System usability of the MedTracks app to aid medication adherence

SBRI MedTracks

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NHS Highlands, RD&I Division

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PROTOCOL VERSIONS

Version Stage	Versions No	Version Date	Protocol updated & finalised by;	Detail of the reason(s) for the protocol update
Submission	V1.1	22-Aug-2024	A Gibson CI	Typographical and consistency corrections
Last Draft	V1	16-Aug-2024	A Gibson CI	Readying For IRAS Submission
Development draft	DV5	08-Aug-2024	A Gibson CI	General revisions at design stage
Development draft	DV4	02-Aug-2024	A Gibson CI	General revisions at design stage
Development draft	DV3	25-Jul-2024	A Gibson CI	General revisions at design stage
Development draft	DV2	18-Jul-2024	A Gibson CI	General revisions at design stage
Development draft	DV1	27-Jun-2024	A Gibson CI	General revisions at design stage

DECLARATIONS

The undersigned confirm that the following protocol has been agreed and accepted and that the investigator agrees to conduct the study in compliance with the approved protocol and will adhere to ICH GCP and other applicable standards, NHS Highlands Data & Information policy, other relevant SOPs and applicable policies and legal frameworks.

I (investigator) agree to ensure that the confidential information contained in this document will not be used for any other purposes other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I (investigator) also confirm that an honest accurate and transparent account of the study will be given; and that any deviations from the study as planned in this protocol will be explained and reported accordingly.

Chief Investigator:

Signature:..... Date...../...../.....

Print Name(in full):.....

Position:.....

On behalf of the Study Sponsor:

Signature:..... Date...../...../.....

Print Name(in full):.....

Position:.....

STUDY SUMMARY

Identifiers	
IRAS Number	347639
REC Reference No	
Sponsor Reference No	NHSH 1961
Other research reference number(s) (if applicable)	
Full (Scientific) title	System Usability of the MedTracks App to aid Medication Adherence (SBRI)
Health condition(s) or problem(s) studied	Medication adherence, treatment compliance
Study Type i.e. Cohort etc	Prospective before and after treatment study
Target sample size	66
STUDY TIMELINES	
Study Duration/length	6 months from green light
Expected Start Date	October 2024
End of Study definition and anticipated date	Last Patient Last Visit Jan/Feb 2025
Key Study milestones	IRAS Submission August 2024, First patient recruited October 2024.
FUNDING & Other	
Funding	The project is funded by the Small Business Research Initiative (SBRI) competition funded by Scottish Health Industry Partnership (SHIP).
Other support	This project will be supported by staff of the NHS Highlands Clinical Research Facility.
STORAGE of SAMPLES (if applicable)	
Human tissue samples	Not Applicable
Data collected / Storage	Pseudo-anonymised data will be shared with Memory Tracks Ltd
KEY STUDY CONTACTS	Full contact details including phone, email and fax numbers
Chief Investigator	Andrew.gibson5@nhs.scot, 01463-255028

KEY ROLES AND RESPONSIBILITIES

SPONSOR: The sponsor is responsible for ensuring before a study begins that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also has to be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATOR (CI): The person who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether or not he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant regulatory approvals are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards.

The Chief Investigator is responsible for submission of annual reports as required. The Chief Investigator will notify the RE of the end of the study, including the reasons for the premature termination. Within one year after the end of study, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC.

PRINCIPLE INVESTIGATOR (PI): Individually or as leader of the researchers at a site; ensuring that the study is conducted as per the approved study protocol, and report/notify the relevant parties – this includes the CI of any breaches or incidents related to the study.

OTHER:

Project Coordinator: Tatyana Brown
Data Managers: NHSH Clinical Research Facility team
Trials Assistants: NHSH Clinical Trials Assistant Team
Primary Care Research Coordinator: Samantha Holden
Research, Development and Innovation Governance Manager: Anna McIver
Memory Tracks Ltd Team

LIST OF ABBREVIATIONS

AE	Adverse Event
App	Mobile phone application
AR	Adverse Reaction
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
DMC	Data Monitoring Committee
GAfREC	Governance Arrangement for NHS Research Ethics
HTA	Human Tissue Authority
IB	Investigator Brochure
ICF	Informed Consent Form
MD	Medical Device
NHSH	NHS Highland
ISRCTN	International Standard Randomised Controlled Studies Number
PI	Principle Investigator
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
RCT	Randomised Clinical Study
REC	Research Ethics committee
SAR	Serious Adverse Reaction
SAE	Serious Adverse Event
SDV	Source Data Verification
SOP	Standard Operating Procedure
SSI	Site Specific Information
TMF	Trial Master File

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1 INTRODUCTION

Digital solutions to act as an aide memoire for taking medication are becoming increasingly available yet little is known about the actual efficacy of the technology. The MedTracks mobile phone application (app) combines a music-based notification platform to provide reminders to take medication whilst providing performance reporting. The app uses a music-based push notification irrespective of whether the app is open or not using memorable music from the users' formative years. Using music in this way can engage multiple areas of the brain creating positive responses which in turn encourage action (Janata, 2009). Personalisation features within the app such as using associated images can enhance engagement and encourage continued use (Cunningham, 2019).

