NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES

UNIVERSITY OF OXFORD

STATISTICAL ANALYSIS PLAN

Study Title:

Adults Regulating Their weight Everyday with Mobile Internet Support (ARTEMIS)

NCT number: NCT05787652

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Version History

Version:	Version Date:	Changes:
1.0	**2nd June 2023**	
2.0	**1st June 2024**	• Final follow-up moved from 52 to 26 weeks due to low retention, meaning the primary outcome changed. • Process measures altered due to data availability. • Definition of per-protocol analysis altered.

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INTRODUCTION

BACKGROUND

A recent pilot study (People REgulating themselVes to Achieve weIght Loss (PREVAIL)) examined the effectiveness of an iterative computerised self-regulation intervention to promote weight loss among adults living with obesity (1). The intervention involved daily self-weighing, daily weight recording, daily action planning, weekly weight change reports, and weekly reflection, compared to a control group who solely engaged in daily self-weighing. A significant difference was observed in mean weight change between the self-regulation intervention (-4.2 kg) and the control group (-1.0 kg) at eight-week follow up (Δ= -3.2 kg (95% CI=4.5, - 1.9), p <0.05. Participants in the self-regulation intervention group, rated the intervention's usefulness to aid in promoting weight loss as 8.3/10 (SD = 2.0). While promising, further evidence that the intervention leads to long-term benefits among a more representative sample, and is safe to deliver, is required before widespread implementation. Further, participants communicated directly with a sole researcher throughout the trial period, which may have introduced researcher bias i.e., led to participants feeling committed to the project and the intervention, which may have overestimated the true benefit, and limited the external validity of findings. This present study will build upon the pilot study with a larger scale, randomised controlled trial examining the effectiveness of the self-regulation intervention to promote weight loss, when delivered through a mobile application, with no in-person contact.

STUDY OVERVIEW

This is a parallel group, randomised, controlled superiority trial among community-dwelling adults. This study aims to test the effectiveness of an online self-regulation intervention to promote weight loss among adults living with obesity. Approximately 1,500 adults ≥18 years of age, living with BMI ≥ 30 kg/m^2 (if of white ethnicity; ≥ 27.5 for all other ethnic groups), will be randomly allocated to either the self-regulation intervention or a no treatment control on a 1:1 basis. Participation lasts 26 weeks. The intervention is the ARTEMIS app which will guide participants through the self-regulation process, and prompt them to weigh daily, track their weight, plan daily actions for weight loss, and reflect on their action plans on a weekly basis. Participants can explore and engage in all these actions for as long as they wish within the 26-weeks of the intervention but will be recommended to continue within the 'active exploratory phase' of the intervention for at least four weeks, before moving to a 'maintenance phase', where they continue with the actions which worked best for them in the 'active exploratory phase'. Control group participants will receive no intervention. All participants, in both experimental testing conditions, will be asked to complete four assessments: at baseline, 12- and 26-week follow up. At each assessment, participants will be asked to report their weight, complete a six-item disordered eating questionnaire (modified Eating Disorders Examination – Questionnaire Short) Form (EDE-QS), and a study specific weight management questionnaire. Process measures will be collected throughout the intervention period.

OBJECTIVES

Primary

The primary aim of this study is to examine the effectiveness of a computerised online self-regulation intervention to promote weight loss among adults living with obesity, at 26 weeks, comparing the intervention with a no-treatment control.

Secondary

The secondary aim is to examine the effectiveness of the intervention to promote weight loss in the short term (12 weeks), as well as to examine the safety of the intervention by assessing if it affects disordered eating behaviours, comparing intervention and control groups.

Process evaluation

A mix of quantitative and qualitative measures will be used to undertake a process evaluation of the intervention. This will include a quantitative assessment of participants' engagement with the intervention. The resulting measures will be used to assess whether engagement with the intervention is predictive of weight change. Qualitative analysis of the free-text responses to the daily action completion question inputting into the app, will help to evaluate any barriers to completing the daily action planning.

STUDY DESIGN

OUTCOME MEASURES

PRIMARY OUTCOME

Primary Objective	Measures	Timepoints
To assess if the intervention achieves significantly greater weight loss than the no-treatment control group assessed by co-primary outcomes	Change in body weight Proportion of participant achieving 5% loss in body weight	Baseline, 26 weeks Baseline, 26 weeks

SECONDARY OUTCOMES

Objectives	Measures	Timepoints
To assess if the intervention achieves significantly greater weight loss than the no-treatment control group in the short-term	Change in body weight Proportion of participants achieving > 5% loss in body weight	Baseline, 12 weeks Baseline, 12 weeks
To assess the impact of self-regulation intervention on disordered weight control	Change in the proportion of participants scoring above threshold (>7) on the modified Eating Disorders Examination - Questionnaire Short Form (EDE-QS) questionnaire	Baseline, 12, 26 weeks

PROCESS EVALUATION

Objectives	Measures	Timepoints
To assess whether the intervention engaged participants	Number of days with any app engagement Number of daily weight readings Number of daily actions selected Number of daily action plans Number of weekly reflections completed Proportion of daily action plans successfully completed Perceived barriers to non-completion of daily action plans Assessment of other weight management programmes accessed	Throughout the intervention period (26 weeks)

BLINDING IN THE ANALYSIS STAGE

All follow-up is done remotely and will therefore be unbiased, and members of the research team analysing the primary outcome will be blind to group allocation.

ANALYSIS – GENERAL CONSIDERATIONS

Quantitative analysis will be carried out using R Studio, version 4.2.1. All of the analyses will be done at a 5% two-sided significance level.

DATA CLEANING AND PREPARATION

Prior to the data analysis, data cleaning will be performed, including checking that all appropriate data has been reported.

