with friends or colleagues	Plan a meeting with friends, or one of your work meetings to done whilst walking.	You burn more calories while walking than sitting. Any extra physical activity helps to burn more calories.	C, F, G
10	Fit mini workouts into your daily routine	Do some stretching exercises when you get out of bed in the morning, squats, lunges or push ups before you get in the shower, run up flights of stairs throughout your day, walk at a fast pace pushing hard off your toes with each step, or bicep curl your shopping bags while walking.	Any extra physical activity helps to burn more calories.	C, F, H7

11	Do some physical chores around the house	Do some physically demanding chores today such as mowing the lawn, cleaning the windows, rearranging the furniture, cleaning out the garage, or brushing / hoovering the floors.	Any extra physical activity in your day helps to burn more calories.	C, F

Tips and Tricks: What to do to succeed

If you are experiencing difficulties completing your planned action today, have a look at the tips below *(check the right-side column of the action plan list to discover which tips are relevant)*.

A) Dealing with cravings

1. Make a bargain with yourself to wait a minute to see if the craving passes. Then see if you can last another day.
2. Eat chewing gum or brush your teeth instead. You might not feel like chocolate after that!
3. Distract yourself e.g., by walking up and down the stairs or phoning a friend.
4. Think about how it will be once you have lost weight. Really try to imagine what it will feel like.
5. Acknowledge the feeling of craving, think about how it feels. Don't wrestle with it and don't stress about it. You don't need to worry about what it means or what will happen, just notice the feeling. Be mindful.
6. Drink a glass of water. If you dislike the taste of plain water, try infusing it with lemon, cucumber, ginger, or mint leaves.

B) Dealing with temptation

1. Avoid places with food and drink temptations, such as fast-food restaurants, ice cream parlours, or coffee shops.
2. Do not go shopping when you are hungry.
3. Make a shopping list and stick to it.

4. If you have food or drinks in your house that aren't part of your eating plan, give them to a local food bank or your friends/neighbours.
5. Don't bring unhealthy foods/drinks into the house.
6. If you're having an unhealthy snack (e.g., a piece of chocolate), take only a small amount and return the rest to the fridge/cupboard.
7. Make sure you have healthy snacks at home and a bottle of water with you when you're out.
8. When you are going to eat out, check the menu beforehand and choose what you will eat. Restaurants are required by law to provide nutritional information about their dishes, including calorie content. If the information is not included on the menu, ask the waiter. In chain restaurants the nutritional information might also be available online.
9. If you tend to reward yourself by eating food or having certain drinks, try to find a reward in something else, e.g., going to the cinema, or taking a hot bath.
10. If you think you might struggle to find healthy foods in your lunch break, prepare your lunch at home and bring it with you to work.
11. Turn off distracting notifications on your phone
12. Try charging your phone at the other side of your bedroom, or in another room, or putting it away at least half an hour before bed.
13. Create a night-time routine that doesn't include your phone, computer, or television such as going straight to sleep, reading a book, or journaling.

C) Dealing with drops in motivation

1. Imagine how you will feel once you have lost weight: What will you look like? What will you be able to do? What will it mean to you?
2. Plan a (non-food) reward for yourself once you have lost a certain amount of weight.
3. Write down a list of reasons why you want to lose weight and stick it on your wall.
4. Stick a photo on your wall from a time when you were happy with your weight.
5. Review your progress so far in the weight tracking app. What does it mean to you? Where would you like to see the graph go?
6. Go through your wardrobe and find clothes that currently don't fit. Imagine wearing them again.

D) Staying strong despite social influences

1. Learn to say "no". Practice saying "thanks, but no" until it becomes a habit.
2. If you feel uncomfortable using a written food diary in public, make notes on your phone. Or take a photo and write it down later.
3. Explain to family and friends why losing weight is important to you and ask for their support.
4. Ask those around you to keep unhealthy foods and drinks out of your sight.
5. If you are attending a social gathering, make sure you bring yourself some healthy food options.
6. If people around you are drinking alcohol choose a low-calorie beverage instead e.g., spirit and diet mixer.

E) If you're not sure about the food and drink alternatives

1. If you struggle drinking plain water, try infusing it. Perhaps with slices of lemon, orange, cucumber, ginger, or mint leaves. Or try sparkling water.
2. If you're not a fan of cooked/boiled vegetables, try roasting them or eating them raw.
3. If you don't like green vegetables, try mashing them together with other vegetables to create a combined flavour.
4. If you dislike the taste of boiled or steamed vegetables, add lemon juice, herbs, or spices.

F) Dealing with barriers to exercise

1. If you are feeling stiff or sore, try exercising a different part of the body. Also try stretching the sore bits or taking a hot shower and you will feel better. Fitness exercises that are not primarily focused on building muscles, such as walking, swimming, cycling or jogging, can help muscle soreness go away.
2. Find an exercise buddy. Having someone to exercise with is more fun and you won't want to let them down by not showing up.
3. If you find exercising boring, listen to music, or watch television while working out.
4. If you feel uncomfortable exercising around people you don't know, choose a time when it's less crowded, go with a friend, or exercise at home.

G) Dealing with bad weather

1. Buy appropriate clothes for the weather e.g., a waterproof jacket and trousers, or comfortable t-shirt and shorts.

2. Check the weather forecast. If the weather is going to improve, move your action to a later time of the day.
3. Find an indoor exercise. For instance, if you planned to go for a run, go running on a treadmill instead.

H) Time, cost, and organisation issues

1. Prepare your meals in advance as this will be cheaper than eating out.
2. Look out for special offers on fruits and vegetables.
3. Prepare meals in bulk and put them in the fridge or freeze them for when you don't have much time.
4. Have healthy ready meals in the freezer for when time is short.
5. Buy healthy prepared foods such as a green salad or a lean soup for when you're busy.
6. If gym membership is too expensive, find things to do without a gym, such as going for a run or following an exercise video on YouTube.
7. Plan in advance. Put your weekly schedule in your calendar including wake-up times, bedtimes, mealtimes, and exercise times.
8. Keep a record for what's working for you and what's not.

APPENDIX 3.3: ARTEMIS ELECTRONIC CASE REPORT FORMS (SCREENING, BASELINE AND FOLLOW-UP ASSESSMENTS)

Screening

The following text will be presented to all participants within the REDCap eCRF interface. Note. All participant facing text is non-italicised:

To determine your eligibility for this study, please answer the following 17 questions about yourself. This will take 1-2 minutes.

Date of birth (dd/mm/yyyy): *(dropdown box) (18 or above=eligible; below 18=ineligible)*

Sex: *(Dropdown box with three options: male, female, prefer not to say)*

Ethnicity: *(Dropdown box with five possible options: i.e., Asian or Asian British (e.g., Indian, Pakistani, Bangladeshi, Chinese, any other Asian background); Black, Black British, Caribbean or African (e.g., Caribbean, African, any other Black, Black British, or Caribbean background); Mixed or multiple ethnic groups (e.g., White and Black Caribbean, White and Black African, White and Asian, any other mixed or multiple ethnic background); White (English, Welsh, Scottish, Northern Irish (or British), Irish, Gypsy or Irish Traveller, Roma, any other White background); Other ethnic group (Arab, any other ethnic group); prefer not to say.*

Height (cm, for conversion from feet/inches to cm, please click here): *(dropdown box)*

Weight (kg, for conversion from stones/pounds to kg please click here): *(dropdown box)*
The answers to the two previous questions will be used to calculate BMI (weight (kg)/height (m)^2). If ethnicity has been answered "White (English, Welsh, Scottish, Northern Irish (or British), Irish, Gypsy or Irish Traveller, Roma, any other White background)", the BMI variable must be ≥ 30 to be eligible; ≥ 27.5 for all other ethnic groups.

What was the highest level of education you achieved? *(Dropdown box with five options: No formal education;*
Some education (no qualification), GCSE/O-level (or equivalent); A level / BTEC (or equivalent); undergraduate or postgraduate degree; prefer not to say.

