Statistical Analysis Plan

Supporting Weight Management during COVID-19 (SWiM-C): 12-month follow-up

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

Date	Version	Justification for SAP version
19/01/2022	1	First draft sent to SJS
20/01/2022	2	Comments from SJS incorporated, version sent round to wider team
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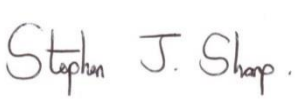
Overseeing statistician	Stephen Sharp, MRC Unit, University of Cambridge	16/3/22	

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.

If the SWiM-C intervention proves to be effective it could be rolled out on a larger scale to support people in situations involving high levels of stress, reduced access to resources, and/or low levels of mobility.

We previously evaluated the effect of SWiM-C on bodyweight in adults with overweight and obesity at 4 months post intervention compared to standard advice (written materials giving advice on diet, physical activity and mental health during the COVID-19 pandemic). The data were compatible with no effect of the intervention on bodyweight, physical activity, mental health, or emotional eating. The intervention improved psychological determinants known to lead to successful weight management in the longer term (uncontrolled eating, cognitive restraint, and experiential avoidance) and had a protective effect on wellbeing.

The current study compares the effectiveness of SWiM-C with standard advice at 12 months post intervention.

1.2 Trial objectives/hypotheses

Primary objective:

To evaluate the effect of SWiM-C on weight over 12 months compared to current standard advice for people with overweight and obesity.

Secondary objectives:

- To evaluate the effect of SWiM-C over 12 months on eating behaviour, physical activity, health-related quality of life, capability and wellbeing, depression, anxiety, perceived stress, and experiential avoidance/psychological flexibility, compared to standard advice.
- To evaluate the effect of SWiM-C on change in weight from 4 months to 12 months, compared to standard advice

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 Control

The wait-list control group received standard advice in the form of a leaflet from the European Association for the Study of Obesity (EASO) on diet, physical activity, and mood during the COVID 19 pandemic, tailored to people living with obesity. After completing 4-month follow-up assessments, participants in the standard advice group were provided access to SWiM-C.

2.3 Trial design

This is a randomised, parallel two-group 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, at 4 months and at 12 months.

2.4 Randomisation

See section 4.2 in the study protocol.

2.5 Sample size

We recruited 388 participants (192 in intervention, 196 in standard advice). Details are provided in the consort flow diagram (Figure 1).