The app is designed to benefit both patients and healthcare providers by improving health outcomes, lowering medication wastage and reducing escalation of treatment. By targeting a wide range of end-users, including those with chronic conditions, the project aims to have a significant impact on medication adherence.

This project aims to examine whether the MedTracks app is useful and easy to use for a cohort of adults taking two or more oral medications. It will also aim to indicate if use of the app changes attitudes and improves self-reported medication adherence. Qualitative interviews will be conducted with a sub-set of participants to examine issues in greater depth. The qualitative interview will be selected at random from those who consent to this part of the study with a maximum of 20 interviews being undertaken.

2 BACKGROUND AND RATIONALE

Poor adherence to medication for chronic diseases has been shown to be a worldwide problem(WHO 2003). The implications for poor adherence to medication impact negatively on the burden of chronic health, increase the likelihood of poor outcomes and increased healthcare costs(WHO 2003). In the intervening years since, work has been done to address this issue but non-adherence is still thought to contribute to poor healthcare outcomes and increased healthcare costs (Kim, Combs et al. 2019).

An early Cochrane review found that there was "no evidence that low adherence can be cured"(Haynes, McDonald et al. 2002) and pointed to the effects of improving adherence having a wide ranging impact. There is also evidence that prevalence in non-adherence tends to be worse in chronic conditions rather than for acute episodes (Cea-Calvo, Marin-Jimenez et al. 2020).

Interventions to improve adherence with face to face interactions have been shown to be successful but digital solutions have also shown to have merit (Kim, Combs et al. 2019). There are many reasons for non-adherence of medication which can be thought of as intentional non-adherence and unintentional non-adherence (Furmedge, Stevenson et al. 2018). The most common reason for unintentional non-adherence being simply forgetting to take the medication. This is where reminder notifications could play a role.

In the UK and devolved nations there are no national approaches to aids for improving medication compliance (Walters, Chakravorty et al. 2022) and there is little evidence for patient benefits for things like dosette boxes. A recent national census gave estimates of smart phone use for adults over 16 at 84% (ONS 2022). Increased smart phone availability is a worldwide

phenomenon as is the growth of apps to facilitate adherence and there is some evidence of efficacy (Perez-Jover, Sala-Gonzalez et al. 2019). Evidence exists to show that electronic reminders via text do improve adherence (Kim, Combs et al. 2019).

Simple before and after studies have shown significant improvements in adherence with a high level of user satisfaction(Perez-Jover, Sala-Gonzalez et al. 2019). A key concept for building sustainable habits of adherence is the notion of building the routine over time (Mathur, Dhodapkar et al. 2022). Using technology to create individualised approaches seems to be a good avenue for future investigation.

Studies in music and memory have shown that memories involving music may remain even into cognitive decline(Cunningham, Brill et al. 2019). This is where the MedTracks app could provide an aid to improve adherence through an individualised approach. With music chosen specifically by the user it is thought to be the most evocative for the individual and maximise effectiveness.

The purpose of this study is to examine the usability and usefulness of the MedTracks app and to see if it has a positive impact on self-reported adherence. With medication adherence still being a problem the need to evaluate potential technological solutions remains a relevant priority.

3 OBJECTIVES

3.1 Primary Objective

- The Primary Objective of the study is to measure the MedTracks app's ease of use by using the System Usability Scale (SUS) self-reported questionnaire. This is an industry standard test which has been used to appraise hardware and software. SUS measures the perceived ease of use with 10 standard questions in a Likert scale that goes from Strongly Disagree to Strongly agree.

3.2 Secondary Objectives

- The main Secondary Objective of the study is to measure the impact of the MedTracks app on medication adherence using the MARS-10 and MARS-5 scales.
- MARS-10 is a questionnaire that consists of 10 items designed to measure medication adherence. Each item is typically scored on a Likert scale, where participants indicate the frequency with which they engage in specific behaviours related to medication adherence.
- MARS-5 is a shortened version of the MARS-10, consisting of 5 items that also aim to measure medication adherence but in a more concise format.
- We will also carry out qualitative interviews to detail user experience for a subset of participants selected randomly. The objective of these interviews is to gain a greater understanding of the participants experiences with the MedTracks app to further develop the communication strategy for the launch and promotion of the finished service.
- Measure of agreement between medications prescribed and those added to the app to check that the prescribed treatment regime has been added correctly. Participants will be instructed to enter only prescription tablets onto the app. The app will also restrict to reminders for medication only for the duration of the study.

4 STUDY DESIGN

The study design is a prospective before and after design which is appropriate for testing a digital application at this phase of its development(Gov.Uk 2020). In the fast-paced world of app development this offers the benefits of fast and cost-efficient means of testing the intervention. The drawback is that it is offset by being indicative only and any change could be down to external factors(Streiner and Norman 2009).

Baseline data will be collected prior to a 28-day (4 week) intervention period. Post-intervention data will be collected and measured against the pre-intervention data where possible.

The intervention consists of a 28-day period using the app to remind participants to take their medication. Sample size needed has been calculated to be 60 participants with 10 percent added to account for potential drop out. The sample size was calculated using estimated responses to the MARS-10 questionnaire to give an estimated standard deviation. Calculations were based on equations advocated by (Bland) and (Allgar 2011).