Are you currently living in the UK? *(Yes/No) (Yes=eligible; no=ineligible)*

Do you have access to the internet via a smartphone or tablet? *(Yes/No) (Yes=eligible; no=ineligible)*

Do you have access to a digital weighing scales? *(Yes/No) (Yes=eligible; no=ineligible)*

Have you attended a weight management programme in the past three months? *(Yes/No) (Yes=ineligible; no=eligible)*

Are you currently taking part in any other weight management study? *(Yes/No) (Yes=ineligible; no=eligible)*

Have you lost more than 5kg (10 pounds) body weight in the previous six months? *(Yes/No) (Yes=ineligible; no=eligible)*

Have you ever undergone bariatric surgery, or are you presently scheduled to have bariatric surgery? *(Yes/No) (Yes=ineligible; no=eligible)*

Are you pregnant, or planning a pregnancy in the next 12 months? *(Yes/No) (Yes=ineligible; no=eligible)*

Have you ever been diagnosed with an eating disorder? *(Yes/No) (Yes=ineligible; no=eligible)*

Have you recently been diagnosed with a disease, or expected to undergo treatment for a disease, associated with substantial weight loss e.g., cancer treatment? *(Yes/No) (Yes=ineligible; no=eligible)*

If ineligible:

We're sorry, based on the answers you have provided you are not eligible for this study. If there has been an error, please refresh this page, or contact us on artemis@phc.ox.ac.uk.

If eligible:

Based on the answers you have provided we can confirm you are eligible to take part in the study. Please click here to continue to the remainder of the assessment. This should take less than 15 minutes.

Baseline assessment

The following text will be presented to all participants within the REDCap eCRF interface. Note. All participant facing text is non-italicised:

Socio-demographic information:

Please enter your information into the spaces provided:

Title: *(Dropdown box with four options: Mr. Ms, Mrs, Dr)*
First name: *(Free text)*
Surname: *(Free text)*
Email address: *(Free text)*
Mobile number: *(Free text)*
Postal address: *(Free text)*
Postcode: (Free text)
Date of birth (dd/mm/yyyy): *(Drop down box)*
Current employment status (please select all that apply: *(Dropdown box with nine options, with the possibility to select multiple options: Retired, employed, self-employed, long-term sick or disabled, looking after home or family, in education or training, unemployed, other (please specify))*

Anthropometric measurements:

Please weigh yourself on a digital weighing scale and report your exact weight into the text box provided. Please do this soon after you wake up and after you have been to the toilet. It will be most accurate if you have not eaten or drunk anything. Please take a photograph of your weight displayed on the digital scales by clicking here and pressing submit. *Note. Important that participants cannot progress until this is completed.*

These next questions are about how you feel about yourself, your weight, and your food and physical activity.

On how many of the past seven days…

Has thinking about food, eating or calories made it very difficult to concentrate on things you are interested in (such as working, following a conversation or reading)? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Has thinking about your weight or shape made it very difficult to concentrate on things you are interested in (such as working, following a conversation or reading)? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you had a definite fear that you might gain weight? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you tried to control your weight or shape by making yourself sick (vomit) or taking laxatives? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you exercised in a compulsive way as a means of controlling your weight, shape or body fat, or to burn off calories? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you had a sense of having lost control over your eating (at the time that you were eating)? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Finally, we are going to ask you three questions about how your wellbeing:

In general, would you say your health is ... Excellent, Very good, Good, Fair, Poor.

In general, would you say your quality of life is ... Excellent, Very good, Good, Fair, Poor.

How satisfied are you with your body at this moment? Very satisfied, Satisfied, Neither satisfied nor dissatisfied, Dissatisfied, Very dissatisfied

You have now finished the baseline assessments. Please click next where we will tell you whether you get to use the app or will try to lose weight by yourself.

Participant randomised to intervention or control and presented with the below information.
Randomised to the control group:

You have been randomised by a computer to the control group. This means you will not get access to the ARTEMIS app and you may want to try to lose weight on your own. In a study like this, the only way we know whether the ARTEMIS app is effective is by comparing what happens to people who use it, and people who do not. It is therefore vital for the study that we find out what happens to you over the next year. We will get in touch with you in three months to ask you to provide us with your weight and to ask a few questions. This should take less than 10 minutes of your time and we will give you £5 to recognise your efforts. In six months, we will ask you to give us the same information and will give you £8 to recognise the time you spend. In 12 months, we will ask again for your weight and give you £12 to thank you for your time. Thank you for taking part in this study and helping others who want to lose weight in the future.

Randomised to the intervention group:

You have been randomised by a computer to the group who gets access to the ARTEMIS app to help you lose weight. Please click here to download the ARTEMIS study app from the Apple store, or here from the Android store. Once downloaded and opened on your phone, the app will guide you through the process. Here is your one-time username and passcode to be entered on the first screen. You will only need to enter this once.

Passcode: *(Participants unique one-time log in passcode)*

We will be in touch with you in three months to ask you to provide us with your weight and to ask a few questions. This should take less than 10 minutes of your time and we will give you £5 to recognise your efforts. In six months, we will ask you to give us the same information and will give you £8 to recognise the time you spend. In 12 months, we will again ask for your weight and give you £12 to thank you for your time. We thank you for taking part in this study and helping others who want to lose weight in the future. Even if you give up using the app, it really helps us to know how well it works if we find out from everyone who tried it, not just those who found it useful.

Follow up assessments

The following text will be presented to all participants within the REDCap eCRF interface at assessment timepoints at 12 and 26 weeks. Note. All participant facing text is non-italicised:

Follow up assessment (12 weeks)

Please complete the survey below.

Thank you!

Anthropometric measurements:

Please weigh yourself on a digital weighing scale and report your exact weight into the text box provided. Ideally this should be done within an hour of waking up, on an empty stomach, having consumed no food or liquid in the previous six hours, and having refrained from vigorous physical activity for the same period of time. Where possible please use the same scale as at your previous weight in.

Please take a photograph of your weight displayed on the digital scales by clicking 'upload file'. Then 'choose file', and then 'Take a photo' or you can choose a photo already in your library, and press submit. Alternatively, you can also send your photo to artemis@phc.ox.ac.uk at a later time. This will not effect your reimbursement

Eating Disorders Evaluation Questionnaire Short form (modified six-item questionnaire).

We are now going to ask you some questions about disordered weight management behaviours. It is important for us to collect this information as we will want to monitor any changes in these throughout the study for your safety.

On how many of the past seven days…

Has thinking about food, eating or calories made it very difficult to concentrate on things you are interested in (such as working, following a conversation or reading)? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Has thinking about your weight or shape made it very difficult to concentrate on things you are interested in (such as working, following a conversation or reading)? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you had a definite fear that you might gain weight? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you tried to control your weight or shape by making yourself sick (vomit) or taking laxatives? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you exercised in a compulsive way as a means of controlling your weight, shape or body fat, or to burn off calories? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Have you had a sense of having lost control over your eating (at the time that you were eating)? *(0 days; 1-2 days; 3-5 days; 6-7 days)*

Weight management questionnaire

1. Have you taken any actions to manage your weight since the last assessment? *(Yes / No)*

If yes:

2. What have you being doing to manage your weight (please click all that apply): *(participants should be able to click on multiple options from the following drop box of options: Actively using the ARTEMIS app; using learned strategies from the ARTEMIS app, but not actively using app; using another online or app based weight loss programme; attending a weight loss programme where I see someone face-to-face; using weight loss medication; using a meal replacement programme; other (please specify further in the text box below). If participant choses other options a text box should be available to provide further detail.*

If 26-week assessment:

3. (Intervention only) On a scale of 1 (not useful)-10 (very useful), how useful have you found the app to assist you in losing weight overall? *(Dropdown box)*

Finally, we are going to ask you three questions about how your wellbeing.

In general, would you say your health is ... Excellent, Very good, Good, Fair, Poor.

In general, would you say your quality of life is ... Excellent, Very good, Good, Fair, Poor.

How satisfied are you with your body at this moment? Very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, Very dissatisfied.

Thank you, you have now finished the (12, 26) week follow up assessments. You will receive an email shortly with confirmation our your (£8, £20) reimbursement.

Randomised to the control group:
If 12-week assessment:

We will contact you again in advance of the next follow up in 14-weeks to input your weight and upload your photo verification again, at which time you will receive a further (£20). We look forward to seeing you then and appreciate your continued support with this study.

All the best.
The ARTEMIS study team
Department of Primary Care Health Sciences
University of Oxford

If 26-week assessment:
As this was the final assessment timepoint, your participation in the study is now complete. Once again, we at the ARTEMIS study team would like to thank you for your contributions to this research study. We will be in contact on the email address provided to let you know the results of the study in due course.

All the best.
The ARTEMIS study team
Department of Primary Care Health Sciences
University of Oxford

Randomised to the intervention group:
If 12-week assessment:
We will also contact you again in advance of the next follow up assessment in 14-weeks to input your weight and upload your photo verification again, at which time you will receive a further £20. We look forward to seeing you again tomorrow in the ARTEMIS app (if you are still engaging with the active intervention phase). Thank you, we greatly appreciate your continued support with this research.

