Statistical Analysis Plan

TRIAL FULL TITLE	Development of an online mindfulness program for stroke survivors and their caregivers
SAP VERSION DATE	08-13-21
Clinical trial number	NCT04553679
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1. SAP Signatures

I give my approval for the attached SAP entitled Development of an online mindfulness program for stroke survivors and their caregivers dated August 13, 2021.

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Date: August 13, 2021

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Date: August 13, 2001

2. Table of Contents

3. Abbreviations and Definitions

HADS	Hospital Anxiety and Depression Scale
NIH PSS	National Institute of Health Perceived Stress Scale
PSSUQ	Post-Study System Usability Questionnaire
SAP	Statistical Analysis Plan
SIS	Stroke Impact Scale
WHOQOL-BREF	World Health Organization Quality of Life-BREF

4. Introduction

4.1 Preface

The incidence of depression and anxiety is much higher in stroke survivors and their caregivers compared to age-matched peers. Previous work suggests that mindfulness delivered in an online format is promising for both individuals with neurological disorders and caregivers to improve quality of life and psychological well-being. The potential application of a non-meditative Langerian mindfulness intervention, however, has never been explored.

This statistical analysis plan (SAP) will give more detailed descriptions of the endpoints in the study and the corresponding analyses.

5. Study Objectives and Endpoints

5.1 Study Objectives

1. To pilot test the online mindfulness program with potential users to evaluate the acceptability, ease-of-use, and satisfaction.
2. To estimate the potential impact on quality of life, anxiety, depression and sleep quality in the short term.
3. To obtain a final version suitable for individuals who have had a stroke with a wide range of impairments and their caregivers.

5.2 Endpoints

Stroke survivors:

- Change in Stroke Impact Scale (SIS): quality of life and impact of stroke (primary, post-intervention)
- Change in Hospital Anxiety and Depression Scale (HADS): anxiety and depression (secondary, post-intervention).
- Change in NIH Perceived Stress Survey (NIH PSS): perceived stress (secondary, post-intervention).
- Change in Single-Item Sleep Quality Scale: Sleep quality (secondary, post-intervention).
- Post-Study System Usability Questionnaire (PSSUQ): Usability of the online platform used to host the intervention (secondary, post-intervention).

Caregivers:

- Change in World Health Organization Quality of Life-BREF (WHOQOL-BREF): quality of life (secondary, post-intervention).
- Change in Zarit Burden Interview: perceived burden (secondary, post-intervention).
- Change in Hospital Anxiety and Depression Scale (HADS): anxiety and depression (secondary, post-intervention).
- Change in NIH Perceived Stress Survey: perceived stress (secondary, post-intervention).
- Change in Single-Item Sleep Quality Scale: Sleep quality (secondary, post-intervention).
- Post-Study System Usability Questionnaire (PSSUQ)

All outcome measures are administered at 3 time points: pre-intervention, within 48 hours of the end of the intervention and at 1-month follow-up (+/- 1 week). All outcome measures are administered via REDCap. A qualitative semi-structured interview is also conducted post-intervention to capture satisfaction and usability of the mindfulness intervention.

Safety outcomes

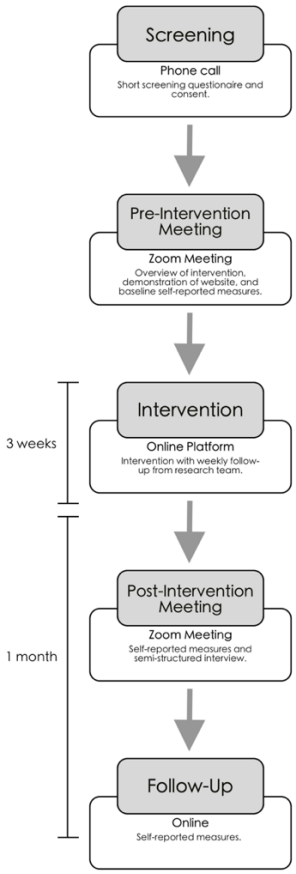
Adverse events are reported at each meeting. Participants are asked about any change in their medical status or hospitalization, since the last meeting.

6. Study Methods

6.1 General Study Design and Plan

The project uses a non-randomized pilot study to establish the relevance, feasibility and usability of the online Mindfulness program for community-dwelling stroke survivors and their caregivers.

Fig. 1. Flow chart



6.2 Inclusion-Exclusion Criteria and General Study Population

Stroke survivors and caregivers are purposefully selected to be representative of individuals who have had a stroke and caregivers (wide range of impairments, familiarity with computers, age, sex, gender, ethnicity, race and socio-economic backgrounds).

