**RECALL – REducing Cognitive decline and dementiA by Lowering bLood pressure- PILOT**

**STATISTICAL ANALYSIS PLAN (FINAL ANALYSIS)**

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|---|---|
| Study Title | REducing Cognitive decline and dementiA by Lowering bLood pressure- PILOT |
| Short Title | RECALL Pilot |
| ISRCTN Number | 256896 |
| Sponsor | UoD-NHS Tayside |
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| Protocol Version and Date | V5 dated 26 March 2021 |
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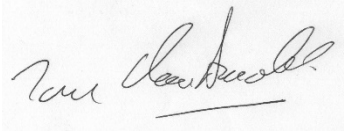

10th September 2021

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# 1. INTRODUCTION

## 1.1. STUDY BACKGROUND

Dementia is the leading cause of death in the UK and the biggest health and social care challenge of the 21st century. There is no effective treatment available or imminent for the commonest causes, which are Alzheimer's disease and vascular dementia. About half of cases have a significant vascular component. There is evidence that other end-organ damage driven by vascular disease is preventable (for example, cardiac, renal and stroke disease). Primary prevention is therefore also a realistic possibility for dementia.

Complex interventions aiming to slow cognitive decline have been disappointing, are time consuming and labour intensive and require extensive commitment on behalf of the health services, individual therapist, and participant. Mounting evidence supports the beneficial effects of reducing blood pressure to ameliorate cognitive decline and to prevent dementia. We intend to conduct a large online study of blood pressure lowering medication to lower blood pressure and prevent dementia. Although elements of the proposed study methodology have been used in other studies, they have not yet been tested in the target population. We therefore plan a pilot study to assess the feasibility of several aspects of the proposed method.

## 1.2. STUDY OBJECTIVES

### 1.2.1. Primary Objective

- Determine the feasibility of carrying out a larger trial by testing the recruitment and screening processes in primary care

### 1.2.2. Secondary Objectives

- Assess suitability of online cognitive testing for study cohort
- Assess baseline cognitive function
- Assess feasibility of requiring each participant to identify two individuals who agree to act as alternative contacts
- Assess feasibility of home blood pressure monitoring using study supplied HBPM machine
- Assess baseline blood pressure suitability of study cohort
- Assess feasibility of using portable i-STAT Alinity device for providing blood results
- Assess the likely number of eligible patients signing up

## 1.3. STUDY DESIGN

Cohort feasibility study.

## 1.4. SAMPLE SIZE AND POWER

This is a feasibility study to test proposed methods for a large online study of dementia prevention. No formal sample size calculation has been done. We estimate that at least 100 participants from at least 5 practices will be required to fully test the methodology.

## 1.5. STUDY POPULATION

Adults aged 60 years or over.

1.5.1. Inclusion and Exclusion Criteria

A list of inclusion and exclusion criteria can be found in the current version of the protocol (see section 1.6.3 below).

## 1.6. STATISTICAL ANALYSIS PLAN (SAP)

1.6.1. SAP Objectives

The objective of this SAP is to describe the statistical reporting to be carried out for the final analysis of the RECALL Pilot Study.

1.6.2. General Principles

Descriptive statistics (e.g. range, mean, standard deviation, percentage) for each outcome will be generated to support the planning (including sample size calculation) of a large, randomised study.

1.6.3. Current Protocol

The current study protocol at the time of writing is version 5, dated 26 March 2021. This SAP has been created in line with the current version of the protocol.

1.6.4. Deviations to those Specified in the Protocol

There are currently no deviations to those specified in the protocol.

1.6.5. Additional Analyses to those Specified in the Protocol

There are currently no planned additional analyses to those specified in the current version of the protocol.

1.6.6. Software

All analyses will be performed using excel or R version 3 or higher. The data will be extracted from the database using SQL and / or c# code.

# 2. ANALYSIS

## 2.1. STUDY POPULATIONS AND ANALYSIS SETS

The study population will consist of all participants with valid consent for the study.

## 2.2. SUBJECT DISPOSITION

The following information, which will help to prepare the CONSORT diagram, will be summarised:

- The number of patients on the initial GP database search list(s)
- The number of patients removed from this list by the GP as they were deemed unsuitable to participate
- The number of patients invited to sign-up to the study (Docmail invite send outs)
- The number of participants consented to the study
- The number of participants who entered demographic details
- The number of participants* who completed baseline data (past medical history, medications, lifestyle etc)
- The number of participants* who attempted online cognitive function testing
- The number of participants* who completed all online cognitive function tests

- The number of participants* who had a HBPM sent by the study team to the address they provided to the study team
- The number of participants* who attempted home blood pressure submission
- The number of participants* who completed all home blood pressure submissions
- The number of participants* who were invited to attend for a blood test using a portable i-STAT Alinity device
- The number of participants who attended for a blood test using portable i-STAT Alinity device
- The number of participants who completed at least one participant feedback questionnaire
- The number of participants who completed all participant feedback questionnaires
- The number and percentage of participants who withdrew from the study and the reasons for withdrawal (if available / participant completed the withdrawal questionnaire)
- The number of patients who completed the study overall

* Those who consented and provided demographic details confirming they were part of a General Practice participating in the RECALL Pilot Study.