All the best.
The ARTEMIS study team
Department of Primary Care Health Sciences
University of Oxford

If 26 week assessment:
Thank you for completing this assessment. This completes your involvement in the study. We will email you the results of the study when we have analysed the results from everyone.

All the best.
The ARTEMIS study team
Department of Primary Care Health Sciences
University of Oxford

APPENDIX 3.4: ARTEMIS SENSITIVITY ANALYSIS

Table A: Sensitivity analysis excluding those who did not have a valid baseline weight verification photo and did not have a valid follow-up weight verification photo.

Timepoint	Variable	Mean (SD) change from baseline				Adjusted difference (95% CI)	P - value
		Control	n	Intervention	n		
12 weeks	Weight (kg)	-1·54 (3·6)	290	-2·90 (4·3)	262	-1·41* (-2·15 to -0·67)	***<0·001***
	n (%) losing ≥5% weight	40 (13·8)	290	72 (27·5)	262	2·36† (1·54 to 3·67)	***<0·001***
26 weeks	Weight (kg)	-2·14 (4·4)	280	-4·12 (6·5)	249	-1·95* (-2·69 to -1·20)	***<0·001***
	N (%) lost ≥5% weight	56 (20·0)	280	91 (36·5)	249	2·32† (1·57 to 3·44)	***<0·001***

*Adjusted mean difference (kg) (95% CI) calculated using linear mixed effects models with fixed effects for condition, week and group*week interaction, and a random effect for participant. IMD and baseline BMI were included as covariates as baseline values were predictive of missingness in the data.

†Odds ratio.

CHAPTER 4: APPENDIX

APPENDIX 4.1: HEALTH COACH INTRODUCTORY CALL INTERVENTION MATERIALS

Booking Email

Welcome to Second Nature

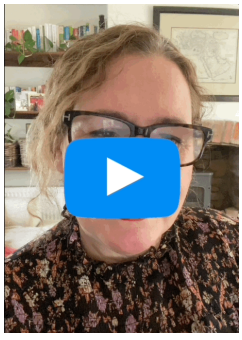
Book an intro call with your health coach!

Hi there,

My name is Kirstie and I'll be your health coach during your time on the Second Nature programme. It can be a lot to take on a new programme, so I will be here to support you every step of the way on your journey!

I wanted to offer the opportunity to book a 20-minute introduction call with me.

You'll find a hello video from me below or by clicking here.



To book in a Zoom call with me, click on this link here and choose a time that works for you.

I look forward to meeting you soon!

Best wishes,
Kirstie

Book a call with Kirstie →

Conversation Guide

NOTE: the aim of the call is primarily for rapport building. Some of the calls may go off in a certain direction depending on the user. But we mainly want to keep the call to getting to know each other and answering any initial questions. Ideally within 20 mins.

Time	Section	Questions
5 mins	Introduce yourself	· Hi, my name is ____ and I'm your health coach. It's great to meet you and thanks for taking the time to chat with me today. · I'd like to take the time to get to know you a little better so I can make sure I support you in the best way possible going forward. This will also be a great chance for you to ask any questions you might have at this point. · Firstly, just a little about me. I joined Second Nature __ years ago. I'm a registered nutritionist/dietitian and I have a degree/qualification in ___. Before Second Nature I worked as a __. · I'll be your health coach for the duration of your time in the Second Nature programme. I'm here to guide you throughout your journey and provide personalised support to help you reach your goals. Feel free to ask me any questions you have, you can message me in the group and 1-1 chat channels. I'll normally be available on weekdays between 8am to 5pm. · Some of the common things we get asked are....how to adapt the programme to dietary requirements, help with snacking, what to do when weight loss has slowed or stopped.
5 mins	Participant introduces themselves	· I'd love to hear a little more about you. (This is to be guided by what the user wants to share but if needed, some prompts are: What do you do for work? Who do you live with? What do you do in your free time?) · Why did you join Second Nature? · What does success look like for you on the programme?
5 mins	Answer any questions	· Do you have any questions for me that you want to ask about the programme or the app?

1-2 mins	Wrap up	· Thank you so much for taking the time to chat with me today. I hope you've found it useful. · Going forwards, our communications will be via the chat in the app. How often would you like me to check in with you, we will normally be in touch on a weekly basis. · Feel free to message me if you have any more questions or concerns. Speak soon!

APPENDIX 4.2: COACHING DROP-IN WEBCHAT SESSIONS INTERVENTION MATERIALS

Booking Message

Hey [insert username],

Hope you've had a good first week and you are settling into your Kickstart habits well. To keep up the great momentum and support you in making progress towards your goals, I wanted to invite you to schedule some 1:1 coaching time with me. This will be roughly 30 minutes each week where we can chat together live in the private chat, which can help towards motivation and accountability. How does that sound?

You can now go ahead and book your first 30-minute live session using this link:

[insert Calendly link]

During this session, we will chat live on the app here in the 1:1 channel. You can reach out to me at any time, and I will try to get back to you as soon as possible. These 1:1 coaching session just allow us to have a set time for a 'back and forth' conversation. Members find having this dedicated time beneficial for asking any questions, reassessing goals, or navigating any challenges or hurdles.

Please let me know if you have any questions or need any support with booking this in - I'm very happy to help 🙂

Conversation Guide

NOTE: discussions can be completely user-led. If you need to facilitate conversation you can use the prompts, but this is just a guide.

At the start of the allotted time

'Hi there [insert name], how are you doing today? This is your 30 minute 1:1 coaching slot for us to discuss anything that you'd like to chat about :) How have you been getting on?'

Introduction:

If they don't mention their previous goals, check in to see how they got on with them.

Identify what challenges they faced when trying to meet them and work with them to find out how to overcome those challenges

Identify what helped them reach those goals and highlight how we want to focus on replicating that

Articles & Activities

Check in to see how they have gotten on with the articles

- Have they read them?
- If yes, what stood out to them?
- If not, what's getting in the way?
- How have they gotten on with the activities?
- Have there been any aha-moments?

Celebrate Wins

- What's been the biggest win this week?
- What helped them achieve that?

Meal plan + food choices

- Tease out what's helping them make healthy choices
- Assess their understanding of the balanced food plate

Progress

- Check in against their measures of progress (e.g. more energised)

Wrapping up

- Is there anything else on your mind that you would like to discuss?
- Set goals for the next session?

ONLY Week 13/14 - end of the coaching session

For the last month of 'core' programme make people aware that you are coming to the last few structured coaching sessions with something like*:*

As we only have a couple of weeks left on the programme, I just wanted to let you know that we have X amount of 1:1 coaching session left. You can space out the remaining sessions over the coming weeks in whichever way suits you best, however as a heads up these sessions will not continue into the next stage of the programme. You can go ahead and book your next session here [} and please let me know if you have any questions.

Schedule next session - recommended schedule is weekly for the first month, and then once every fortnight thereafter

'We're coming to the end of our 30-minute slot. You can book back in for next week using this link: [insert your calendly link] - remember that you can also continue to discuss this here any day, and I'll get back to you as and when I can.'

ONLY Final Session

Let them know this is the final session:

Just to let you know that this is our final 1:1 coaching session as these sessions will not continue into the next stage of the programme. I've really enjoyed working with you over the past few months, if you have any questions, you can still reach me in the private chat, and I will try to get back to you as soon as possible.

Notes

- If everything is going well, feel free to prompt thought and reflection around planning ahead for any challenges
- For example: "Thinking ahead, do you feel there might be any hurdles or barriers that might prevent you from maintaining your habits in the short term? E.g., an upcoming holiday/birthday/big social outing/restaurant etc"
- "Are there any situations/events that you feel might be a challenge navigating with your new habits and lifestyle?"
- Throughout the session keep reinforcing wins and also compare how they're doing things differently now and how doing things this way is better than before.
- If they've made any unplanned changes that haven't been related to their goals, celebrate that and highlight how they're taking initiative and focusing on what's most important to them. Help them build consistency with this

APPENDIX 4.3: GOAL SETTING STATEMENTS INTERVENTION MATERIALS

Goal Setting Template

Hi everyone,

Today's article emphasises the importance of goal setting for providing a clear direction and focus. To assist you with this, we'd like you to complete an activity this week.

You can view our short video which will explain what's involved and why it's important by clicking the link here.

Once you've watched the video, please complete the template below as a journal entry in the app. It's a great way to focus on your goals and what actions you'll take to get there. I've added some example goals to get you started, but feel free to write your own as you complete your journal entry.