The study population will include NHSH adult patients who take two or more oral medications regularly. Patients on inhalers and also taking injections will be excluded from the trial at this stage of the investigation to mitigate for risk and maintain the simplicity of the design in this early phase. These groups are also more likely to use targeted apps to aid with disease management such as “MySugr” and “MyLife” for diabetes management. Interference with well managed regimens of complex conditions could introduce risk. In the event of a larger, randomised controlled trial these groups may need to be included. Patients using topical medication can be in the study if they also take 2 or more oral medications.

5 STUDY SCHEDULE

- PIC search and mailout from GP sites chosen.
- Upon receiving the invitation letter and patient information leaflet interested people can self-refer to the study by responding to the contact details.
- Phone call and near me booking
- Near Me call and consent process see below. Near Me is a Video consulting service that is widely used across NHS Scotland.
- Complete baseline questionnaires
- Once completed questionnaire is received send out link and downloading instructions
- Day zero from this point

- Between day 3 and 6 check if participant has started their use of the app. If not a reminder will be sent by the research team. MedTracks will be notified when a new participant has been recruited and will in turn let the research team know if the new participant does not download the app between days 3-6. Only one reminder will be sent. People who fail to download the app will still be followed up at day 29.
- Day 29 email questionnaires
- Day 35 chase if not received
- Day 42 Final chase, if not received consider as lost to follow-up
- Day 42- invite subset for interview
- End of study defined as last patient interview complete.
- SAE reporting ends on day 29 and only covers the period from consent to day 28 inclusive.
- Withdrawal will be on the request of the participant. Participants who fail to download or engage with the app will still be followed up at day 29.

6 SCREENING, CONSENT AND BASELINE

Search happens and mail outs from Primary care. Includes invite letter and PIS.

People self-select if they are interested and email or phone the research team.

- Arrange time to call and send Near Me link. Warn them they will need a means of verifying ID. This will involve holding photographic ID to the camera during the consultation. Acceptable Identification is detailed in NHSH RD&I SOP CLIN009.
- Consent discussion on Near Me video consultation.
- Ask screening questions as part of consent conversation. Verbal consent will be sought to check eligibility criteria as part of the consent discussion prior to full consent. Reasons for being ineligible will be recorded with no identifiable data on a screening log in order to account for the consort diagram.
- Answer any questions
- If they indicate they are happy to take part:
    - Verify ID
    - Send eConsent envelope with attached participant identification number
    - Talk through envelope and get to sign in real time
    - Get participant to send envelope back
    - Confirm signed envelope
    - If eConsent is unavailable a paper alternative will be available as a fall back.
- email baseline questionnaire
- Confirm receipt of baseline checking for completeness and send download plus instructions. Explain further questionnaire bundle will be sent out after 28 days.

7 ELIGIBILITY CRITERIA

7.1 Inclusion Criteria

- NHS registered patient
- Adults aged 40 and above
- Able to understand the Participant Information Sheet, able to provide written informed consent electronically and complete self-reporting eligibility questionnaire
- Volunteers who take 2 or more different prescription oral medications
- Owning a compatible smartphone (device with Android 8.0 or higher (mid-2017) or alternatively iPhone with iOS 12.0 or higher (mid 2018).
- Willing for the MedTracks app to be 'active' on the smartphone device for the duration of the Test Phase, including active reliable internet connection.

7.2 Exclusion Criteria

- Non-NHS patient
- Age <40
- Unable to provide written informed consent electronically or not able to understand the Participant Information Sheet.
- Currently using an existing app to help with remembering to take their medication
- Vulnerable people deemed inappropriate to approach e.g. prisoners.
- Not owning* a smartphone suitable for accessing the app (*for purposes of the study "own" means to consider the device to be their own personal item that they access independently.
- Currently taking part in an interventional trial if being in another study is an exclusion criteria for the other study.*

*Note participation in this study may make people ineligible for other studies for the duration of this trial.

8 RECRUITMENT

The NHS Research Scotland Primary Care Coordinator will recruit GP Practices to help support identification of potential participants. Searches of the GP Practice patient management system will be undertaken at each GP practice and the list generated by the search will be screened by a GP from the practice before invitations are mailed out. A Letter of Invitation on Practice Letterhead and Patient Information Sheet (PIS), are sent out on behalf of the practice using an NHS approved web mailing provider. Patients are asked to contact the research team if they are interested in participating in the study as per the PIS. Patient details are not disclosed to the research team during the invitation process.

Following self-referral by interested parties a member of the research team will contact the individual to discuss the study further to pre-screen and consent, if applicable (See consent for full details). The participant will then be sent baseline eQuestionnaires to complete before being sent a

link to download the app. Ineligible people will be recorded on a screening log using a screening number and reason they don't meet the eligibility criteria.

9 STATISTICAL METHODS

This is a pragmatic early phase proof of concept trial to evaluate a digital health product. Governmental guidance advocates that a before and after design is appropriate at this stage in the development of a product(Gov.Uk 2020). Any changes in the outcomes are attributed to the intervention but the design cannot rule out that something else is responsible for the result. A randomised controlled trial would be the most reliable means to test this but they are more expensive and involved to run.

