**Statistical Analysis Plan**

**Supporting Weight Management during COVID-19 (SWiM-C)**

Scientific title: An acceptance-based programme for weight management during the COVID-19 pandemic in people with overweight and obesity (SWiM-C Study).

Trial registration number: ISRCTN 12107048

**SAP revision history**

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| --- | --- | --- |
| **Date** | **Version** | **Justification for SAP version** |
| 20/01/2021 | 1.0 | First draft sent out to AA and SJS |
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| 09/03/2021 | 4.0 | Incorporated comments by RAJ, AJH, JW, CAH, RR, |
| 10/03/2021 | 5.0 | Incorporated comments by SG |

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# 1 Introduction

## 1.1 Trial background and rationale

The social distancing and isolation measures imposed during the COVID-19 pandemic beginning March 2020, including the closure or reduced operating of some weight management programmes and services, mean that adults with overweight and obesity in the UK are at increasing vulnerability to weight gain, and associated negative impacts on physical health and mental wellbeing. There is good evidence that interventions based on acceptance and commitment therapy (ACT) are effective for weight management and may improve mental wellbeing and psychological determinants of weight control.(4) However, acceptance-based programmes are usually psychologist-led and the cost and scarcity of psychologists specialising in obesity mean it is not possible to support everyone who would benefit from this type of intervention.

We developed a supported self-help intervention (SWiM-C; Supporting Weight Management during COVID 19) that aims to help adults with overweight and obesity to manage their weight and eating behaviour, be more physically active, and protect their emotional wellbeing during the COVID pandemic. The 12-week intervention is based on ACT, targets known psychological determinants of weight management and is delivered via an online platform with remote support from a guide or coach.

The current study compares the effectiveness of SWiM-C with standard written materials giving advice on diet, physical activity and mental health during the COVID-19 pandemic. If the SWiM-C intervention proves to be effective it could be rolled out on a larger scale to support people through the current crisis. Findings may also be generalisable to other situations involving high levels of stress, reduced access to resources, and/or low levels of mobility.

## 1.2 Trial objectives/hypotheses

**Primary objective:**

To evaluate the effect of SWiM-C on weight over 4 months compared to current standard advice for people with overweight and obesity.

**Secondary objectives:**

* To evaluate whether SWiM-C achieves greater improvements over 4 months in eating behaviour, physical activity, and wellbeing (health-related quality of life, capability and wellbeing, depression, anxiety, perceived stress, experiential avoidance/psychological flexibility) compared to standard advice.
* To explore if the intervention effect differs by age, gender, education level, and baseline BMI category.

A mixed-methods process evaluation (to be published separately to the main trial findings) will explore potential causal mechanisms and contextual factors that may be associated with variations in outcome.

# 2 Methods

## 2.1 Intervention

A detailed description of the intervention is provided in section 5 of the protocol. Briefly, the intervention includes access to an online web platform with 12 modules (SWiM sessions) consisting of psychoeducational content, reflective exercises, and behavioural experiments, to be completed weekly. After participants had completed session 4, they received a telephone call from their SWiM Coach. The coach also sent a tailored email at week 10.

## 2.2 Trial design

This is a pragmatic, randomised, single-blind, parallel group, two-arm trial. Participants were randomised to either the SWiM-C intervention or to a standard advice wait list control. Participants completed quantitative outcome assessments online at baseline and at 4 months follow-up. We chose to conduct follow-up at 4 months rather than 3 months, although the intended intervention duration is 3 months (12 sessions, 1 session per week), to allow for people who may require more time to complete the intervention.

## 2.3 Randomisation

See section 4.2 in the study protocol.

## 2.4 Sample size

We aimed to recruit 360 participants (180 per group); for details please see section 8.2 in the study protocol.

## 2.5 Framework

We will adopt a superiority trial hypothesis testing framework, testing whether the SWiM-C intervention is superior to current standard advice for people with overweight and obesity (standard advice from the European Association for the Study of Obesity (EASO) on diet, physical activity and mood during the COVID 19 pandemic).

## 2.6 Measures

The following measures were assessed:

* Weight (kg)
* Patient Health Questionnaire 8-item (PHQ-8)
* Generalized Anxiety Disorder 7-item (GAD-7) scale
* Perceived Stress Scale (PSS-4)
* Acceptance and Action Questionnaire Weight Related (Revised) (AAQW-R)
* Three-Factor Eating Questionnaire (TFEQ-R21)
* International Physical Activity Questionnaire (IPAQ )
* Health related quality of life and wellbeing (EQ-5D-L ; ICECAP-A )
* Demographics
* Website Usage (data analytics)
* Intervention adherence (number of sessions and coach calls completed)

(For details and references, see section 6 in the study protocol)

## 2.7 Timing of outcome assessments

Time points for assessments of the different measures are shown in Table 1.

