PROTOCOL FULL TITLE

A randomised feasibility trial of a patient app and clinical workflow-integrated care team interface to facilitate shared decision making for people with bipolar disorders (SDM-BD)

Study Identifiers

ISRCTN:	15425950		
REC Number:	25/WS/0092		
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Protocol Version Number:	2.0	Date:	19/11/2025

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1. Study Synopsis

TITLE OF STUDY:	A randomised feasibility trial of a patient app and clinical workflow-integrated care team interface to facilitate shared decision making for people with bipolar disorders under maintenance care versus usual care (SDM-BD).
Protocol Short Title/ Acronym:	SDM-BD
Study Phase If Not Mentioned In Title:	Feasibility
Sponsor Name:	King's College London & South London and Maudsley NHS Foundation Trust
Chief Investigator:	Prof Allan Young
Medical Condition or Disease Under Investigation:	Bipolar disorder
Purpose Of Clinical Study:	To determine whether implementation of a new digital health service (Fora Health) could be studied in substantive clinical trials for its ability to improve care for people with bipolar disorders (BD) under maintenance care i.e., feasibility of intervention.
Primary Objective:	The primary objective of the study is to determine whether a UK-adapted Fora Health service can be delivered alongside NHS care for adults with bipolar disorder and whether it is feasible, acceptable to patients, and safe to evaluate the intervention in a definitive trial. This includes assessing intervention fidelity, integration into care pathways, adequacy of staff training, participant engagement, usability, and satisfaction.
Secondary Objective(s):	1. To explore the potential clinical utility of Fora Health by estimating preliminary effect sizes for mood state and patient adherence to prescribed treatment. 2. To evaluate health economic outcomes, including service use, intervention costs, and quality-adjusted life years (QALYs) derived from EQ-5D-5L. 3. To qualitatively explore patient and clinician experiences, including barriers and facilitators to implementation, and to gather feedback to refine the intervention for a future definitive trial. 4. To assess whether the Fora Health service is acceptable to clinicians alongside its compatibility with and integration within existing NHS care pathways and care coordination.

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Study Design:	Single site, randomised controlled feasibility trial.
Endpoints:	Primary: • Recruitment, retention, and completeness of outcome data • Patient acceptability and engagement with the intervention • Fidelity of intervention delivery Secondary: • Patient experience • Mood stability • Patient health confidence and engagement • Shared decision making • Health economic outcomes • Clinician acceptability and service integration
Sample Size:	120 individuals.
Summary Of Eligibility Criteria:	Aged 18 or older at study entry. Meet DSM-5 criteria for a bipolar disorder (type I, type II, or NOS), with onset prior to age 50. Undergoing care within South London & Maudsley NHS Trust and has an identified clinician who is willing and able to provide separate written informed consent. Not currently in an acute bipolar episode. Ability to provide informed consent to participate. Access to internet-enabled device that is supported by the Fora Health application No comorbid substance use disorder. No comorbid organic neurological disorder. Able to read and understand the participant information sheet plus ability to communicate with the researcher throughout screening assessment. Not participating in another clinical trial or research study that may interfere with the objectives/assessments of the present study
Intervention (Description, frequency, details of delivery):	A digital health service (“Fora Health”), a UK and BD-specific service consisting of a patient smartphone app (iOS and Android) and a clinical workflow-integrated and web-app-based Care Team Interface (CTI). The patient app supports patients in preparing for medical appointments, by helping them to review their treatment options and express their treatment preferences using interactive patient decision aids. The app also allows treatment review, to track symptoms, side-effects, medication adherence, and record Patient Reported Outcome Measures (PROMs), and can engage patients in shared decision making (SDM) before, during, and after appointments to support regular treatment review. Information gathered by the patient using the app will be shared with their relevant clinical support team in advance of any clinical encounter and can be used to inform the conversation between the patient and their clinical team.