Outcome goal	Examples: • I want to lose [x] amount of weight by [*specific date*] • I want to fit into my favourite jeans/shirt/dress by [*specific date*] or [*specific event*] • I want to reduce my blood sugar levels by [*specific date*] • I want to have more energy by [*specific date*] • I want to improve my fitness levels by [*specific date*] • I want to improve my sleep by [*specific date*]
Process goal	Examples: • I want to have a more structured eating routine • I want to choose the right portion sizes for me • I want to reduce my alcohol intake to [x] drinks per week • I want to drink 2L of water throughout the day • I want to walk [x] steps per day • I want to exercise for at least [x] minutes [y] times per week • I want to get 7-8 hours of sleep each night
Actions	Examples: • Create a meal plan for the week ahead each weekend • Eat three evenly spaced, balanced meals per day • Follow portion size guide for one meal per day • Have one alcohol free night per week • Carry a water bottle with me and refill it often • Start by walking [x] steps per day • Find a fitness class and/or a workout buddy • Set a bedtime routine and stick to it as much as possible

Please let me know if you have any questions or feel free to message me in the private chat!

Reflection Template

This week we have been talking about goal setting. At the end of each week, we are going to be inviting you to pause and reflect on your action goals and the progress you've made through the week. This task is self-guided, allowing you the flexibility to complete it over the weekend or at your convenience.

Regular reflection will help you to focus on what you want to achieve and reinforce your commitment to your goals. It will also allow you to learn from your experiences, both good and bad. Understanding what has worked well and what hasn't, enables you to make informed decisions moving forward.

To make it easier for you, please use the questions below to guide your reflection and write your responses in the journal to keep track of your progress.

- Did you complete the actions you set out to do this week?
- What actions went well?
- What actions didn't go well?
- What did you learn from this week and what will you do differently?

Please let me know if you have any questions or feel free to message me in the private chat!

APPENDIX 4.4: FOOD DIARY REVIEW PLUS FEEDBACK INTERVENTION MATERIALS

Introductory Message

Hi everyone,

Welcome to week 3 where we're focusing on nutrition in practice.

Your task this week is to start monitoring your eating habits using the 'Food diary' in the app. This can be a great way to start recognising patterns in your food choices and increase awareness of your food intake.

You'll also have the opportunity to receive personalised feedback from me on your food diary entries. We have a 2-minute video explaining how to complete your food diary, which you can view by clicking the link here.

(OR use this link if the hyperlink doesn't work:
https://vimeo.com/896967356/101cda4729?share=copy)

Once you have finished logging your meals for the week, please let me know, and I can go in and take a look. I'll aim to send your personalised feedback by the end of next week.

If you have any questions, let me know!

Feedback Template

To be completed by health coach and returned to user in private chat by the end of the following week

“Hi, [insert name],

Thank you so much for filling in the food diary this week. I have just a few of points to consider which will help you progress even further with your health goals:

If you have any questions, do let me know. Otherwise, keep up the great work!”

Points to consider:

- Balanced plate model - ½ veg, ¼ protein, ¼ carbs, and one serving of fat
- Portion sizes - check any photos or recorded food quantities. Remind users they can use the hand portion guide to serve balanced meals.
- Hydration - aim to drink 1-2L of water per day. Suggest energy-free drink alternatives such as flavoured water, sparkling water, or unsweetened tea/coffee.
- Limit caffeine intake within 4-5hrs of sleep or consider switching to decaf. Check any added sugar.
- Limit intake of ultra-processed food - base most of the diet on whole foods. Suggest some healthier food swaps e.g., swapping crisps for veg sticks.
- Meal timing - leave gaps of 3-5 hours between meals and enjoy healthy snacks in between when needed
- Skipping main meals - aim to eat 3 balanced meals per day following the balanced plate model
- Snacking - review current snacks and comment on any healthy swaps or how to build a balanced snack e.g., include a source of protein and/or fat
- Limit alcohol intake - 1-2 drinks max in one sitting, note high sugar drinks (e.g., beer, cider, mixers)
- Check hunger/fullness comments - eat until comfortably full

- Limit sugar intake - note excess consumption of sweet foods, check added sugars in meals and fruit juice etc.

CHAPTER 5: APPENDIX

APPENDIX 5.1: FACTORIAL TRIAL SENSITIVITY ANALYSES TO ASSESS DIFFERENT MISSING DATA ASSUMPTIONS

Table A : Results of mixed effects models examining effects of candidate components on weight loss over a 24-week period, using different missing data approaches.

Term	BOCF (n = 1,335)			LOCF (n = 1,335)		
	Coef	90% CI	P-value	Coef	90% CI	P-value
Week (ref = 0)						
4	-0.71	(-0.8,-0.62)	***<0.001***	-0.71	(-0.8,-0.62)	***<0.001***
16	-0.78	(-0.87,-0.68)	***<0.001***	-1.09	(-1.18,-1.0)	***<0.001***
24	-0.60	(-0.69,-0.51)	***<0.001***	-1.18	(-1.27,-1.09)	***<0.001***
Week4:CS	0	(-0.1,0.09)	0.95	0	(-0.09,0.09)	0.95
Week4:FD	0.05	(-0.04,0.14)	0.37	0.05	(-0.04,0.14)	0.35
Week4:GS	0.01	(-0.08,0.11)	0.81	0.01	(-0.08,0.1)	0.81
Week4:HC	-0.03	(-0.13,0.06)	0.55	-0.03	(-0.12,0.06)	0.54
Week4:CS:FD	-0.06	(-0.15,0.03)	0.31	-0.06	(-0.15,0.03)	0.29
Week4:CS:GS	0.05	(-0.04,0.14)	0.38	0.05	(-0.04,0.14)	0.37
Week4:GS:FD	0.02	(-0.07,0.11)	0.74	0.02	(-0.07,0.11)	0.74
Week4:HC:CS	-0.03	(-0.12,0.06)	0.57	-0.03	(-0.12,0.06)	0.56
Week4:HC:FD	0.05	(-0.04,0.14)	0.37	0.05	(-0.04,0.14)	0.35
Week4:HC:GS	0.01	(-0.08,0.1)	0.84	0.01	(-0.08,0.1)	0.84
Week4:CS:GS:FD	0.04	(-0.05,0.13)	0.48	0.04	(-0.05,0.13)	0.47
Week4:HC:CS:FD	0.02	(-0.07,0.11)	0.71	0.02	(-0.07,0.11)	0.70
Week4:HC:CS:GS	0.02	(-0.08,0.11)	0.78	0.02	(-0.07,0.1)	0.77
Week4:HC:GS:FD	0.02	(-0.07,0.11)	0.72	0.02	(-0.07,0.11)	0.71
Week4:HC:CS:GS:FD	-0.01	(-0.11,0.08)	0.81	-0.01	(-0.1,0.08)	0.81
Week16:CS	-0.01	(-0.1,0.08)	0.82	-0.02	(-0.11,0.06)	0.65
Week16:FD	0.11	(0.03,0.21)	***0.03***	0.12	(0.03,0.21)	***0.03***
Week16:GS	-0.08	(-0.17,0.01)	0.16	-0.06	(-0.15,0.03)	0.25
Week16:HC	-0.05	(-0.14,0.04)	0.39	-0.06	(-0.15,0.03)	0.29
Week16:CS:FD	-0.08	(-0.17,0.02)	0.17	-0.09	(-0.18,-0.0)	0.10
Week16:CS:GS	0.03	(-0.06,0.12)	0.61	0.06	(-0.03,0.15)	0.27
Week16:GS:FD	-0.03	(-0.12,0.06)	0.63	-0.03	(-0.12,0.06)	0.58
Week16:HC:CS	-0.06	(-0.15,0.03)	0.27	-0.06	(-0.15,0.03)	0.27