Table 1. Schedule of assessments.

|  |  |  |
| --- | --- | --- |
| TIMEPOINT | 0 (baseline) | 4 months |
| Height | X |  |
| Weight | X | X |
| Demographics | X |  |
| Mental wellbeing (depression, anxiety, stress) | x | x |
| Psychological flexibility | x | x |
| Eating Behaviour | X | X |
| Physical Activity | X | X |
| Quality of Life /Wellbeing | X | X |
| Intervention Engagement |  | X |
| Adherence to intervention |  | X |

## 2.8 Interim analyses and stopping guidance

No interim analyses are planned for this study.

## 2.9 Timing of final analysis

All statistical analyses will be undertaken following completion of the study (when the database is closed for 4 month follow up data).

# 3 Statistical principles

## 3.1 Confidence intervals and p-values

95% confidence intervals will be calculated around relevant parameters (e.g. means).

**Multiplicity**: As we have specified a single primary endpoint (weight change) to test the effectiveness of the intervention (confirmatory analysis), adjustments for multiple endpoints are unnecessary (1). All other outcome measures are secondary and therefore subsidiary and exploratory (1,2). P-values will only be reported for the main effects and interaction analyses of the primary outcome; 95% confidence intervals will be reported for all outcomes/comparisons.

## 3.2 Adherence and protocol deviations

Intervention usage will be assessed through website analytics. Reports on frequency and duration of visits, as well as activities completed during each visit, will be available via secure download directly from the SWiM-C online platform.

For the main trial paper we will report basic statistics on intervention adherence, including:

* Average number of sessions completed by participants
* Number and proportion of people completing the first 4 sessions and coach contact (this provides an indication of how participants engaged with the intervention prior to and leading up to the first coach contact)
* Number and proportion of people completing the first 8 sessions (=2/3 of the total intervention)
* Number and proportion of people completing all 12 sessions (i.e. the total number of sessions)

Any deviations from the study protocol will be recorded, including:

* + Completion of telephone and email contacts with coaches
  + Any technical failures (e.g. reminders not sent, questionnaires not sent)

## 3.3 Analysis population

The analysis will be based on the intention-to-treat principle, whereby all individuals are included in the group to which they were randomised, regardless of the extent to which they adhered to the intervention. Participants with missing outcome data at follow-up will be excluded. A sensitivity analysis will be performed using multiple imputation for missing data (see section 5.2).

# 4 Trial population

## 4.1 Screening data

Participants completed an online screening questionnaire which assessed:

* Age
* Weight, height (to assess BMI)
* Good understanding of written English (yes/no)
* Bariatric surgery (yes/no)
* Whether they own a set of scales

## Eligibility criteria

See section 4 in the study protocol.

## Recruitment

We will report:

* Number of participants assessed for eligibility
* Number of participants excluded based on online screening questionnaire
* Number of participants randomised to each study arm
* Number of participants who complete baseline measures (record reasons if participants did not receive the allocated intervention)
* Number of participants who complete 4-month follow-up (record reasons where possible if participants discontinued the intervention)
* Number of participants included in the analysis (record reasons for any exclusions)

## 4.4 Withdrawal/loss to follow-up

Withdrawal/loss to follow-up will be presented by randomised group, specifically:

* Number and proportion of participants who do not complete baseline measures following informed consent (proportion out of study group, proportion out of total sample)
* Number and proportion of participants who do not complete follow-up measures at four-month follow-up (proportion out of study group, proportion out of total sample)
* Number and reasons for withdrawal (proportion out of study group, proportion out of total sample)

## 4.5 Baseline characteristics

The following baseline characteristics of the study sample will be summarised separately within each randomised group and for the total sample:

* Age (years) (range, mean, SD)
* Sex (female/male/other)
* Ethnicity
* Educational qualifications
* Occupational status
* Current situation under lockdown (e.g. working from home, furloughed)
* Marital status
* Number of adults and number of children living in household
* Caring responsibilities
* Body-mass-index (kg/m²)
* Proportion of participants reporting BMI in the following categories: 25-<30, 30-<40, 40+

Questions specific to the Covid-19 lockdown situation:

* Current cost of living situation (from “Find it a strain to get by from week to week” to “Quite comfortably off”
* Walking distance (in minutes) from home to nearest accessible open recreation area
* Access to (communal) garden or private outdoor space
* (Lack of) access to food due to a lack of money, access or other resources
* Social support during social distancing

For continuous variables, means and standard deviations (SDs) will be presented, unless the variable has a skewed distribution, in which case medians, 25th and 75th percentiles will be presented. For categorical variables, the number and percentage of individuals within each category will be presented. For each variable (continuous or categorical), the percent of missing values will be calculated. For the categorical variables, percentages within sub-categories will be calculated using the number of non-missing values as the denominator.

P-values for comparing the two study groups on baseline characteristics will not be reported as per the CONSORT statement (4).

# 5 Analysis

## 5.1 Outcome definitions

## Primary Outcome

Change in self-reported weight from baseline to 4-month follow-up (kg).

## Secondary Outcomes

All secondary outcomes will be defined as change in outcomes (Table 2) from baseline to follow-up.