The primary outcome is the Self-reported System Usability Scale (SUS) which is a 10 item questionnaire giving a score from 0-100 (Brooke 2013). Despite giving a range of 0-100 the result should not be reported as a percentage (Sauro 2011) and should instead be reported as a percentile. For the purposes of this study the SUS will be reported using an adjective rating scale (Bangor, Kortum et al. 2009).

The secondary outcome of the MARS-10 and MARS-5 questionnaires can be treated in the before and after design as a test of two means. The sample size has been calculated based on 90% power and 5% level of significance. Using formula for a test of means (Bland , Allgar 2011) with an assumed standard deviation of 3.36 (for the MARS-10) and clinically significant difference of 4 between the scores. This gives the numbers needed for a sample size for a statistically significant difference at approximately 60 participants.

The MARS-5 can be derived from the MARS-10 and will also be reported but would need slightly more participants to be powered correctly (67). As such the sample size is calculated against the MARS-10 and we will aim to recruit 66 participants factoring in a 10% dropout rate. Both the MARS-10 and Mars-5 scores will be reported. The results will be analysed by T-test or Wilcoxon sign rank test dependent on the distribution of the data.

Bland-Altman plots will be used to measure agreement between the number of medications that are prescribed for taking at set times compared to those entered onto the app(Bowers 2008).

Demographics and baseline characteristics will be described using appropriate measures of summary.

10 PATIENT AND PUBLIC INVOLVEMENT (PPI)

Public involvement is central to high-quality, ethical research.

As the purpose of this study is to examine the usability and usefulness of the MedTracks app and to see if it has a positive impact on self-reported adherence, PPIE contributors don't have to have a special skills or experience. 2-3 people from the general public who expressed interest will be involved in the study. To find these people, these not exhaustive channels will be used:

- advertising in NHS Highland weekly newsletter
- through personal connections of the research team
- inviting existing patients or research participants
- asking existing PPI contributors find others
- advertising through University of Highlands and Islands building facility network

Patients and public members will be involved in reviewing patient facing study documents such as PIS, ICF, invitation to participate in the study letter, advertising flyer, public study summary, etc., to make sure that the study information is understandable and acceptable to participants.

Also, PPIE contributors will support the communication of findings to have better communication of results at the end of the study. They will review a research findings summary to make sure that the information is understandable for members of public.

They will disseminate the results through their networks to make sure is accessible to a public audience.

11 FUNDING AND SUPPLY OF EQUIPMENT

The study funding has been reviewed by the NHSH RD&I Finance Lead, and deemed sufficient to cover the requirements of the study. NHS costs will be supported via the funding grant.

The research costs for the study have been supported by the Small Business Research Initiative (SBRI) competition funded by Scottish Health Industry Partnership (SHIP).

There is no equipment provided for this study; participants will be using their own devices for the app intervention.

12 DATA HANDLING AND MANAGEMENT

The RDI Division of NHS Highland will review all aspects of Information Governance to ensure all IG issues are addressed.

NRS Primary Care Network will work with GP practices to enable recruitment of suitable patients. The Network provides an expert service, recruiting Practices, undertaking searches of their electronic Patient Managment Systems, identifing potentially eligible patients and preparing the ethically approved invitations to be sent out to patients on behalf of the practice. Patient details are not disclosed to the research team during this process. Invitations are uploaded and sent out via an NHS approved web mailing service.

Network staff work on behalf of the healthcare team with the permission of the Practice. Network staff must have a current substantive or honorary NHS contract to allow them to carry out these duties. Memorandum of Agreements between the Network and GP practices are signed to set out responsibilities regarding Data Protection and GDPR. A Data Protection Impact Assessment is in place to support this role.

NRS Primary Care Network is funded by the Scottish Government, Chief Scientist Office (CSO) and facilitates research in primary care across Scotland.

Participant identifiable data will not be required for the MedTracks log-in process which will be managed using an anonymised code which will be entered on the Study Participant Log. This will be held in electronic format on the NHS Highland RD&I secure drive. When the links for downloading the app are sent out participants will be issued with a study ID number and initial password needed to log in.

The Chief Investigator will act as custodian for the study data. The following guidelines will be strictly adhered to:

- Participant data will be pseudo-anonymised and all pseudo-anonymised data will be stored on a secure server. The only patient identifying data shared with memory tracks will be for the purpose of enabling the sub-group qualitative interviews.
- All consent will be logged on the Study Consent Log and copies of the consent will be held in the TMF.
- All study data will be stored in line with the Medicines for Human Use (Clinical Trials) Amended Regulations 2006 and the Data Protection Act 2018, and the General Data Protection Regulation 2016/679/EU.
- NHS Highland will provide the MedTRacks team with a time point related report accompanied by all pseudo-anonymised data collected to that date and a basic analysis of interim findings
- All pseudo-anonymised data will be transferred to and fully owned by MedTracks as agreed within the study Agreement.

Data will be handled by using a Project Participant Log. Data analysis will be from a fully anonymised dataset.

13 MATERIAL/SAMPLE STORAGE

There is no sampling of human tissues for this trial.