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	The details of the frequency of patient interaction will depend on the frequency of the medication they take, the PROMs that are included into the app and the frequency of their appointment with the care teams. Patients randomised to receive this tool will, after randomisation, be trained in using the tool and supported in downloading it. They may then access it at their convenience over a 6-month period. Participants who discontinue will remain in the study if they are willing. Participants will also continue usual care.
Comparator Intervention:	Usual care (the trial team will not interfere with this in any regard, although the care received (e.g., frequency, type) will be recorded.
Maximum Duration Of Treatment Of A Participant:	6 months / 26 weeks (i.e., from baseline up until the final follow-up assessment).
Version And Date Of Final Protocol:	V2.0, 19/11/2025
Version And Date Of Protocol Amendments:	n/a

2. Revision History

Document ID – (Document Title) revision X.Y	Description of changes from previous revision	Effective Date
Protocol v1.1	• Timepoints for the delivery of CollaboRATE & M-PICS reduced from Baseline, Weeks 3, 8, 13 and 26, to Baseline and Week 26 only • SUS and Audit Questionnaire timepoints corrected to Week 26 only and Weeks 13 and 26, respectively	04/07/2025

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Protocol v2.0	• General formatting changes • Rephrasing title to refer to clinical workflow integration, as opposed to health record integration • Removal of references to health record integration • Revision of primary and secondary objectives following input from statisticians • Revision of endpoints following input from statisticians • Revisions to Analysis section following input from statisticians • Correction of outcome measure titles/descriptions • Replacement of the Patient Health Engagement Scale with the Altarum Consumer Engagement scale • Inclusion of 'Randomisation' as part of Table 1 • Elaboration on intervention adherence approach and classification • Revisions to Blinding Procedures • Restructuring of Study Procedures section to include per visit descriptions • Decoupling of patient and clinician outcome measure timelines following input from statisticians.	

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3. Glossary of terms

ACE: Altarum Consumer Engagement measure
AE: adverse event
AHY: Prof Allan Young
AR: adverse reaction
ASSIST: Alcohol, Smoking and Substance Involvement Screening Test
BD: bipolar disorder
CI: chief investigator
CRF: clinical research facility
CSRI: client service receipt inventory
GCP: good clinical practice
IQR: Inter-quartile range
IRAS: integrated research application system
ISRCTN: international Standard Randomised Controlled Trial Number
KCL: King's College London
KCTU: King's Clinical Trials Unit
MVAS: Maudsley Visual Analogue Scales, comprising measures of:

- depression (M3VAS-D)
- mania (M3VAS-M)
- anxiety (M1VAS-A)

NHS: National Health Service (UK)
NOS: Not otherwise specified
PHQ-9: Patient Health Questionnaire-9
PI: principal investigator
PIS: participant information sheet
PPI: patient and public involvement
QIDS-C: Quick Inventory for Depressive Symptomatology
REC: research ethics committee
RCT: randomised controlled trial
RS: Dr Rebecca Strawbridge
SAE: serious adverse event
SAP: statistical analysis plan
SAR: serious adverse reaction
SD: standard deviation
SDM: Shared Decision Making
SLaM: South London & Maudsley NHS Trust
SOP: standard operating procedure
SSC: study steering committee
SUS: System Usability Scale
SUSAR: suspected unexpected serious adverse reaction
TAU: Treatment as Usual
UAR: unexpected adverse reaction
UK: United Kingdom
YMRS: Young Mania Rating Scale

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4. Protocol Contents

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5. Background & Rationale

Bipolar disorder (BD) is a long-term, recurrent mental health disorder with frequent hospitalisations, serious physical comorbidity, and a reduced life expectancy of approximately 13 years [9,10]. BD is associated with decreased quality of life, severe loss of functioning, and increased rates of suicide [11,12]. In 2010, the annual NHS cost of bipolar disorder was estimated to be £342 million, where hospitalisations accounted for 60% of costs [11]. There is more need than ever to help prevent avoidable hospital admissions associated with BD [13].

Treatment for BD includes medication therapy, often requiring combinations of various medication classes and doses. People with BD need to make a series of complex decisions about medications throughout their life. Despite the documented efficacy of medication to improve BD outcomes, non-adherence rates of BD patients to medication ranges from 50-80%, with medication non-adherence associated with significant relapse rates, hospital admissions, suicides, and higher healthcare costs [14–16]. BD patients who are non-adherent to maintenance medication have associated poorer long-term clinical outcomes and higher economic costs (costing ~£3,000 more per patient over two years) [15,17,18].