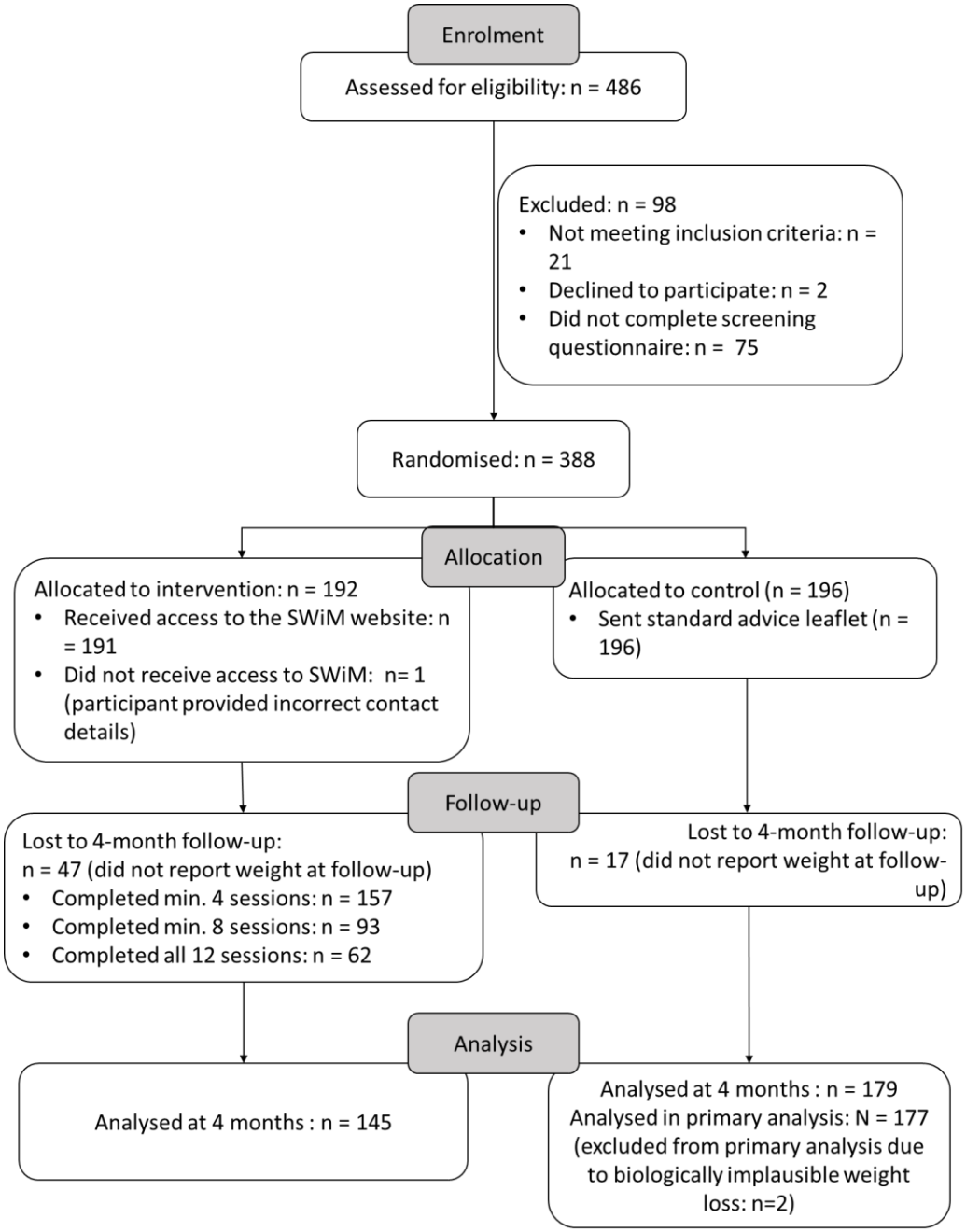


Figure 1. Consort flow diagram.

2.6 Framework

We will adopt a superiority 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) at 12-month follow-up.

2.7 Measures

The following measures were assessed:

- Self-reported 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)

2.8 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	12 months
Height	X		
Weight	X	X	X
Demographics	X		
Mental wellbeing (depression, anxiety, stress)	X	X	X
Psychological flexibility	X	X	X
Eating Behaviour	X	X	X
Physical Activity	X	X	X
Quality of Life /Wellbeing	X	X	X
Intervention Engagement		X	X
Adherence to intervention		X	X

2.9 Interim analyses and stopping guidance

No interim analyses are planned for this study.

2.10 Timing of final analysis

All statistical analyses will be undertaken following completion of the study (when the database is closed for 12 month follow up data).

3 Statistical principles

3.1 Confidence intervals and p-values

95% confidence intervals will be calculated around relevant estimates of effect.

Multiplicity: As we have specified a single primary endpoint (weight change from baseline to 12 months) 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

Reported in the 4-month assessment and the process evaluation.

In the 12-month evaluation, we will report on the number of control participants who accessed the SWiM website (1 session, 4 sessions, 8 sessions, 12 sessions) after being provided access after the 4-month assessment.

3.3 Analysis population

Individuals will be included in the analysis 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. Two per-protocol analyses will be conducted (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

4.2 Eligibility criteria

See section 4 in the study protocol.

4.3 Recruitment

We will report:

- Number of participants assessed for eligibility
- Number of participants randomised to each study arm
- Number of participants who completed baseline measures
- Number of participants who completed 4-month follow-up
- Number of participants who completed 12-month follow-up
- Number of participants included in the main analysis (record reasons for any exclusions) and in the 2 per-protocol analyses.