14 PEER AND REGULATORY REVIEW

Peer Review -

As proportionate to the study design, the Sponsor considers the review undertaken by the funding body and via the PPI activities, to have been of sufficient and adequate rigour and independence.

Following submission via IRAS, the protocol and study documents will undergo ethical and regulatory review from NHS REC and NHS RD&I Governance, with NHS REC favourable opinion and NHSH Management Approval sought prior to research activities being initiated at site. Any subsequent amendments to study protocol or study documents will be submitted, as per national process and RDI LWI001 GOV, and were applicable will not be implemented until review by NSH REC and NHS RDI has been completed and agreed.

15 ASSESMENT AND MANAGEMENT OF RISK

This is considered a low-risk study, with no changes to participants medication regime. The potential for participants to take too much or too little of their medication or taking it at the wrong times is deemed to be no more likely than standard of care or their usual routine. Post consent advice will be given to all participants with regards to contacting NHS 24 immediately upon any concerns with regards to under or over dosage of their medication including missed doses, as per standard of care. Participants will be asked to report to the study team during the next available office hours. SAE recording will cover the intervention period only and will be picked up at day 29 via the eQuestionnaire and/or review of patient records. Patient NHSH records will always be checked prior to sending out study material to ensure the participant is not incapacitated or deceased which would trigger SAE reporting. The CI will follow up all SAEs for causality and report as per NHSH SOP CLIN006b.

16 RECORDING AND REPORTING OF EVENTS AND INCIDENTS

16.1 Definitions of Adverse Events

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or study participant, which does not necessarily have a causal relationship with the procedure involved. **Only Adverse events that fulfil the Seriousness criteria below will be recorded.**
Serious Adverse Event (SAE).	Any adverse event that: • results in death, • is life-threatening*, • requires hospitalisation or prolongation of existing

	hospitalisation**, • results in persistent or significant disability or incapacity, or • consists of a congenital anomaly or birth defect
*A life- threatening event, this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. ** Hospitalisation is defined as an in-patient admission, regardless of length of stay. Hospitalisation for pre-existing conditions, including elective procedures do not constitute an SAE.	

16.2 Assessments of Adverse Events

Each adverse event will be assessed for severity, causality and seriousness.

16.3 Causality

The assessment of relationship of adverse events to the procedure is a clinical decision based on all available information at the time of the completion of the case report form NHSH Form035 and recorded on an SAE log on Form013.

It is of particular importance in this study to capture events related to the product application. The assessment of relationship of an adverse event to this/these additional safety issue(s) will also be carried out as part of the study.

The following categories will be used to define the causality of the adverse event:

Category	Definition
Definitely:	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
Probably:	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely
Possibly	There is some evidence to suggest a causal relationship (e.g. the event occurred within a reasonable time after administration of the study procedure). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant events).
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the study procedure). There is another reasonable explanation for the event (e.g. the participant's clinical condition).
Not related	There is no evidence of any causal relationship.
Not Assessable	Unable to assess on information available.

16.4 Expectedness

There will be no reporting of SUSARs as this is not a CTIMP.

~~16.3~~16.5 Recording adverse events

Only Adverse Events that satisfy the seriousness criteria will be explored with the participants if they answer "yes" to the appropriate follow up question or an admission to hospital or death is noted in the medical review on day 29-33.

16.6 Procedures for recording and reporting Serious Adverse Events

Following consent and up to and including Day-28 all serious adverse events will be recorded in the CRF. Any SAEs thought to be causally related will be reviewed by the Sponsor and escalated as appropriate in line with NHSH RD&I SOP CLIN006b.

All SAEs (except those specified in section 16.5 as not requiring reporting to the Sponsor) must be recorded on a serious adverse event (SAE) form. The Chief Investigator will respond to any SAE queries raised by the sponsor as soon as possible.

Completed forms for SAES thought to be causally related must be sent within 24 hours of becoming aware of the event to the Sponsor

Email forms to: randd.nhsh@nhs.scot

16.7 Serious Adverse Events that do not require reporting

All SAEs will be recorded.

16.8 Reporting Urgent Safety Measures

If any urgent safety measures are taken the CI shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant REC and Sponsor of the measures taken and the circumstances giving rise to those measures, as per RD&I SOP CLIN008.

17 PROTOCOL DEVIATIONS AND NOTIFICATION OF PROTOCOL VIOLATIONS

A deviation is usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the sponsor. The CI will monitor protocol deviations.

A protocol violation is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study.

The CI and sponsor will be notified immediately of any case where the above definition applies during the study conduct phase.

18 MONITORING AND AUDITING

The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The Chief Investigator will inform the sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

RDI Monitoring and audit SOP

See the appendix for further details about the monitoring and audit plan.

19 TRAINING

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files. Staff training will be given at SIV for the team taking consent and carrying out Trial related activity.

20 INTELLECTUAL PROPERTY

Memory Tracks Ltd will retain all intellectual property (IP) created during the NHS research project titled SBRI: Medicines and Dementia – MedTracks. This includes, but is not limited to, any inventions, discoveries, designs, software, and methodologies developed as part of the research activities.