Shared decision-making (SDM) helps clinicians and service users to use the best available evidence to reach a shared agreement on treatment options [19]. NICE recommends that a “SDM approach should be facilitated across all adult mental health services” [20]. The implementation of SDM to support prescription decisions, in addition to psychoeducation implementation, is evidenced to help patients, including those with BD avoid future medication nonadherence [15,21,22]. However, currently the global implementation of SDM into routine mental health care is limited, due to limited access to high-quality decision support tools and restricted patient access to the potential benefits SDM could bring to optimise treatment efficiency [23]. We will address this by creating UK and BD-specific content and functionality to support SDM around maintenance therapy for BD.

The NHS Long Term Plan, Core20PLUS5 statement, and NetZero policy aim to improve mental health services, personalised care and public health, in addition to deploying digital technology and improving healthcare inequalities. Fora Health Ltd. (who have an existing digital health service called ‘Fora Health’), and King’s College

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London (KCL) are working together to develop a UK and BD-specific version of Fora Health to address these ambitions. Fora Health consists of a patient smartphone app (multi-language in iOS and Android) and a clinical workflow-integrated and web-app-based Care Team Interface (CTI). The patient app supports patients in preparing for medical appointments by helping them to review treatment options and express their treatment preferences using interactive patient decision aids. The app also allows treatment review to track symptoms, side-effects, medication adherence, and record Patient Reported Outcome Measures (PROMs), and can engage patients in SDM before, during, and after appointments to support regular treatment review.

We want Fora Health to improve treatment as usual (TAU) for BD service users at scale, by digitally enabling NICE guidance for SDM and BD assessment and management [24,25]. Existing uses of Fora Health by people with depression in the US indicate it can improve patient engagement, decrease depression severity, encourage remission, and reduce health service use by up to 40% (after 1 year of use) [26]. Fora Health hopes to help to reduce avoidable hospital admissions and mental health service use [27]. With the median length of hospital inpatient stay for a BD relapse being 31 days,[28] and a mental health bed costing £404.11 per night, we anticipate one avoided hospital BD admission will save ~£12,000 per patient [29]. We also hope Fora Health will improve patient adherence to maintenance treatment and reduce waste from unwanted prescriptions, helping to tackle NetZero priorities. Data on patient demand for treatment can be used to improve proactive Integrated Care System (ICS) resource planning when needing to alleviate compound pressures.

Supportive technologies for people with serious mental illness are increasingly recognised as being a cost-effective way to provide more continuous care between medical appointments especially when linked to the mental health teams using electronic record systems [30,31]. BD patients prefer making decisions with their clinician, where better clinician-patient relationships improve patient treatment adherence [30]. Better support can lead to reductions in relapses [33] and readmissions [34]. To support SDM, existing web-based and BD-specific patient decision aids have been shown to be acceptable, feasible, safe, and potentially effective [35]. Furthermore, remote interventions to support SDM are possible and have been shown to reduce overall medical costs and result in fewer hospital admissions [36]. Mobile health tools for BD have also been shown to be feasible in BD care for patients and their carers [37,38]. Studies have highlighted the need for detailed decision aids [39] and for psychoeducation and an ability to track treatment effectiveness, inform their clinical team, and maintain access to highly valued face-to-face contact when required [40]. Building on this work, this application brings together expertise from an experienced mental health research team, SDM expertise, and experienced commercial entity a with proven record of accomplishment. Fora Health is of Technology Readiness Level 5-6 [41] and is considered a Tier C Digital Health Technology as per the NICE Evidence Standards Framework (ESF) [42]. From 2018-2021 in the US, Fora Health has been used to support people with depression (as a real-world effectiveness and feasibility study (40 patients) and a cluster randomised trial (76 patients) [26,43] and has been deployed to be used by people with a rare disease [44]. In 2022, Fora Health was integrated into the EPIC EPR in a 200-patient pilot study within a large US Accountable Care Organisation to support patients with depression [45]. Initial results have shown an increased patient engagement, greater remission, and reduced referrals for patients using Fora Health [46]. In 2023, Fora Health is being piloted within Access Community Health Network [47], a network of Federally Qualified Health Centres in South Chicago supporting underserved communities. Fora Health is also working with Professor Elwyn at The Dartmouth Institute for Health Policy and Clinical Practice to support the use of conversation aids and shared decision-making with adolescent patients and their carers who are taking multiple medications polypharmacy and who have been prescribed off-label antipsychotics [48,49]. Fora Health has been developed in line with ISO 13485 standards, is Health Insurance Portability and Accountability Act (HIPAA) and General Data Protection Regulation (GDPR) compliant and is progressing with Digital Technology Assessment Criteria (DTAC) regulation. The current barriers stopping Fora Health from being commissioned within the UK are 1) an absence of UK real-world evidence (as stipulated by standards 14-17 of the NICE ESF), and 2) a need for Fora Health to be integrated within NHS systems.