Week16:HC:FD	0.01	(-0.08,0.1)	0.87	0.05	(-0.04,0.14)	0.38
Week16:HC:GS	0.02	(-0.07,0.12)	0.66	0.02	(-0.07,0.11)	0.77
Week16:CS:GS:FD	0.14	(0.05,0.23)	***0.01***	0.14	(0.05,0.23)	***0.01***
Week16:HC:CS:FD	0	(-0.09,0.09)	0.96	0.01	(-0.07,0.1)	0.79
Week16:HC:CS:GS	0.04	(-0.06,0.13)	0.53	0.05	(-0.04,0.14)	0.34
Week16:HC:GS:FD	0.06	(-0.03,0.15)	0.30	0.05	(-0.03,0.14)	0.32
Week16:HC:CS:GS:FD	0	(-0.09,0.09)	0.98	0.01	(-0.08,0.1)	0.83
Week24:CS	-0.04	(-0.13,0.05)	0.48	-0.06	(-0.15,0.03)	0.29
Week24:FD	0.12	(0.03,0.21)	***0.03***	0.14	(0.05,0.23)	***0.01***
Week24:GS	-0.01	(-0.1,0.08)	0.86	-0.04	(-0.13,0.04)	0.42
Week24:HC	-0.1	(-0.19,-0.01)	***0.07***	-0.13	(-0.22,-0.04)	***0.02***
Week24:CS:FD	-0.11	(-0.21,-0.02)	***0.04***	-0.12	(-0.21,-0.03)	***0.04***
Week24:CS:GS	-0.03	(-0.12,0.07)	0.64	0.03	(-0.06,0.12)	0.56
Week24:GS:FD	0	(-0.09,0.09)	0.96	-0.01	(-0.1,0.08)	0.86
Week24:HC:CS	-0.02	(-0.11,0.07)	0.68	-0.05	(-0.14,0.04)	0.38
Week24:HC:FD	0.08	(-0.01,0.17)	0.15	0.11	(0.02,0.2)	***0.04***
Week24:HC:GS	0.03	(-0.06,0.12)	0.56	0	(-0.09,0.09)	0.97
Week24:CS:GS:FD	0.08	(-0.02,0.17)	0.18	0.13	(0.04,0.22)	***0.02***
Week24:HC:CS:FD	0.01	(-0.08,0.1)	0.86	0.02	(-0.07,0.11)	0.77
Week24:HC:CS:GS	-0.07	(-0.16,0.02)	0.23	0.04	(-0.05,0.13)	0.47
Week24:HC:GS:FD	0.08	(-0.01,0.17)	0.16	0.05	(-0.04,0.13)	0.41
Week24:HC:CS:GS:FD	0	(-0.09,0.1)	0.95	-0.01	(-0.1,0.08)	0.82

Main effects at baseline (time zero) do not test the hypotheses of interest and have been omitted from the table for brevity. All models used effect coding. Reported coefficients represent half the difference between component levels; multiply by 2 for the full effect size. Missing data were imputed by carrying forward the baseline weight (BOCF) or carrying forward the last-measured weight (LOCF). Significant effects (p<.10) are highlighted in bold. Abbreviations: BOCF = baseline observation carried forward; CS = coaching drop-in webchat sessions; FD = food diary review and feedback; GS = goal setting statements; HC = health coach introductory video call; LOCF: last observation carried forward.

APPENDIX 5.2: FACTORIAL TRIAL SUBGROUP ANALYSES BY GENDER, AGE, IMD TERTILE, AND BMI CATEGORY

Table B : Subgroup analysis by gender. Results of mixed effects models examining effects of candidate components on weight loss over a 24-week period, comparing females (n = 1205) to males (n = 130).

Term	All Data (n = 1,335)		
	Coef	90% CI	P-value
Week (ref = 0)			
4	-1.31	(-1.5, -1.12)	***<0.001***
16	-2.58	(-2.83, -2.34)	***<0.001***
24	-2.89	(-3.17, -2.61)	***<0.001***
Gender (ref = female)			
Male	16.42	(13.4, 19.44)	***<0.001***
Interaction terms			
Week4:Male	-0.39	(-1.07, 0.29)	0.35
Week4:CS	-0.05	(-0.24, 0.14)	0.66
Week4:Male:CS	0.15	(-0.53, 0.82)	0.72
Week4:FD	0.05	(-0.14, 0.23)	0.68
Week4:Male:FD	-0.09	(-0.81, 0.64)	0.84
Week4:GS	0.07	(-0.12, 0.26)	0.53
Week4:Male:GS	-0.34	(-1.04, 0.35)	0.41
Week4:HC	-0.04	(-0.22, 0.15)	0.76
Week4:Male:HC	-0.35	(-1.06, 0.37)	0.42
Week16:Male	-0.64	(-1.58, 0.3)	0.27
Week16:CS	-0.1	(-0.34, 0.15)	0.53
Week16:Male:CS	0.55	(-0.34, 1.44)	0.31
Week16:FD	0.18	(-0.07, 0.43)	0.24
Week16:Male:FD	0.80	(-0.11, 1.71)	0.15
Week16:GS	-0.16	(-0.4, 0.09)	0.30
Week16:Male:GS	-0.17	(-1.17, 0.83)	0.78
Week16:HC	-0.26	(-0.5, -0.01)	***0.09***
Week16:Male:HC	0.61	(-0.3, 1.53)	0.27
Week24:Male	0.26	(-0.91, 1.43)	0.72
Week24:CS	-0.25	(-0.53, 0.03)	0.14
Week24:Male:CS	0.56	(-0.49, 1.62)	0.38

Week24:FD	0.31	(0.04, 0.59)	***0.06***
Week24:Male:FD	-0.16	(-1.24, 0.93)	0.81
Week24:GS	0.03	(-0.25, 0.31)	0.87
Week24:Male:GS	-1.54	(-2.74, -0.35)	***0.034***
Week24:HC	-0.58	(-0.86, -0.3)	***<0.001***
Week24:Male:HC	0.84	(-0.22, 1.9)	0.19

Main effects at baseline (time zero) do not test the hypotheses of interest and have been omitted from the table for brevity. All models used effect coding. Reported coefficients represent half the difference between component levels; multiply by 2 for the full effect size. Significant effects ($p < .10$) are highlighted in bold. Subgroup effects were tested by adding gender into the primary linear mixed-effect model and estimating three-way interactions between time, intervention component, and gender. Abbreviations: CS = coaching drop-in webchat sessions; FD = food diary review and feedback; GS = goal setting statements; HC = health coach introductory video call.

Table C : Subgroup analysis by age. Results of mixed effects models examining effects of candidate components on weight loss over a 24-week period, comparing participants above (n = 684) and below (n = 632) the median age of 50 years.

Term	All Data (n = 1,316)		
	Coef	90% CI	P-value
Week (ref = 0)			
4	-1.28	(-1.53, -1.04)	***<0.001***
16	-2.38	(-2.70, -2.06)	***<0.001***
24	-2.41	(-2.77, -2.06)	***<0.001***
Age (ref = > 50 years)			
Age <50 years	2.88	(1.08, 4.69)	***0.01***
Interaction terms			
Week4:Age <50 years	-0.17	(-0.53, 0.20)	0.45
Week4:CS	-0.08	(-0.33, 0.17)	0.59
Week4:Age <50 years:CS	0.12	(-0.25, 0.49)	0.60
Week4:FD	-0.04	(-0.29, 0.21)	0.77
Week4:Age <50 years:FD	0.17	(-0.20, 0.54)	0.45
Week4:GS	0.06	(-0.19, 0.31)	0.69
Week4:Age <50 years:GS	-0.06	(-0.43, 0.31)	0.79
Week4:HC	-0.02	(-0.27, 0.23)	0.88
Week4:Age <50 years:HC	-0.07	(-0.44, 0.29)	0.75
Week16:Age <50 years	-0.69	(-1.18, -0.21)	***0.02***
Week16:CS	-0.24	(-0.56, 0.08)	0.22
Week16:Age <50 years:CS	0.53	(0.04, 1.02)	***0.08***
Week16:FD	0.21	(-0.11, 0.53)	0.28
Week16:Age <50 years:FD	-0.12	(-0.61, 0.37)	0.70
Week16:GS	-0.21	(-0.54, 0.11)	0.28
Week16:Age <50 years:GS	0.21	(-0.28, 0.70)	0.48
Week16:HC	-0.17	(-0.49, 0.16)	0.40
Week16:Age <50 years:HC	-0.20	(-0.68, 0.29)	0.50
Week24:Age <50 years	-1.18	(-1.72, -0.64)	***<0.001***
Week24:CS	-0.19	(-0.55, 0.18)	0.40
Week24:Age <50 years:CS	0.06	(-0.49, 0.60)	0.87
Week24:FD	0.26	(-0.11, 0.62)	0.25
Week24:Age <50 years:FD	0.01	(-0.55, 0.56)	0.99
Week24:GS	-0.14	(-0.51, 0.23)	0.52
Week24:Age <50 years:GS	0.22	(-0.33, 0.77)	0.51

Week24:HC	-0.46	(-0.82, -0.09)	***0.04***
Week24:Age <50 years:HC	-0.15	(-0.70, 0.39)	0.65

Main effects at baseline (time zero) do not test the hypotheses of interest and have been omitted from the table for brevity. All models used effect coding. Reported coefficients represent half the difference between component levels; multiply by 2 for the full effect size. Significant effects ($p < .10$) are highlighted in bold. Subgroups were determined based on the median age of the study population (50 years). Subgroup effects were tested by adding age subgroup into the primary linear mixed-effect model and estimating three-way interactions between time, intervention component, and age subgroup. $n = 19$ had missing data for age. Abbreviations: CS = coaching drop-in webchat sessions; FD = food diary review and feedback; GS = goal setting statements; HC = health coach introductory video call.