DERIVED VARIABLES

User engagement

User engagement from baseline to 26 weeks will be calculated for each participant. We will calculate the following variables:

Number of days with any app engagement: calculated as the number of days with at least one engagement in the intervention period and treated as a continuous variable.

Number of daily weight readings: calculated as the number of weight readings entered in the app and treated as a continuous variable.

Number of daily actions selection: calculated as the number of daily actions selected and treated as a continuous variable.

Number of daily action plans: calculated as the number of daily action plans completed and treated as a continuous variable.

Number of weekly reflections: calculated as the number of weekly reflections completed and treated as a continuous variable.

Successful completion of daily action plans: calculated as the percentage of daily action plans successfully completed in the 'exploratory phase' of the intervention. Calculated as follows: number of days where participants have responded 'yes' to completing their daily action plans/total number of action plans completed*100.

MODEL ASSUMPTIONS

All model assumptions will be checked before analysis and if assumptions are not met an appropriate transformation will be applied. For the primary analysis, the normality of all model residuals will be assessed using histograms. Where model assumptions are not met, an appropriate transformation will be applied.

DESCRIPTIVE STATISTICS

A table will present the baseline characteristics overall and by group allocation (Appendix 1).

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

PRIMARY & SECONDARY ANALYSIS

Before analysis of outcomes, we will assess the association between baseline variables and loss to follow-up at 26 weeks. Any variables that are associated with loss to follow-up will be included as covariates.

PRIMARY OUTCOME

The statistical analysis of the primary outcome, effectiveness of the intervention for weight loss, will be prioritised based on intention-to-treat (ITT). For the ITT analysis, participants will be analysed according to their allocated group (control or intervention). We will endeavour to obtain full follow-up data on every participant to allow full ITT analysis, by sending text/email reminders and calling the participant where necessary.

Where this is not possible, we will assess 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). We will also conduct per-protocol (PP) analysis, we will include only 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

Mixed-model repeated-measures analyses will be used to assess weight change from baseline, over the 26-week period. The primary outcome will be weight at 26 weeks. A between-subjects factor of condition, a within-subjects factor of week, and the interaction between week and condition will be included as fixed effects, to assess whether weight at each time point differed from baseline. Participant ID will be included as a random effect to account for the repeated weight measures on the same participant at 12 and 26 weeks. Secondary dependent variables regarding the proportion of participants achieving a > 5% loss in body weight from baseline to 12- and 26 weeks will be assessed using analogous logistic models. We will also conduct sensitivity analysis excluding those who utilised other effective strategies for weight loss.

Further we will conduct exploratory subgroup analyses by age, sex, level of education attainment, employment status, indices of multiple deprivation (IMD) decile, and ethnicity.

SECONDARY OUTCOMES

Analysis of change in the proportion of participants scoring above the threshold (>7) on the modified EDE-QS will be assessed as a binary variable by logistic regression at each follow-up time point (12 and 26 weeks).

PROCESS EVALUATION

For quantitative process outcomes, means and standard deviations of user engagement rates, will be descriptively assessed. We will also descriptively assess the actions participants used to manage their weight, including accessing other weight management programmes.

EXPLORATORY ANALYSES

Engagement: to analyse whether engagement predicts weight change from baseline to week 26, we will use a multivariable linear regression model with weight change as the dependent variable and all possible predictors included in one single model. Possible predictors are: 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.

Barriers to daily action planning: the free-text responses to the daily action completion question will be analysed. Responses will be analysed qualitatively using content analysis. With responses coded and then grouped into broader categories of shared meaning.

APPENDICES

Appendix 1. Template tables for presentation of results

Baseline Demographic Characteristics

N (%), unless otherwise specified	**Control (n=)**	**Intervention (n=)**	**Total (n=)**
Age, years, mean (SD)			
Gender, % female			
BMI, kg/m^2, mean (SD)			
Ethnicity			
Asian or Asian British			
Black or Black British			
Mixed or multiple ethnic groups			
White			
Other/prefer not to say			
IMD decile			
1-3			
4-7			
8-10			
Highest Educational Qualification			
No formal qualifications			
GCSE/O-level			
A levels/BTEC			
Undergraduate/postgraduate degree			
Prefer not to say			
Employment Status			
Employed			
Self-employed			
Unemployed			
Looking after home and family			
In education or training			
Retired			
Long-term sick or disabled			
Other			
Proportion scoring >7 on EDE-QS			

Primary (weight change & proportion achieving 5% loss in body weight) and secondary outcome (proportion scoring above threshold (>7) on the EDE-QS) by group allocation

Mixed-model repeated-measures analyses

		Intervention (n =)	Control (n =)	Adjusted difference (95% CI)	*P value*
12 weeks	Weight (kg), mean (SD)				
	N (%) lost ≥5% weight				
	N (%) >7 on the EDE-QS				
26 weeks	Weight (kg), mean (SD)				
	N (%) lost ≥5% weight				
	N (%) >7 on the EDE-QS				

Process Evaluation

Engagement

Intervention Component	**Mean (SD)**
Number of days with any activity	
Number of daily weight readings	
Number of daily actions selected	
Number of daily action plans	
Percentage of actions successfully completed	
Number of weekly reflections	

Exploratory Analysis

Multivariable regression

	B	95% CI	P value
Number of days with any activity			
Number of daily weight readings			
Number of daily actions selected			
Number of daily action plans			
Percentage of actions successfully completed			
Number of weekly reflections			

1. Frie K, Hartmann-Boyce J, Jebb SA, Aveyard P. Effectiveness of a self-regulation intervention for weight loss: A randomized controlled trial. Br J Health Psychol. 2020;25(3):652-76.