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6. Objectives and Design

6.1. Objectives

The primary objective of the study is to determine whether a UK-adapted Fora Health service can be delivered alongside NHS care for adults with bipolar disorder and whether it is feasible, acceptable to patients, and safe to evaluate the intervention in a definitive trial. This includes assessing intervention fidelity, integration into care pathways, adequacy of staff training, participant engagement, usability, and satisfaction.

The secondary objectives include:

- To explore the potential clinical utility of Fora Health by estimating preliminary effect sizes for mood state and patient adherence to prescribed treatment.
- To evaluate health economic outcomes, including service use, intervention costs, and quality-adjusted life years (QALYs) derived from EQ-5D-5L.
- To qualitatively explore patient and clinician experiences, including barriers and facilitators to implementation, and to gather feedback to refine the intervention for a future definitive trial.
- To assess whether the Fora Health service is acceptable to clinicians alongside its compatibility with and integration within existing NHS care pathways and care coordination.

6.2. Outcome measures

6.2.1. Primary outcome measures

1. Recruitment, retention, and completeness of outcome data
    - Number of participants randomized per month.
    - Proportion of participants retained at 26 weeks, with reasons for withdrawal and loss to follow-up.
    - Proportion with complete data for key assessments (mood state, patient engagement, EQ-5D-5L) at 26 weeks.
2. Patient acceptability and engagement with the intervention
    - Usability and satisfaction with the app, assessed using the System Usability Scale (SUS) and qualitative interviews.
    - Distribution of participants in the intervention arm across categories of intervention engagement (i.e., no, low, moderate, and high engagement).
3. Fidelity of intervention delivery
    - Adoption by staff (training completion and uptake).
    - Delivery of core intervention functions and consistency across sites.
    - Anticipated adaptations, costs, and resources, documented through structured fidelity audits guided by the RE-AIM framework.

6.2.2. Secondary outcome measures

The secondary outcomes are exploratory. They will inform the choice of a primary endpoint for a future definitive trial and provide estimates of effect size, variability, and data completeness.

1. Mood stability (at week 26)
    - Patient-reported measures: Maudsley Visual Analogue Scales (M-VAS), Patient Health Questionnaire-9 (PHQ-9) [2, 51].
    - Interviewer-rated measures: Quick Inventory of Depressive Symptomatology (QIDS), Young Mania Rating Scale (YMRS) [3,4].

    These mood stability measures are designated as the main clinical outcomes to be piloted in this feasibility study. These will inform decisions relating to the primary endpoint(s) for a future definitive trial and provide preliminary estimates to support potential superiority or non-inferiority designs.

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2. Patient experience
    - Perceptions of the intervention compared with usual NHS care (convenience, effectiveness, and whether the service meets patient needs).
    - Measured through semi-structured interviews with patients, analysed using the RE-AIM framework.
3. Patient health confidence and engagement
    - Self-reported confidence in managing health and treatment, measured using the Health Confidence Scale [5].
    - Patient engagement, measured by the Altarum Consumer Engagement scale [1].
4. Shared decision making
    - Patient-reported involvement in care decisions, measured using the CollaboRATE tool [6] and the Modified Patient Involvement in Care Scale [63].
5. Health economic outcomes
    - Health-related quality of life: EQ-5D-5L [7].
    - Service use: Client Service Receipt Inventory (CSRI) [8].
    - Appointment outcomes: did-not-attend (DNA) rates and appointment duration.
6. Clinician acceptability and service integration
    - Clinician accessibility and workflow integration, assessed using the Mini-Z Burnout Scale and qualitative interviews.
    - Integration into existing NHS care pathways and care coordination, assessed in semi-structured interviews using the RE-AIM framework.

Additional tertiary/exploratory analyses may be undertaken.