21 INDEMNITY ARRANGEMENTS

NHSH will provide NHS indemnity cover for negligent harm via CNORIS, as appropriate and is not in the position to indemnify for non-negligent harm. NHS indemnity arrangements do not extend to non-negligent harm and NHS bodies cannot purchase commercial insurance for this purpose; it cannot give advance undertaking to pay compensation when there is no negligence attributable to their vicarious liability. The Board will only extend NHS indemnity cover for negligent harm to its employees, both substantive and honorary, conducting research studies that have been approved by the R&D Department. The Board cannot accept liability for any activity that has not been properly registered and Board approved. Potential claims should be reported immediately to the NHSH RD&I Governance Lead.

22 ARCHIVING

NHSH recognises that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The study master file will be archived in accordance with the NHSH SOP ADM006. It will be archived for a minimum of 10 years from the study end.

23 PUBLICATION AND DISSEMINATION POLICY

Our research publication strategy aims to disseminate findings, maximize impact, and engage with a diverse audience across academic, professional, and public domains. The

following plan outlines our approach using impact statements, academic papers, LinkedIn, AHSNs, and ORCHA.

We plan to develop concise and engaging impact statement for our research findings, highlighting the benefits, potential applications, and societal impact. This statement will be included in all research publications and reports, shared on institutional and personal websites and used in grant applications, funding reports, and presentations to stakeholders.

We would like to contribute to the scientific community by publishing in peer-reviewed journals relevant to our research field. This will involve thorough literature reviews to position our research within the existing body of knowledge, and the preparation of papers to submit to target journals.

We plan to leverage our own professional networks on LinkedIn for wider dissemination and engagement. This will involve regularly sharing updates on research progress, publications, and impact statements. We will encourage discussions and connect with other researchers, practitioners, and stakeholders in related fields.

We will collaborate with regional health networks for enhanced research impact and implementation, across Scotland through the North of Scotland Innovation Hub, and in England via the Academic Health Science Networks (AHSNs). This will involve participation in events, workshops, and collaborative projects, sharing our research findings and where possible contributing to newsletters, blogs, and reports.

We will work with the Organisation for the Review of Care and Health Apps (ORCHA) to

ensure our app and digital solution are reviewed and recognized for quality and efficacy.

Using the ORCHA platform we can promote the application to a broader audience. We can also highlight the ORCHA reviews in impact statements, academic papers, and LinkedIn posts.

We will also aim to provide a lay summary of the results to all participants; this will be available on the NHS Highlands RD&I website and also the MedTracks web page.

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25 APPENDICES

25.1 Appendix 1: System Usability Scale

Please check the box that reflects your immediate response to each statement. Don't think too long about each statement. Make sure you respond to every statement. If you don't know how to respond, simply check box "3".

Questions	Strongly Agree				Strongly Disagree
1. I think that I would like to use this app frequently.	1	2	3	4	5
2. Found the app unnecessarily complex.	1	2	3	4	5
3. I thought the app was easy to use.	1	2	3	4	5
4. I think that I would need the help of a technical person to be able to use this app.	1	2	3	4	5
5. I found the various functions in the app were well integrated.	1	2	3	4	5
6. I thought there was too much inconsistency in the app.	1	2	3	4	5
7. I Imagine that most people would learn to use this app very quickly.	1	2	3	4	5
8. I found the app very awkward to use.	1	2	3	4	5
9. I felt very confident using the app.	1	2	3	4	5
10. I needed to learn lots of things before I could get going with this app.	1	2	3	4	5

This data is collected after the 28 day intervention period only.

Scoring SUS

- For odd items: subtract one from the user response.
- For even-numbered items: Subtract the user response from 5.
- This scales all values from 0-4 with 4 being the most positive response.
- Add up the converted scores and multiply the total by 2.5. This gives a range of 0-100 instead of 0-40.

References: (Bangor, Kortum et al. 2009, Sauro 2011, Brooke 2013).

25.2 Appendix 2: Baseline Data to Collect

1. Age on date of consent in whole years. For example someone 48 years and 300 days would be recorded as 48.
2. Gender
3. Postcode. This is used to determine the decile score from the SIMD website: https://simd.scot/#/simd2020/BTTTFTT/9/-4.0000/55.9000/
4. And also the six-fold rurality score from the web page: https://www.gov.scot/publications/scottish-government-urban-rural-classification-2020/pages/2/

Postcode will not be shared outside of NHSH.

5. Self-reported Gender
6. Type of phone: Make, model (settings-about phone)
7. Number of prescription oral medications taken daily?
8. Number of regular OTC medications you take daily?
9. How do you usually remind yourself to take your medication?
    a. Set an alarm on my phone or other device
    b. I use an medication reminder app
    c. Fit it around regular activities, such as meal times
    d. None

25.3 Appendix 3: MARS-10 and MARS-5 (Medication Adherence Report Scale)

Many people find a way of using their medicines which suit them. This may differ from the instructions on the label or from what their doctor has said. Here are some ways in which people have said they use their medicines. For each statement please tick the box which best applies to you.