Table D : Subgroup analysis by IMD tertile. Results of mixed effects models examining effects of candidate components on weight loss over a 24-week period, comparing participants with IMD 1-6 (n = 404), to participants with IMD 6-8 (n = 403) and participants with IMD 8-10 (n = 403).

Term	All Data (n = 1,210)		
	Coef	90% CI	P-value
Week (ref = 0)			
4	-1.37	(-1.7, -1.05)	***<0.001***
16	-3.43	(-3.86, -2.99)	***<0.001***
24	-3.41	(-3.9, -2.92)	***<0.001***
IMD Tertile (ref = Low [1-6])			
IMD_Medium (6-8)	-1.94	(-4.25, 0.38)	0.17
IMD_High (8-10)	-4.37	(-6.69, -2.05)	***0.002***
Interaction terms			
Week4:IMD_Medium	-0.03	(-0.49, 0.44)	0.92
Week4:IMD_High	-0.03	(-0.49, 0.44)	0.92
Week4:CS	-0.01	(-0.34, 0.31)	0.94
Week4:IMD_Medium:CS	0.03	(-0.43, 0.5)	0.91
Week4:IMD_High:CS	-0.15	(-0.61, 0.31)	0.60
Week4:FD	-0.06	(-0.39, 0.26)	0.75
Week4:IMD_Medium:FD	0.20	(-0.26, 0.67)	0.48
Week4:IMD_High:FD	0.09	(-0.37, 0.56)	0.74
Week4:GS	-0.13	(-0.45, 0.19)	0.51
Week4:IMD_Medium:GS	0.26	(-0.2, 0.73)	0.35
Week4:IMD_High:GS	0.23	(-0.23, 0.69)	0.40
Week4:HC	-0.12	(-0.45, 0.21)	0.55
Week4:IMD_Medium:HC	0.11	(-0.36, 0.58)	0.70
Week4:IMD_High:HC	-0.04	(-0.5, 0.43)	0.89
Week16:IMD_Medium	0.61	(-0.01, 1.22)	0.11
Week16:IMD_High	1.16	(0.54, 1.78)	***0.002***
Week16:CS	-0.36	(-0.79, 0.07)	0.17
Week16:IMD_Medium:CS	0.52	(-0.09, 1.14)	0.16
Week16:IMD_High:CS	0.04	(-0.58, 0.65)	0.92
Week16:FD	0.06	(-0.38, 0.5)	0.81
Week16:IMD_Medium:FD	0.32	(-0.31, 0.94)	0.40
Week16:IMD_High:FD	0.20	(-0.42, 0.82)	0.60
Week16:GS	-0.69	(-1.12, -0.26)	***0.009***
Week16:IMD_Medium:GS	0.68	(0.07, 1.3)	***0.07***
Week16:IMD_High:GS	0.60	(-0.01, 1.22)	0.11
Week16:HC	0.01	(-0.43, 0.45)	0.97

Week16:IMD_Medium:HC	-0.27	(-0.89, 0.35)	0.48
Week16:IMD_High:HC	-0.32	(-0.94, 0.3)	0.39
Week24:IMD_Medium	0.23	(-0.45, 0.91)	0.58
Week24:IMD_High	0.31	(-0.4, 1.03)	0.47
Week24:CS	-0.66	(-1.15, -0.17)	***0.03***
Week24:IMD_Medium:CS	0.69	(0.01, 1.37)	0.10
Week24:IMD_High:CS	0.58	(-0.13, 1.29)	0.18
Week24:FD	-0.04	(-0.54, 0.45)	0.89
Week24:IMD_Medium:FD	0.26	(-0.42, 0.95)	0.53
Week24:IMD_High:FD	0.92	(0.21, 1.63)	***0.034***
Week24:GS	-1.39	(-1.88, -0.91)	***<0.001***
Week24:IMD_Medium:GS	1.74	(1.06, 2.42)	***<0.001***
Week24:IMD_High:GS	2.01	(1.3, 2.72)	***<0.001***
Week24:HC	-0.39	(-0.89, 0.12)	0.21
Week24:IMD_Medium:HC	0.11	(-0.58, 0.79)	0.80
Week24:IMD_High:HC	-0.65	(-1.37, 0.07)	0.14

Main effects at baseline (time zero) do not test the hypotheses of interest and have been omitted from the table for brevity. All models used effect coding. Reported coefficients represent half the difference between component levels; multiply by 2 for the full effect size. Significant effects ($p < .10$) are highlighted in bold. Subgroups were determined based on tertiles from the total study population. The lowest tertile included IMD 1-6, the middle tertile included IMD 6-8, and the highest tertile included IMD 8-10. Subgroup effects were tested by adding IMD subgroup into the primary linear mixed-effect model and estimating three-way interactions between time, intervention component, and IMD subgroup. $n = 125$ had missing data for IMD. Abbreviations: CS = coaching drop-in webchat sessions; FD = food diary review and feedback; GS = goal setting statements; HC = health coach introductory video call; IMD = index of multiple deprivation.

Table E : Subgroup analysis by BMI category. Results of mixed effects models examining effects of candidate components on weight loss over a 24-week period, comparing participants with BMI 21-25kg/m² (n = 119), to participants with overweight BMI 25-30 kg/m² (n = 454) and participants with obesity BMI > 30kg/m² (n = 758).

Term	All Data (n = 1,331)		
	Coef	90% CI	P-value
Week (ref = 0)			
4	-1.02	(-1.68, -0.37)	***0.01***
16	-1.77	(-2.69, -0.84)	***0.002***
24	-1.67	(-2.61, -0.73)	***0.003***
BMI Category (ref = 21-25kg/m²)			
Overweight (BMI 25-30 kg/m²)	10.58	(8.01, 13.14)	***<0.001***
Obesity (BMI > 30kg/m²)	34.49	(32.03, 36.96)	***<0.001***
Interaction terms			
Week4:Overweight	-0.11	(-0.83, 0.61)	0.80
Week4:Obesity	-0.54	(-1.23, 0.16)	0.20
Week4:CS	-0.02	(-0.68, 0.64)	0.97
Week4:Overweight:CS	0.02	(-0.71, 0.75)	0.96
Week4:Obesity:CS	-0.01	(-0.71, 0.69)	0.98
Week4:FD	0.13	(-0.54, 0.8)	0.74
Week4:Overweight:FD	-0.24	(-0.98, 0.49)	0.59
Week4:Obesity:FD	-0.01	(-0.72, 0.7)	0.97
Week4:GS	-0.22	(-0.89, 0.45)	0.59
Week4:Overweight:GS	0.23	(-0.5, 0.96)	0.61
Week4:Obesity:GS	0.29	(-0.42, 1.0)	0.50
Week4:HC	-0.11	(-0.79, 0.56)	0.79
Week4:Overweight:HC	0.02	(-0.72, 0.76)	0.96
Week4:Obesity:HC	0.05	(-0.67, 0.76)	0.91
Week16:Overweight	-0.22	(-1.23, 0.78)	0.72
Week16:Obesity	-1.39	(-2.37, -0.42)	***0.02***
Week16:CS	0.36	(-0.59, 1.31)	0.54
Week16:Overweight:CS	-0.41	(-1.45, 0.62)	0.51
Week16:Obesity:CS	-0.48	(-1.48, 0.53)	0.44
Week16:FD	0.26	(-0.68, 1.2)	0.65
Week16:Overweight:FD	-0.37	(-1.39, 0.65)	0.55
Week16:Obesity:FD	0.14	(-0.85, 1.13)	0.81
Week16:GS	-0.19	(-1.14, 0.77)	0.75