6.3. Study Design

A phase II, parallel group, single site, two-arm randomised feasibility study. A total of 120 patients with BD will be recruited and randomised in a 1:1 ratio to either:

- Treatment as Usual
- Treatment as Usual plus access (themselves and their clinician) to the app/interface for use over a six-month period

6.4. Study Flowchart

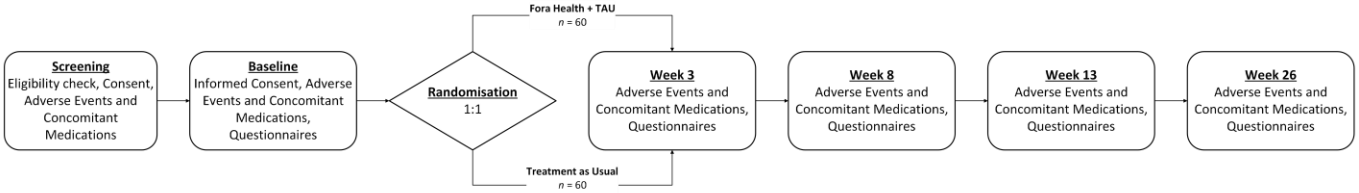

Table 1: Summary of study procedures and measures.

Procedures/Measures	**Screening**	**Baseline (week 0)**	**Week 3**	**Week 8**	**Week 13**	**week 26**
Day *[window]*	**n/a**	**0**	**21** [±14]	**56** [±14]	**91** [±14]	**182** [±14]
Eligibility assessment (clinician report)	X					
Informed consent (patient)	X	X				
Informed consent (clinician)		X				

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Procedures/Measures	Screening	Baseline (week 0)	Week 3	Week 8	Week 13	week 26
Eligibility assessment (patient report)	X					
Eligibility assessment (substance use disorders; ASSIST)	X					
Randomisation		X				
Sociodemographic		X				
Adverse Events	X	X	X	X	X	X
Concomitant Medications & Therapies	X	X	X	X	X	X
Interviewer-rated depressive symptoms (QIDS-C)		X	X	X	X	X
Patient-rated depressive, anxious & manic symptoms		X	X	X	X	X
Patient-rated depressive symptoms (PHQ-9)		X	X	X	X	X
Interviewer-rated manic symptoms (YMRS)		X	X	X	X	X
Health-related quality of life (EQ5D) & service use (CSRI)		X			X	X
Participant engagement (ACE)		X	X	X	X	X
Patient confidence (Health Confidence Scale)		X	X	X	X	X
Extent of shared decision making (CollaboRATE & M-PICS)		X				X
Clinician Burnout (Mini-Z)‡		X				X
System Usability Scale (SUS)*†						X
Audit Questionnaire - Patient*					X	X
Audit Questionnaire – Clinicians*‡						X
**Intervention Group Only, †Completed by Participants and Clinicians, ‡Completed by Clinicians Only*						

7. Study Intervention

7.1. Therapy/Intervention Details

This section relates to the Fora Health service.

A digital health service ("Fora Health") will contain a UK and BD-specific application consisting of a patient smartphone app (iOS and Android) and a clinical workflow-integrated and web-app-based Care Team Interface (CTI). This patient app will be introduced to the patient by their clinical team members. Clinicians will be given training and granted access to the CTI at enrolment.

The patient app supports patients in preparing for medical appointments, by helping them to review their treatment options and express their treatment preferences using interactive patient decision aids. The app also allows treatment review to track symptoms, side-effects, medication adherence, early warning signs and record Patient Reported Outcome Measures (PROMs).

Information gathered by the patient using the Fora Health app will be shared with their relevant clinical support team in advance of any clinical encounter and can be used to inform the conversation between the patient and their clinical team.

If during or after the clinical encounter a decision to change or alter treatment is made, then both the patient and the clinical team will be asked to attest to whether this decision would be a shared decision from their perspective. The patient can record this in the app, and the clinical team member can record this in the care team interface. The patient will then be able to continue to use the app to support their adherence to their new treatment and continue to share information with their clinical team to help inform any subsequent conversations.

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The details of the frequency of patient interaction will depend on the frequency of the medication they take, the PROMs that are included into the app and the frequency of their appointment with the care teams.

Fora Health has undertaken a self-assessment of the Fora Health service using US, EU and UK guidelines. Please see the summary of these assessments below:

- Fora Health **does not qualify** as a Medical Device in the US and is not subject to regulation by the FDA.
- Fora Health **does not qualify** as a Medical Device in the EU and is not subject to regulation under the MDR. The same "monitoring" caveat as the UK does apply.
- Fora Health **does not qualify** as a Medical Device in the UK and is not subject to regulation by the MHRA. One key assumption here is that the intended use of the data collected by a patient using the Fora Health app is to inform a conversation rather than guide treatment.