Table 2. Secondary outcomes.

|  |  |  |
| --- | --- | --- |
| **Outcome** | **Type of outcome** | **Measure** |
| Depression (depressive symptom severity) | Continuous, summary score | Patient Health Questionnaire 8-item (PHQ-8) |
| Anxiety (anxious symptom severity) | Continuous, summary score | Generalized Anxiety Disorder 7-item (GAD-7) scale |
| Perceived stress | Continuous, summary score | Perceived Stress Scale (PSS-4) |
| Psychological flexibility | Continuous, summary score | Acceptance and Action Questionnaire Weight Related (Revised) (AAQW-R) |
| Eating behaviour:   * cognitive restraint * uncontrolled eating * emotional eating | Continuous, summary score for each subscale | Three-Factor Eating Questionnaire (TFEQ-R21) |
| Volume of total physical activity | Continuous, MET-min per week | International Physical Activity Questionnaire (IPAQ) |
| Health related quality of life | Continuous, summary score | EQ-5D-L |
| Wellbeing/capability | Continuous, summary score | ICECAP-A |

(For details and references, see section 6 in the study protocol)

## 5.2 Analysis methods

### Descriptive analyses

See section 4.5 “Baseline characteristics”.

### Primary outcome

The mean and SD of weight at baseline and 4-month follow-up will be presented, together with the mean and SD of weight change from baseline, separately in each randomised group.

The primary analysis will estimate baseline-adjusted differences between the study groups in change in weight from baseline to 4 months. We will use a linear regression model with change in weight as the outcome, and including baseline weight, the randomisation stratifiers (sex, BMI classification) and intervention group as covariates.

### Secondary outcomes

Continuous secondary outcomes will be analysed using the same approach as described for the primary outcome.

### Sub-group analyses

All subgroup analyses are exploratory as the study is not powered to detect effects in subgroups of the total sample. Subgroup analyses will therefore be interpreted with caution.

We will test whether intervention effects differ among sub-groups by including interaction terms (i.e. the relevant multiplicative parameters) in the model for randomisation group by age, gender, education level (dichotomized into a variable grouping all education categories up to and including A-levels as ‘below post-secondary’ and categories above A-levels as ‘post-secondary and above’), and baseline BMI category (25-30, 30-40, 40+). Where an interaction (p<0.05) is identified, the intervention effect and 95% CIs within each subgroup will be presented (5). For interaction with age, the variable will be split into categories (early and early middle-aged adults [18-40 years] and middle-aged and older adults [>40 years] (6)) to facilitate interpretation (5). The categories for BMI and age will be reviewed when the distribution of these variables is available to avoid creating very unequal groups.

### Testing assumptions

Prior to analyses, we will assess the assumptions underlying linear regression.

***Linear regression***

*Normality of residuals*: Normality will be assessed by visually inspecting the frequency distribution of the standardised residuals. Variables with a skewed distribution will be log-transformed and then re-checked for violations of normality. Violations of normality should not affect the validity of the method as our sample size will be large (7).

*Heteroscedasticity*: Heteroscedasticity will be explored by visually examining the regression plot plotting the standardized residuals of the outcome against the standardized predicted values of the model.

### Missing data

***Missing values of weight at baseline***

Participants with a missing baseline value of weight will be included in the analysis using the missing indicator method (8), which is a valid method for pre-randomisation measures in trials, ensuring that, other than participants with missing outcome data (see below), no further participants are excluded, thereby maximising precision of the effect size estimates.

***Missing values of weight at 4 months***

We will present baseline characteristics of participants with missing outcome data at follow-up and compare these with characteristics of participants without missing data. Participants with missing values of weight at 4 months will be excluded (i.e., a complete-case analysis which assumes outcome data are missing completely at random).

If there are > 5% of participants with missing values of weight at 4-month follow-up, a sensitivity analysis will be performed using multiple imputation by chained equations (MICE) – this assumes data are missing at random. The multiple imputation model will include values of weight at baseline as well as other baseline characteristics that have univariate associations with missingness (p<0.2). MICE involves imputing missing values based on regression models using the remaining variables in the data. This is repeated for a number of cycles to create multiple imputed datasets. Analyses are then performed on these imputed datasets and results are pooled. We will run the MICE procedure with 10 cycles/iterations per dataset, to create 20 imputed datasets (9,10). Analyses will then be run on the imputed datasets and pooled by Rubin’s rules (11).

### Sensitivity analyses

We will conduct a sensitivity analysis with imputed missing data as described above We will also undertake a sensitivity analysis by including only those in the intervention group who completed the first 4 sessions, and those who completed at least 2/3 of the intervention (i.e. 8 sessions)[[1]](#endnote-1), to assess whether the findings are influenced by the degree of compliance.

## 5.3 Safety data

This is a low risk trial with little reason to consider that adverse events would arise as a result of following any one of the interventions. Accordingly no formal adverse event monitoring is planned (12).

## 5.4 Statistical software

Data will be analysed using R version 4.0.0 (unless newer versions become available in the interim) and R Studio version 1.0.153. Where required data will also be analysed using Stata version 16.1.

# 6 References

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1. Feasibility will depend on the number of participants who completed min. 8 sessions. [↑](#endnote-ref-1)