Week16:Overweight:GS	-0.20	(-1.23, 0.84)	0.76
Week16:Obesity:GS	0.05	(-0.95, 1.06)	0.93
Week16:HC	-0.66	(-1.6, 0.28)	0.25
Week16:Overweight:HC	0.52	(-0.5, 1.54)	0.40
Week16:Obesity:HC	0.39	(-0.6, 1.38)	0.52
Week24:Overweight	-0.60	(-1.64, 0.44)	0.34
Week24:Obesity	-1.92	(-2.92, -0.92)	***0.002***
Week24:CS	0.20	(-0.84, 1.24)	0.75
Week24:Overweight:CS	-0.40	(-1.54, 0.73)	0.56
Week24:Obesity:CS	-0.51	(-1.61, 0.59)	0.44
Week24:FD	0.49	(-0.57, 1.56)	0.45
Week24:Overweight:FD	-0.39	(-1.55, 0.76)	0.58
Week24:Obesity:FD	-0.14	(-1.26, 0.99)	0.84
Week24:GS	-0.69	(-1.77, 0.39)	0.29
Week24:Overweight:GS	0.56	(-0.61, 1.73)	0.43
Week24:Obesity:GS	0.68	(-0.46, 1.82)	0.32
Week24:HC	-0.57	(-1.64, 0.5)	0.38
Week24:Overweight:HC	0.43	(-0.72, 1.59)	0.54
Week24:Obesity:HC	-0.33	(-1.46, 0.8)	0.63

Main effects at baseline (time zero) do not test the hypotheses of interest and have been omitted from the table for brevity. All models used effect coding. Reported coefficients represent half the difference between component levels; multiply by 2 for the full effect size. Significant effects ($p < .10$) are highlighted in bold. Subgroup effects were tested by adding BMI category into the primary linear mixed-effect model and estimating three-way interactions between time, intervention component, and BMI category. *n* = 4 had missing data for height so baseline BMI could not be calculated. Abbreviations: BMI = body mass index; CS = coaching drop-in webchat sessions; FD = food diary review and feedback; GS = goal setting statements; HC = health coach introductory video call.

CHAPTER 6: APPENDIX

APPENDIX 6.1: EXAMPLE MEDLINE SEARCH STRATEGY

	Medline
1	Weight Reduction Programs/ and (intermittent or break? or pause? or interrupt? or disrupt?).mp.
2	(caloric restriction/ or diet, reducing/) and (intermittent or break? or pause? or interrupt? or disrupt?).mp.
3	(((calor* or energy or diet) adj3 (restrict* or reduc*)) and (intermittent or break? or pause? or interrupt? or disrupt?)).mp.
4	(dieting and (intermittent or break? or pause? or interrupt? or disrupt?)).mp.
5	(intermittent adj5 (fast* or diet* or restrict* or food depriv* or calori* or low-calorie*)).mp.
6	(intermittent energy adj5 (fast* or diet* or restrict* or food depriv*)).mp.
7	(periodic adj5 (fast* or diet* or restrict* or food depriv*)).mp.
8	((pause? or break? or interrupt? or disrupt?) adj5 (weight adj3 (chang* or loss or maintain* or maintenance or control or management))).mp.
9	((pause? or break? or interrupt? or disrupt?) adj5 ((weight or obes* or overweight) adj10 (intervention? or program*))).mp.
10	((pause? or break? or interrupt? or disrupt?) adj5 ((lifestyle or lifestyle or behav* or diet* or nutrition* or health* eating) adj10 (intervention? or program*))).mp.
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	body weight changes/ or weight loss/
13	body mass index/ or waist-hip ratio/ or Waist Circumference/ or exp Body Composition/
14	(weight adj3 (chang* or loss or lose or losing or maintain* or maintenance or decreas* or reduc* or improv*)).ti,ab,kw.
15	(body weight or body fat or fat mass or body composition or body mass index or bmi or "waist hip ratio" or "waist to hip ratio" or waist circumference).ti,ab,kw.

16	12 or 13 or 14 or 15
17	11 and 16
18	randomized controlled trial.pt.
19	controlled clinical trial.pt.
20	randomized.ab.
21	placebo.ab.
22	drug therapy.fs.
23	randomly.ab.
24	trial.ab.
25	groups.ab.
26	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27	exp animals/ not humans.sh.
28	26 not 27

APPENDIX 6.2: SUBGROUP ANALYSES FOR ATTRITION RATE CATEGORISED BY PAUSE INTERVAL DURATION OR DIETARY REGIMEN IN PAUSE INTERVAL

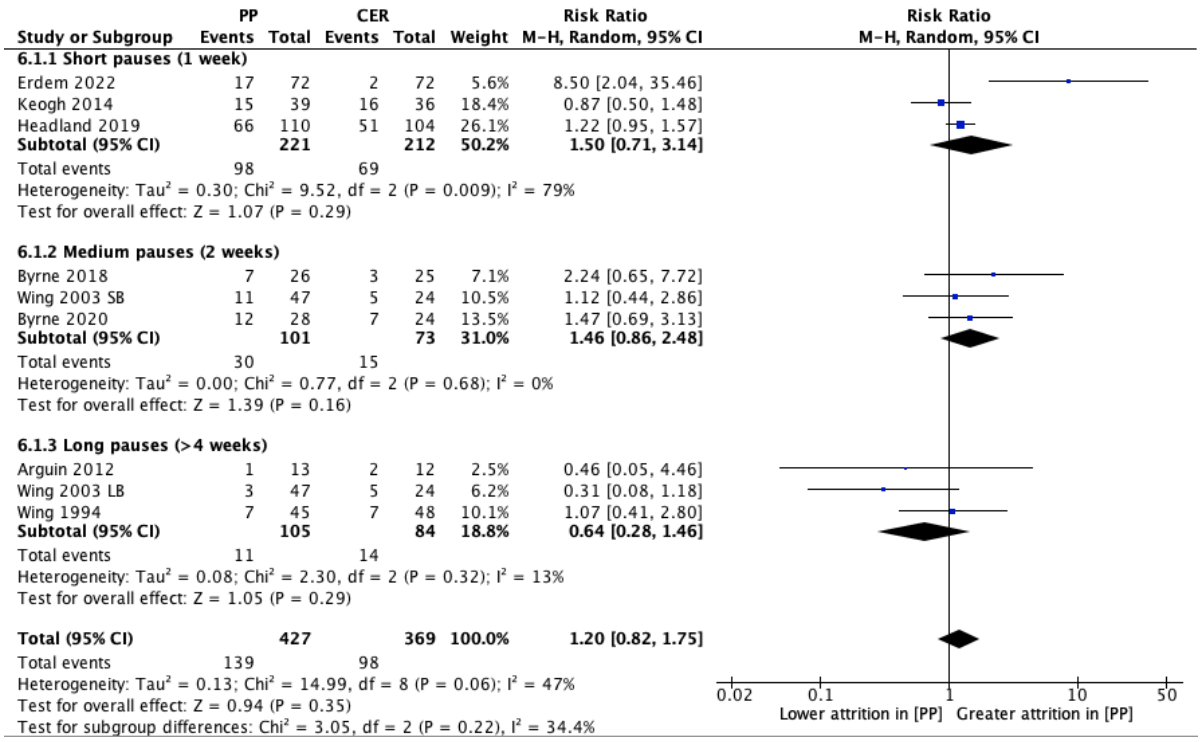


Figure A: Forest plot showing mean risk ratio of attrition at the end of the active intervention in planned pause (PP) interventions versus continuous energy restriction (CER) by pause interval duration. A risk ratio > 1 indicates greater attrition in the PP arm compared to CER, and a risk ratio < 1 indicates lower attrition in the PP arm compared to CER.