Given the nature of the intervention and the length of time the intervention will be in use by patients and clinical teams, we anticipate that minor modifications to the service may be required during the study. These planned minor changes will be formally documented and reviewed to ensure they do not impact the scientific integrity of the study (i.e., ensuring that they do not fundamentally alter the service for either patients or clinical teams).

Updates/amendments to the service may be introduced in response to:

- **Regulatory or technological developments:** e.g., software updates to maintain compliance with new regulations/policies, or to accommodate new devices, operating systems, or browsers).
- **Participant feedback:** e.g., updates to user experience elements or alterations to the workflow, training or defined clinical roles.

7.2. Intervention timeline

The intervention will begin at the start of Week 1, the day after baseline assessment. The intervention will continue for 6 months, until the final assessment at week 26, or as long as participants are willing to continue with the intervention during this time.

7.3. Intervention Adherence

Intervention Adherence, alternatively referred to as 'Engagement', will be examined by assessing, through usage data, the extent to which the patient has engaged with the intervention. Level of engagement across shared-decision functionality, self-management functionality and information functionality will be quantified in terms of the number of "active months" during the intervention period, with an 'active month' defined as any 28-day period in which a participant interacts with the Fora Health application. For each participant, the possible range of engagement is 0 (i.e., none) to 6 (consistent and sustained engagement across the study period), with engagement classified as follows:

- 0 active months = no engagement
- 1-2 active months = low engagement
- 3-4 active months = moderate engagement
- 5-6 active months = high engagement

7.4. Concomitant treatments (usual care)

All participants will continue receiving TAU including all concomitant interventions and service use. We will monitor and record these.

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8. Research environment

By default, all study assessments will be conducted remotely via telephone/videocall (MS Teams). However, participants may opt to attend in-person visits if preferred. In-person visits will be arranged with the study team and are to be held at the King's CRF and carried out by the study team.

9. Selection and Withdrawal of Participants

9.1. Inclusion Criteria

- Aged 18 or older at study entry (via patient report).
- Meet DSM-5 criteria for a bipolar disorder (type I, type II, or NOS), with onset prior to age 50, as reported by clinician.
- Undergoing care within South London & Maudsley NHS Trust and has an identified clinician who is willing and able to provide separate written informed consent. *
- Ability to provide informed consent to participate.
- Access to an internet-enabled device that is supported by the Fora Health application, according to minimum system requirements.

**Please note that there are no specific criteria relating to clinicians' inclusion, besides their responsibility for the patient. Additionally, for the purposes of this trial, a clinician is any healthcare professional within SLaM with responsibility for managing the bipolar disorder treatment of a given participant. This includes, but is not limited to, consultants and care coordinators.*

9.2. Exclusion Criteria

- Currently in an acute bipolar episode (as reported by clinician).
- Comorbid substance dependence, as determined by a score of 27 or higher on any domain of the Alcohol, Smoking and Substance Involvement Screening Test v3.1 (ASSIST) [52].
- Comorbid organic neurological disorder (as per patient report).
- Unable to read and understand the participant information sheet and inability to communicate with the researcher throughout screening assessment.
- Participation/enrolment in another clinical trial or research study that may interfere with the objectives/assessments of the present study

9.3. Selection of Participants

Our participants will be identified via SLaM clinical services, either via research team communications with service members or via CRIS. CRIS allows patients in secondary care to be identified. This service allows approved researchers to rapidly screen case notes of service users who have agreed that researchers can access their contact details and limited clinical information and invite them to participate in research projects. We will utilise the SLaM Consent for Contact (C4C) initiative to recruit Trust patients and will follow the related Trust policy. After potentially eligible individuals are identified through any of these routes, both them and their clinician will be provided with information about the study and a full screening for eligibility will take place subject to verbal consent; for details, see Section 10). Informed consent will be required from both patients and their clinicians to facilitate participation.