4.4 Withdrawal/loss to follow-up

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

- Number of participants who do not complete measures at 12-month follow-up
- Number of participants excluded from the analyses (with reasons)
- Number of participants who withdraw (with reasons)

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
- Marital status
- Body-mass-index (kg/m^2)
- Proportion of participants reporting BMI in the following categories: 25-<30, 30-<40, 40+

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 percentage 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 12-month follow-up (kg).

Secondary Outcomes

All secondary outcomes will be defined as change in outcomes (Table 2) from baseline to 12 month 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, 4-month and 12-month follow-up will be presented, together with the mean and SD of weight change from baseline to 4 months, 4 months to 12 months, and baseline to 12 months, separately in each randomised group.

The intervention effect on weight at 12 months (and 95% CI) will be estimated from a random intercepts linear regression model, using measures of change in weight at 4 months and 12 months as outcomes. The model will include intervention group, assessment timepoint, intervention by assessment timepoint interaction, the randomisation stratifiers (sex, BMI classification), and baseline value of weight as fixed effects, and random intercepts to allow for the repeated measures on each individual:

$$(\text{Change in weight from baseline to timepoint } t)_i = \beta_0 + u_i + \beta_1 \times \text{group}_i + \beta_2 \times (t=4)_i + \beta_{12} \times (t=4)_i * \text{group}_i + \beta_3 \times \text{baselineweight}_i + \text{randomisation stratifiers} + \varepsilon_{it}$$

i*=individual, t=4 or 12 months (follow-up timepoint).*
$\boldsymbol{(t=4)_i}$ *= 1 if timepoint=4 months, 0 otherwise.*
$\boldsymbol{u_i}$ *has a normal distribution with mean 0, variance* σ_u^2 *and represents the (level 2) between-individual error.*
$\boldsymbol{\varepsilon_{it}}$ *has a normal distribution with mean 0, variance* σ^2 *and represents the overall (level 1) residual error.*

Then $\boldsymbol{\beta_1}$ *represents the baseline-adjusted difference in weight change at 12 months comparing intervention vs control.*

NOTE: $\boldsymbol{\beta_1 + \beta_{12}}$ *represents the baseline-adjusted difference in weight change at 4 months comparing intervention vs control – not of interest in this analysis since it has previously been reported.*

Secondary outcomes

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

We will estimate baseline-adjusted differences between the study groups in change in weight from 4 months to 12 months using a linear regression model with change in weight from 4 months to 12 months as the outcome, and including baseline weight, 4 month weight, the randomisation stratifiers (sex, BMI classification) and intervention group as covariates.

Per-protocol analysis

Participants in the control group were given access to the web-based components of the SWiM intervention after the 4-month outcome assessment. In a per-protocol analysis, we will redo the primary outcome analysis comparing intervention participants who engaged with the SWiM intervention with control group participants who did not engage with the SWiM intervention. We will redo the primary outcome analysis including only those in the intervention group who completed at least 4 SWiM sessions and those in the control group who accessed less than 4 SWiM sessions, to assess whether the findings are influenced by the degree of engagement with the intervention. We will also redo the primary outcome analysis including only those in the intervention group who completed at least 8 SWiM sessions and participants in the control group who accessed less than 4 SWiM sessions.

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 (for both within and between person error). 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

We will conduct analyses with all observed data; random intercept models use all available data and assume missing data are missing at random. To explore this assumption, we will descriptively compare participants with and without missing outcome data on baseline characteristics.

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 4.1.2 (unless newer versions become available in the interim) and R Studio version 1.4. Where required data will also be analysed using Stata version 16.1.

5.5. Protocol deviations

The SWiM-C protocol states that we will do a linear regression analysis with change from baseline as the outcome. This protocol was written when only one follow-up assessment at 4 months was planned, before we had decided to include the 12-month follow-up. As we now have two follow-up timepoints, we have opted for a random intercepts model to allow for the repeated measures on each individual.

6 References

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