Inclusion criteria:

- Aged older than 18 years old
- Diagnosis of stroke (for stroke survivors)

- Ability to access Internet using a computer, a tablet and/or a smartphone
- Ability to provide informed consent
- Fluent in English

Exclusion criteria:

- Severe language impairments
- Regular meditation or full participation in a mindfulness program within past 3 months

6.3 Study Assessments

Table 1. Outcome measures at each time point

Visit	Baseline	Post-intervention	Follow-up
Target day of visit	1	22	52
Protocol assessment time windows (days)	1	± 2	± 7
Participant characteristics	x		
SIS*	x	x	x
HADS	x	x	x
NIH PSS	x	x	x
Sleep Quality	x	x	x
WHOQOL-BREF†	x	x	x
Zarit Burden Inventory†	x	x	x
PSSUQ		x	
Qualitative semi-structured interview		x	
Adverse event monitoring	x	x	x

* Stroke survivors only
† Caregivers only

The SIS 3.0 includes 59 items organized in 8 domains about the impact of stroke on health and life. Each question is scored from 1 (severe difficulty) to 5 (no difficulty) and each domain score is normalized. Higher scores indicate lower perceived impact of stroke. Participants also rated their perceived recovery on a sliding scale from 1 (no recovery) to 100 (full recovery).

The HADS is a 14-item scale with 7 items each for anxiety and depression subscales. Each item is scored from 0 to 3, with higher scores indicating higher anxiety or depressive symptoms.

The NIH PSS includes 10 items about the occurrence of life stressors scored from 0 (never) to 4 (very often). Higher scores indicate higher perceived stress.

The Single-item Sleep Quality includes an 11-point visual analogue scale about sleep quality in the past week (0: poor, 10: excellent sleep quality).

The WHOQOL-BREF comprises 26 questions from 4 domains about health and well-being. The scores

are normalized, and higher scores indicate better perceived health and well-being.
The Zarit Burden Interview includes 22 questions about caregiver burden rated from 0 (never) to 4 (nearly always). Higher scores indicate higher perceived burden.

The adapted PSSUQ consists of 5 questions on perceived satisfaction with the website. Each question is scored on a 7-point Likert scale from 1 (Strongly Agree) to 7 (Strongly Disagree). Higher scores indicate lower usability.

7. Sample Size

A convenience sample of 10 stroke survivors is targeted to capture the relevance, feasibility and usability of the Mindfulness Program and to obtain data saturation and richness on the qualitative semi-structured interviews. This study is not powered to detect differences in quality of life or psychological well-being.

8. General Analysis Considerations

8.1 Timing of Analyses

- The qualitative analysis and will be performed by 2 members of the research team after each interview have been transcribed verbatim.
- The final analysis will be performed when qualitative data saturation will be achieved and a sample of 10 stroke survivors have completed the intervention.

8.2 Analysis Populations

8.2.1 Full Analysis Population

- All participants who complete the intervention.

8.2.2 Safety Population

- All participants who received the intervention but excluding participants who drop out prior to receiving any treatment.

All outcomes will be presented using descriptive statistics; normally distributed data by the mean and standard deviation (SD) and skewed distributions by the median and interquartile range (IQR). Binary and categorical variables will be presented using counts and percentages. JASP version 0.14.1. will be used for all statistical analysis.

The subsections below will describe analyses in addition to the descriptive statistics.

The results of the adapted PSSUQ will be averaged for each group. For each group, differences prior to, after the mindfulness program and at 1-month follow-up will be assessed using a repeated measure analysis of variance (ANOVA). If data normality is violated, data will be transformed, or non-parametric statistics will be substituted. The semi-structured interview will be transcribed verbatim and analyzed independently using thematic content analysis by 2 members of the research team to identify codes, themes and overarching categories, using the Braun & Clarke six-step framework for inductive thematic analysis.

9. Summary of Study Data

Participant characteristics and the mean scores for each self-reported measure will be summarized in a table format.
A figure will be created with individual data and mean data for each outcome measure.

All continuous variables will be summarized using the following descriptive statistics: n (sample size), mean and standard deviation. The percentages (based on the sample size) of observed levels will be reported for all categorical measures.

9.1 Demographic and Baseline Variables

The following baseline characteristics and/or baseline variables will be collected:
Birthdate (continuous)
Age (continuous, years)
Sex (categorical)
Gender (categorical)
Ethnicity (categorical)
Race (categorical)
Living situation (qualitative)
Date of stroke onset (continuous)*
Type of stroke (categorical)*
Stroke diagnosis (qualitative)*
tPA administration (categorical)*
Assistive device for ambulation (qualitative)*
Other medical conditions (qualitative)*
Main impairments due to stroke (qualitative)*
Familiarity with mindfulness (qualitative)
Familiarity with technology (qualitative)
Relation to stroke survivor (categorical) †
Caregiving role (qualitative) †
Caregiving duration (hours/day, continuous) †
Caregiver major health complaint (qualitative) †

* Stroke survivors only
† Caregivers only

The summary statistics will be produced in accordance with section 9.

10. Listing of Tables, Listings and Figures

Figure 1. Flow chart
Table 1. Outcome measures at each time point