9.4. Randomisation Procedure / Code Break

Following written consent, participants will be randomised in a 1:1 ratio to one of the two treatment arms (TAU, or TAU + Fora Health) within 24 hours of completing the baseline assessment. A web-based randomisation system

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will be designed, using the bespoke KCTU randomisation system. The randomisation system will be created in collaboration with the trial analyst/s and the CI and maintained by the King's Clinical Trials Unit for the duration of the project. It will be hosted on a dedicated server within KCL. The system will employ block randomisation with randomly varying block sizes. The details needed for randomisation (month/year of birth, initials and unique patient identity number) will be held in a dedicated database. Only the trial coordinator (unblinded) will have access to the randomisation system (or their nominated backup in times of absence; the nominated backup will not be another member of the blinded team but will be a team member whose role on the delegation log specifies this role as contingency Trial Manager). Those randomised to the intervention will then receive an invitation from the clinical team to download and start using the app.

9.5. Blinding Procedures

Due to the nature of the intervention, blinding of participants and their treating clinicians to study arm allocation is not feasible. With this in mind, and to minimise bias, blinding will be implemented at the level of outcome assessment wherever possible. The partial blinding strategy to be implemented as part of this study is as follows:

- **Blinded staff:** members of the study team responsible for administering clinical symptom inventories (e.g., QIDS and YMRS) will remain blinded to participants' treatment allocation. These assessors will not be involved in randomisation, allocation, or delivery of the intervention.
- **Unblinded staff:** Trial coordinators and other team members who are not conducting blinded outcome assessments will be aware of participants' allocation in order to manage randomisation, intervention delivery, and participant support.
- **Blinding maintenance:** Procedures will be in place to reduce the risk of accidental unblinding during assessments, including instructing participants not to disclose their allocation to assessors. If unblinding occurs, this will be documented, and a new blinded assessor will be assigned where feasible.
- **Data analysis:** Outcome data will be analysed by statisticians blinded to treatment allocation until the primary analysis dataset has been finalised.

9.6. Withdrawal of Participants

We will highlight to all participants that they are free to withdraw from the study at any time, without prejudice or consequences for their clinical care or their involvement in any other research studies. Similarly, the study intervention can be discontinued at any point. This will occur where a clinician withdraws their support for their patients' participation, where a participant decides they no longer wish to continue the intervention, or where a participant withdraws from the study entirely. The investigator also has the right to withdraw patients from the therapy and/or study, for any reason e.g., if a participant loses the capacity to consent to the study, they will be withdrawn. This will be assessed by researchers during every contact with participants (e.g., phone calls, study appointments). If needed, researchers will be available throughout the study course to answer further questions about withdrawal. Should a participant decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible.

Participants will be advised that they have the right to dissent to Fora Health's access to and usage of their data. However, this will prevent them from continuing to use the Fora Health platform. To this end, discontinuation from Fora Health does not constitute withdrawal from the study. Thus, should a patient withdraw from the intervention only, efforts will be made to continue to obtain follow-up data, with the permission of the patient; participants who wish to withdraw from Fora Health will be asked to confirm whether they are still willing to provide the study data already provided for research.

In the event that clinicians withdraw from the study, any of their patients that are randomised to the intervention group will no longer be able to access the service. However, they will be asked to continue in the study on an intention-to-treat basis, including attending all remaining study visits.

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9.7. Expected Duration of Study

The total study duration for a given participant will be 26 weeks. Week 0 will comprise the baseline assessment and Fora Health initiation will occur as soon as feasible after this. Intermediary assessments will be conducted at Weeks 3, 8 and 13, followed by the final follow-up assessment and discontinuation of Fora Health use at week 26. The beginning of the study overall will be Week 0 (baseline assessment) of the 1st participant, estimated April 2025. Data collection will end after the last participant's final follow-up assessment, estimated to be in August 2026. The end of study is defined by the completion of the data analysis necessary for the final study report.

10. Study Procedures

10.1. Overview

The trial involves procedures for both patients with bipolar disorder and their clinicians. Patients will use the Fora Health app for six months, with scheduled outcome assessments and engagement in shared decision-making discussions with their clinician. Clinicians, meanwhile, will engage with the platform's care team interface, using it to support clinical conversations and decisions, and will complete certain outcome measures.

To reduce burden while ensuring the collection of meaningful clinician-reported data, clinician measures will not be tied to patient schedules. Instead, each enrolled clinician will be asked to complete measures at two fixed timepoints: at the time of their first patient's baseline visit, and again 26 weeks later. This approach ensures consistent and standardised clinician-level data, irrespective of how many patients each clinician has in the study or the duration of their participation.