## 2.3. BASELINE CHARACTERISTICS

Summaries will be provided of the following baseline characteristics as included in the eCRF:

- Age (mean, range) and gender (n, % for each category)
- Education (n, % for each category)
- Race (n, % for each category)
- Smoking and alcohol consumption (n, % for each category)
- BMI (mean, range)
- Medical history (n, % for each condition)
- Medication - participants reporting at least one medication (n), number of medications added per participants (mean, range)
- Family history (n, % for each condition)
- Socioeconomic deprivation - IMD decile (n, %)
- Lab results (Sodium, Potassium, Glucose, Urea Nitrogen (BUN), Creatinine, calculated eGFR, and Haemoglobin etc (for each analyte: n, result range, n for each result value)

A summary of any missing data will be included.

## 2.4. STUDY OUTCOMES

### 2.4.1. Primary Outcome

The primary outcome is to determine the feasibility of carrying out a larger trial by testing the recruitment and screening processes in primary care. The outcome measures for this will be recruitment numbers (consented and provided demographic details confirming they were part of a General Practice participating in the RECALL Pilot Study (n, % invited)), retention figures (consented and provided demographic details confirming they were part of a General Practice participating in the RECALL Pilot Study – withdrawn and not reconsented (n and % of total consented and provided demographic details confirming they were part of a General Practice participating in the RECALL Pilot Study)), and protocol adherence.

2.4.2. Secondary Outcomes

| **Secondary Objective:** | **Outcome Measure:** |
|---|---|
| Assess suitability of online cognitive testing for study cohort | Proportion of participants who complete a baseline test (n, %[†] ) |
| Assess baseline cognitive function | Proportion of study population completing one, two, three, four, five and all online screening cognitive function test (n, %[†]), and scores obtained (mean, range) |
| Assess feasibility of requiring each participant to identify two individuals who agree to act as alternative contacts | Proportion of participants who have two contacts provided, one contact provided, no contact provided (n, %[†]) |
| Assess feasibility of home blood pressure monitoring using study supplied HBPM machine | Proportion of participants submitting a complete set of home BP measurements (n, %[†]) |
| Assess baseline blood pressure suitability of study cohort | Proportion of participants with a home BP submission averaging 140mmHg or below systolic (n, %[†]) |
| Assess feasibility of using portable i-STAT Alinity device for providing blood results | Proportion of blood results obtained using portable system (n, %[†]) |
| Assess the likely number of eligible patients signing up | Proportion of those invited who meet proposed formal study entry criteria[§] (n, %[†]) |

[†]% of those consented and provided demographic details confirming they were part of a General Practice participating in the RECALL Pilot Study.

[§]Participants aged 60 years or over, who provide at least one alternative contact, have a mean HSBP ≥ 100mmHg and ≤140mmHg, do not have a diagnosis of dementia and are not on treatment for dementia, are not currently taking spironolactone, amiloride or eplerenone, do not have a history of dizziness or syncope, do not have an eGFR<45 mL/min/1.73m$^2$ at baseline, and do not have significant hyperkalaemia or hypokalaemia.

2.4.3. Participant Feedback Questionnaires

3 optional questionnaires are presented to participants throughout the course of the study and one optional questionnaire if they choose to withdraw. These are as follows:

- Website and provision of alternative contact questionnaire – 5 point Likert format
- Blood pressure questionnaire – 5 point Likert format
- Cognitive test questionnaire – 5 point Likert format
- Withdrawal questionnaire – check box as appropriate, and free textbox

Number of completed questionnaires (n, % of consented) will be presented, and percentages used for interpreting the distribution of the responses given by participants to Likert scale results. The Withdrawal questionnaire results will be summarised narratively / in a table.

2.4.4. Subgroup Analysis

Subgroup analysis will be completed as appropriate.

3. TABLES AND FIGURES

Draft reports will be produced and reviewed by the chief investigator. Approval of the final statistical outputs will be documented before database lock.

## 4. LISTINGS

Listings of all derived datasets will be produced as excel spreadsheets. In addition, listings (as excel spreadsheets) will be produced containing the information used for each output table and figure in the report.

## 5. DOCUMENT HISTORY

This is version 1.0 of the RECALL Pilot final analysis SAP, dated 14 July 2021, the initial creation.