Question	Never	Rarely	Sometimes	Often	Always
1. I take my medication only when I need it.	Never	Rarely	Sometimes	Often	Always
2. I take it regularly every day.	Never	Rarely	Sometimes	Often	Always
3. I avoid taking it if I can.	Never	Rarely	Sometimes	Often	Always
4. I forget to take it.	Never	Rarely	Sometimes	Often	Always
5. I alter the dose.	Never	Rarely	Sometimes	Often	Always
6. I stop taking it for a while.	Never	Rarely	Sometimes	Often	Always
7. I take it exactly as prescribed.	Never	Rarely	Sometimes	Often	Always
8. I miss out a dose.	Never	Rarely	Sometimes	Often	Always
9. I take more than instructed.	Never	Rarely	Sometimes	Often	Always
10. I take less than instructed.	Never	Rarely	Sometimes	Often	Always

Items in bold form the MARS-5 questionnaire.

Scoring

Questions	Never	Rarely	Sometimes	Often	Always
1, 3, 4, 5, 6, 8, 9, 10.	5	4	3	2	1
2, 7.	1	2	3	4	5

This is collected after consent at baseline and also after the 28-day intervention.

References: (Anghel, Farcas et al. 2019, Chan, Horne et al. 2020, Spetz, Olbers et al. 2024)

25.4 Appendix 4: - Additional post intervention questions App focused

1. How did you find opening the app from the icon and signing in?
   a. [5 Very easy / 4 Easy / 3 Neutral / 2 Difficult / 1 Very difficult]

2. How did you find the process of setting up the MedTracks reminders?
   a. [5 Very easy / 4 Easy / 3 Neutral / 2 Difficult / 1 Very difficult]

3. How did you find customising the settings, for instance changing the timings, the image, or the music?
   a. [5 Very easy / 4 Easy / 3 Neutral / 2 Difficult / 1 Very difficult]

4. Could you hear the 30-second song notifications on your phone?
   a. [yes / sometimes / no]

5. Do you have your phone on silent (mute notifications and ringtone)?
   a. [5 No, Never / 4 Rarely / 3 Sometimes / 2 Often / 1 Always]

6. Did you see the on-screen notifications (whether you heard the music or not)?
   a. [5 Every time / 4 Most of the time / 3 Sometimes / 2 Occasionally / 1 Never]

7. Did you confirm you had taken your medication from the notification menu?
   a. [5 Every time / 4 Most of the time / 3 Around half the time / 2 Occasionally / 1 Never]

8. Did you use the snooze option available within the notifications
   a. [yes / no / I didn't see this option]
9. Did you confirm your medication/supplement in the app itself?
   a. [yes, most times / yes, sometimes / no / I did it in the notification]

10. Once you heard or saw the notification on your phone, did you take your medication?
    a. [5 Always / 4 Often / 3 Sometimes / 2 Rarely / 1 Never]

11. Did you view the Tracking screen to check your medication adherence over time?

a. [always / most of the time / some of the time /never]

12. Did you use the Prescription Reminder option?

a. [yes / no / I didn't see this option]

13. (If you answered 'yes' to question 12)

Using the scale below, please indicate to what extent the prescription reminder function was useful?

a. Very useful / useful / not that useful / not at all useful

14. Safety questions

a. Whilst using the app did you seek medical attention other than for routine care?

- If yes we may need to contact you for more information.

15. Question at endpoint: how many prescription medications do you take now?

16. Question at endpoint: how many regular OTC medications you take regularly at set times now?

25.5 Appendix 5: - Structured interview questions

Introduction

Thank you for taking part in this study. We are trying to see if using familiar music can help you to reduce missed medications, so we really appreciate you taking the time to participate. Your answers are anonymous and your name will not be associated with this interview. Please try to give your answers as honestly as possible, as understanding any challenges with taking medications can help us to find the best solutions.

- How would you describe your usual medication routine? How many medications (pills or other) do you take and how frequently do you take them?

- Do you have any challenges in remembering to take them regularly? For example, do you sometimes miss taking medications?

- Do you feel that you are good at taking your medications regularly? Do you ever forget or miss taking them for other reasons (for example, because you weren't able to eat)?

Some questions about your technology usage and the app itself …

- What phone do you have?

- How easy do you find using your phone, apps, managing updates or installing them?

- If you get stuck with using or finding something on your phone, what do you do?

- Do you ask a friend or family for help, do you search for a solution online or do you mostly ignore it?

- Did you look at the instructions provided, including the step-by-step video? If you did, what are your thoughts on how helpful they were?

- When you first opened the app, was it clear what to do, such as how to set up a reminder?

- How did you find the process of setting up the reminders overall?

- Were you able to set days and times in a way that worked for you?

- Did you add an image and if so, what did you select? Was it your own? If so, was it a picture of the actual pill or packet?

- How did you find the song selection process? Was the choice of songs appropriate for you?

- Did the notifications appear on your home screen okay?

- Did you hear the music when the notifications happened?

- Did you let the song play for the full 30 seconds or did you cancel it?

- Did you use the options to 'complete' or snooze from within the notifications?

- Did you confirm that you'd taken the medication (complete) in the home screen of the app from the MedTrack Tile menu?

- Did you check your progress in the Tracking section of the app?

- Did you ever play a full song from the MedTrack home screen?

- Overall, how did you find using songs to remind you to take medication?