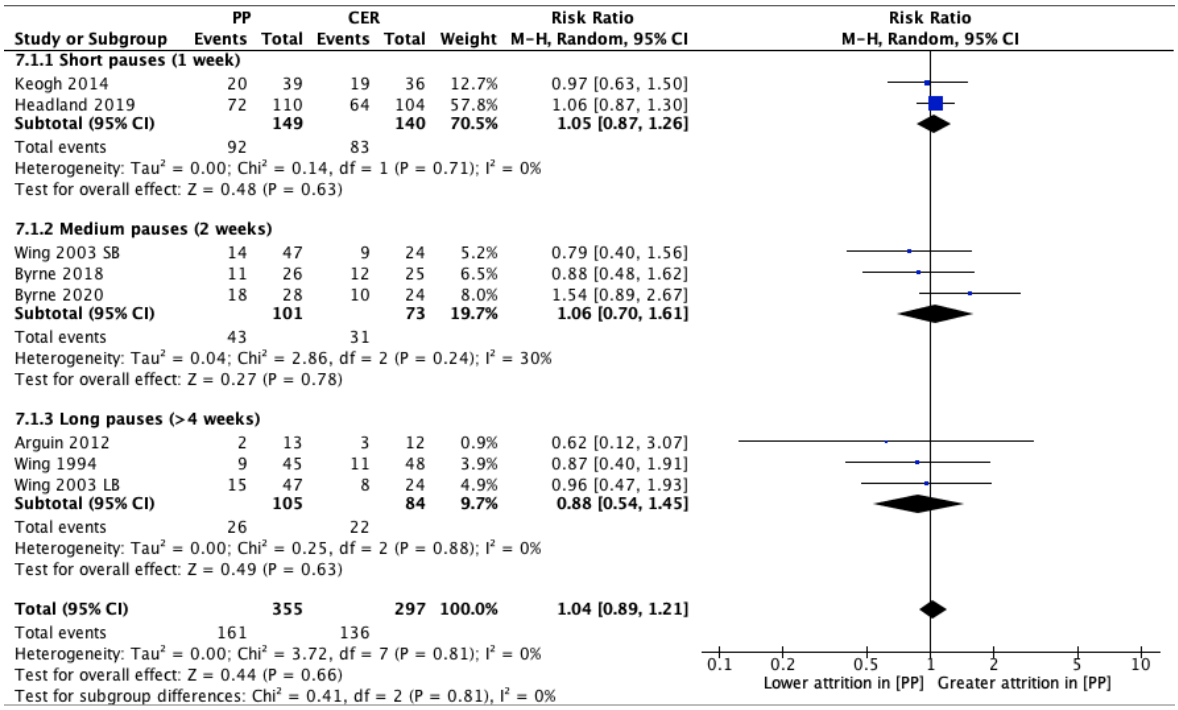


Figure B: Forest plot showing mean risk ratio of attrition at the final follow up in planned pause (PP) interventions versus continuous energy restriction (CER) by pause interval duration. A risk ratio > 1 indicates greater attrition in the PP arm compared to CER, and a risk ratio < 1 indicates lower attrition in the PP arm compared to CER.

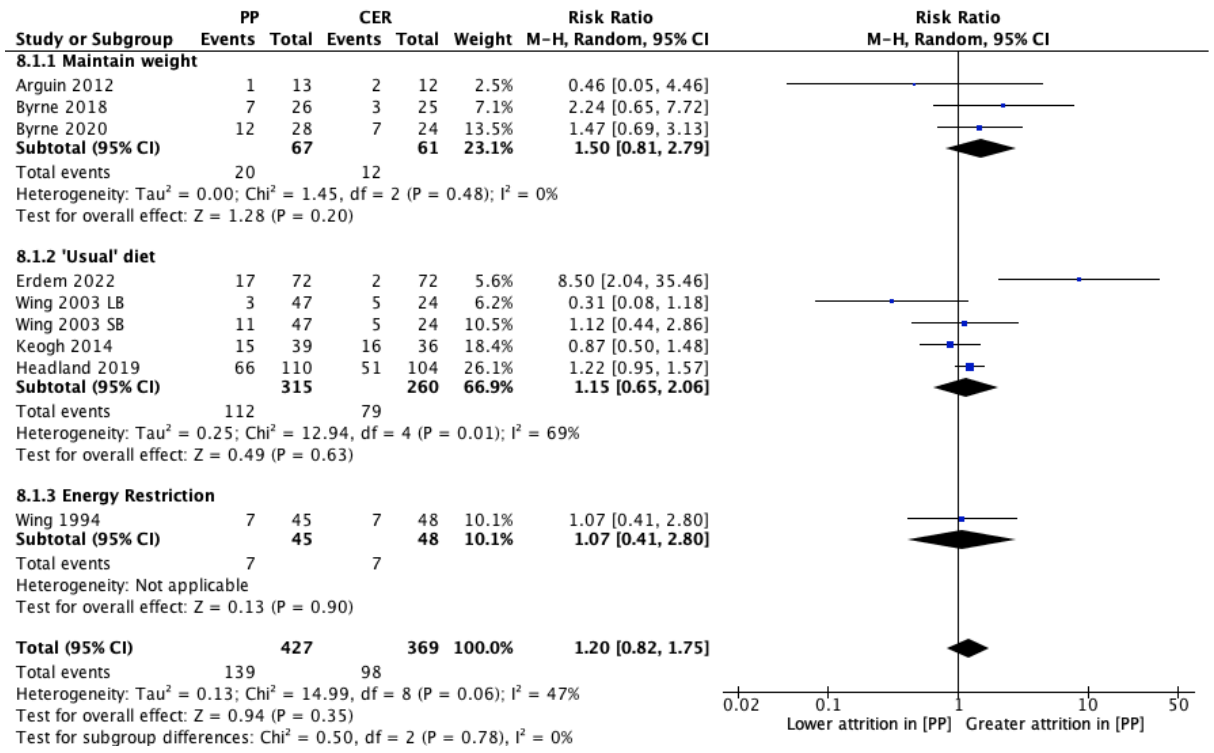


Figure C: Forest plot showing mean risk ratio of attrition at the end of the active intervention in planned pause (PP) interventions versus continuous energy restriction (CER) by dietary regimen in pause interval. A risk ratio > 1 indicates greater attrition in the PP arm compared to CER, and a risk ratio < 1 indicates lower attrition in the PP arm compared to CER.

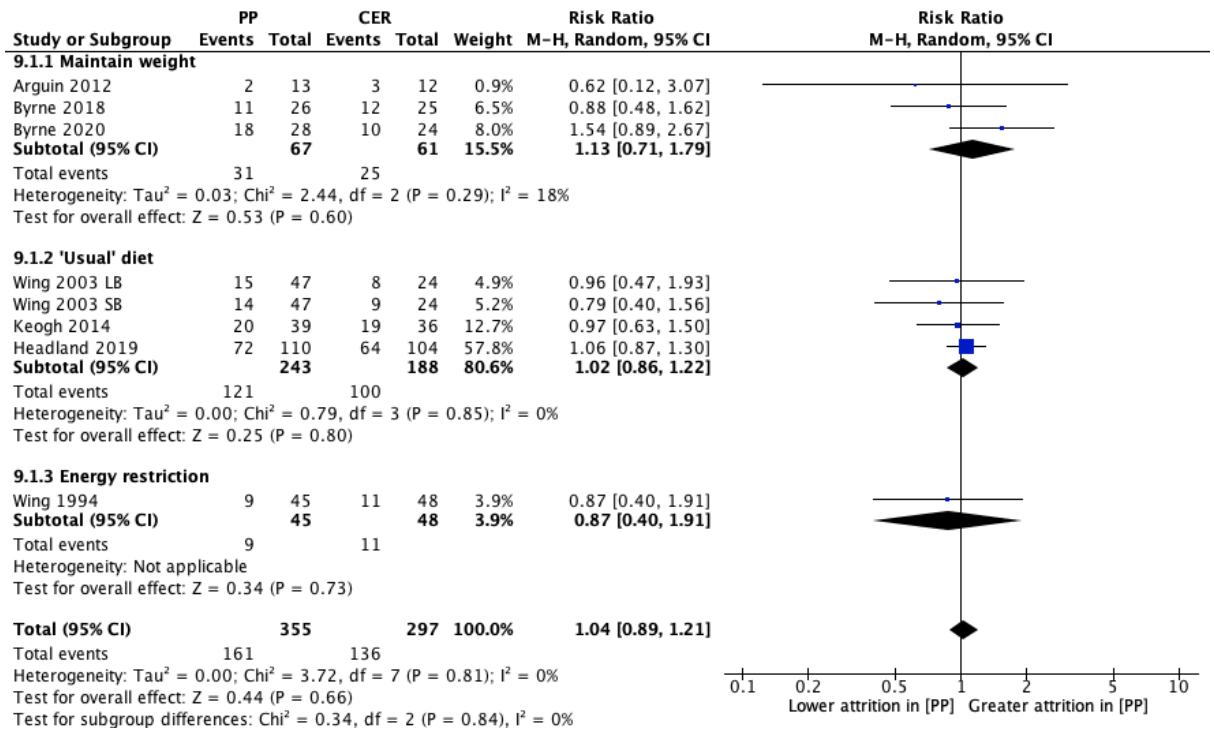


Figure D: Forest plot showing mean risk ratio of attrition at the final follow up in planned pause (PP) interventions versus continuous energy restriction (CER) by dietary regimen in pause interval. A risk ratio > 1 indicates greater attrition in the PP arm compared to CER, and a risk ratio < 1 indicates lower attrition in the PP arm compared to CER.