- How would you describe the app to a friend or a member of your family?

- Would recommend the app to others (assuming it was in the app store)?

25.6 Appendix 6 – Monitoring plan

Reason for Monitoring

The primary objective for conducting monitoring visits is to ensure that the rights, safety and well-being of the trial subjects are being observed as the most important considerations and that they prevail over the interests of science and society. Therefore, the monitoring visits will ensure that the trial documentation is present, complete and in accordance with the principles of GCP and applicable regulations.

Monitoring methods and frequency of visits for this study

The frequency and method of monitoring visits for this study have been determined on the basis of a risk assessment carried out by the trial steering group and CI. The study will be monitored in adherence to the NHS Highland Standard Operating Procedures for monitoring Trust sponsored studies.

For this study the monitoring methods and frequency are outlined below.

Method of Monitoring	**Frequency / timing**
Initiation Visit (On site visit)	On site visit delivered by CI with training to key personnel.
Interim monitoring (On site visit)	In team monitoring after 1st participant for data completeness, eligibility, procedure review and consent documentation. Stop moment. If no problems are identified recommence recruitment. NHS Highlands Governance review after first 10 participants carried out to NHSH SOPs. The study is a low risk.
Heightened monitoring/ Reduced monitoring (Changes to frequency and/or methods of monitoring/ Further investigation into a suspected serious breach/ Further investigation and CAPA/ 'For cause' monitoring/ Terminate the investigator site and notify competent authority and/or REC)	The above scheduled Monitoring Visits may require adjusting due to protocol amendments & changes to risk assessment/ participants recruitment rate/quality concerns/GCP and/or Protocol compliance issues/ staff changes. Escalation procedures should be followed to trigger heightened monitoring on NHSH R&D advice.
Close-out monitoring visit	On site visit close–out via use of NHSH SOPs checklists

(On site visit)	after the end of study date.

4. Initiation Visit

The following activities will be carried out by the Monitor/Trial Co-ordinator during the initiation visit

- Review Investigator Site File – R&D Monitor to check all essential documents in ISF;
  - Protocol
  - Consent forms & Patient Information Sheets (ensure correct versions are filed)
  - Blank Case Report Forms/ access to e-CRFs
  - Delegation Log & training certificates, Screening & Enrolment Log
  - AE/SAE Log & Report Forms, Log/Forms for reporting and documenting Protocol/GCP breaches
  - Amendments Log
  - Regulatory approvals
  - Confirmation of Capacity and Capability
  - Other ……

Discuss:

- Monitoring Plan with investigator team
- Overview of the Protocol/ applicable SOPs and discuss consenting, discontinuation and withdrawal process
- Primary and secondary endpoints
- Definitions of Source Data
- CRF completion procedures, data collection, file notes
- Data management
- Safety reporting requirements and responsibilities
- Documenting and reporting breaches/deviations
- Receiving and implementing amendments
- Other …….

The Monitor/Trial Co-ordinator should also undertake a review of the Sponsor File and ensure it is complete.

5. Interim monitoring conducted after 1, 10, 30, 60 patients are recruited

The following activities will be carried out by the Monitor during the interim monitoring visit*:*

- Preliminary or end discussion with study CI research team (study progress and recruitment, staff changes, amendments submitted, any other identified issues)

- Source Data Verification
  - 100% source data verification on the first patient recruited to the study
  - Data checking: missing data/ CRF data verified against source data – Data Monitor to SDV for completeness for after every 10 participants recruited.
  - Participant Eligibility – Monitor to SDV Eligibility for all patients recruited.
  - Consent forms – Monitor to check validity of consent forms for all participants.

- Review of Investigator Site File and Sponsor File
  - Study documentation up to date
  - Delegation logs
  - Screening logs
  - Recruitment logs
  - Safety reports/reconciliation of investigators AE/SAE Log with Sponsor's records
  - Amendments and completed amendments log
  - Review of recorded/identified Protocol/GCP breaches
  - Check if all findings from previous monitoring visits have been addressed.
  - Review the Sponsor File on at least one occasion during the study.

NOTE: After each monitoring visit the Monitor will:

- Discuss any significant issues immediately with the Research Advisor and/or Head of R&D (sponsor representative). Significant issues or potential risk issues will be escalated to the R&D Group and/or immediately within the organisation.

- Report to the Sponsor, within 24 hours of becoming aware of them, any individual events, or series of events that s/he considers may be a Serious Breach of the Protocol, GCP or other urgent issues the Sponsor should review carefully.

6. Heightened or reduced monitoring and/or changes to monitoring methods

This section is to be completed when changes to the above interim Monitoring Plan have been considered as appropriate.

Changes/ actions to be taken

*Changes to frequency and/or methods of monitoring (specify):

* Further investigation into a suspected serious breach

*Further investigation and CAPA/ 'For cause' monitoring

*Terminate the investigator site and notify competent authority and/or REC

7. Closeout visit

On –site closeout monitoring visit will be conducted at least 30 days after the end of last patient last visit.

The following activities will be carried out by the Monitor during the on-site close out visit monitoring conducted via study specific checklist:

- Full scrutiny of the study ISF and TMF
- Archiving arrangements