10.2. By Visit

The summary table in section 6.3 describes the procedures at each 'visit' (or measurement timepoint) which are also described below. We refer to each timepoint by its week number (W), (except for the first screening, which is not assigned a 'W' timepoint).

Once identified through different recruitment sources, potential patient participants will be first contacted regarding the study by a researcher who will send them a copy of the Participant Information Sheet (PIS; via email, post or in person). The researcher will encourage potential participants to spend as much time as they need asking questions about the study (via email or phone call) and consider whether they wish to participate or not. As a minimum, study information will be provided to potential participants at least 24 hours prior to screening. After reading the PIS and having any questions answered, if the participant is happy to take part in the study, an appointment for screening will be arranged.

10.2.1. Screening

Usually conducted over the phone, or if potential participants are willing, by videocall (i.e., Microsoft Teams). Here, study information will be discussed and verbal consent for screening obtained. If the potential participant is willing, screening will provide an initial determination of eligibility. Specifically, eligibility will be assessed via screening procedures as follows:

- Open questions for self-report:
    - Eligible age range.
    - Clinical health diagnoses (including bipolar disorder).
    - Current neurological disorder/s
- Assessment for substance use disorders via the Alcohol, Smoking and Substance Involvement Screening Test [52]
- Ability to communicate assessed via discussions with researcher about understanding of participant information sheet and prior questions.

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- Ability to provide informed consent to participate assessed by researcher, via communications and understanding of the procedures being consented to.
- Confirmation of access to internet-enabled device that is supported by the Fora Health application

If, following this visit, all inclusion criteria are met and no exclusion criteria are violated, the W0 assessment will be scheduled (within 28 days of screening assessment; if time exceeds this, the relevant parts of the screening assessment would be repeated).

10.2.2. Baseline (Week 0)

The baseline visit will occur after eligibility screening (as outlined above) and clinician consent and onboarding to the Fora Health platform. Patients will enter the study via one of two recruitment streams:

a) **Clinician-led referral:** The clinician refers an eligible patient to the research team.

b) **Patient-led self-referral:** The patient expresses interest and is screened by the research team; following preliminary eligibility confirmation, the patient's clinician is approached for consent and onboarding.

This approach ensures that clinician consent is obtained, and onboarding completed prior to any of their patients formally enrolling in the study.

Prior to completing the baseline assessment, written informed consent will be obtained from the patient electronically. Electronic consent will be obtained via a Qualtrics form that comprises both the information sheet and consent form, with patients and clinicians receiving a copy of their form after submission. Participants' signatures will be verified by (a) their sharing of the completion screen with the researcher and/or (b) confirmation of submission receipt by the researcher.

The following measures will then be administered to the participant.

- Sociodemographic / clinical history measures: Date of birth, gender, ethnicity, education level (highest level of education), employment status, details related to previous episodes and hospitalisations for BD.
- Current treatments: Non-pharmacological and medication therapies currently undergoing (including type, dose, frequency of use, duration of use).
- Symptom assessments:
    - Patient-rated Maudsley visual analogue scales (MVAS) [2] for symptoms of depression, mania and anxiety
    - Patient-rated measure of depression (PHQ-9) [51]
    - Investigator-rated depressive symptoms scale (QIDS-C) [3]
    - Investigator-rated Young Mania Rating Scale (YMRS) [4]
- Assessments for health economic outcomes:
    - Health-related quality of life (EQ-5D-5L) [7]
    - Client service receipt inventory (CSRI) [8]
- Assessment of patient engagement (ACE) [1]
- Assessment of patient confidence (Health Confidence Scale) [5]
- Assessment of extent of shared decision-making (CollaboRATE and M-PICS) [6, 63]

Participants will, at the end of the assessment, be randomised to either the Fora Health + TAU or TAU group. Those randomised to the Fora Health + TAU group will then be supported by the research team in installing the application on their supported device, alongside being provided with written instructions for installing and using the application. In conjunction with the baseline visit for their first enrolled patient, clinicians will complete the measure of clinician burnout (Mini-Z) [61].

The researcher will subsequently send a letter of notification regarding the study (and information about Fora Health) to the participants' named Healthcare Professional.

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10.2.3. Week 3

As part of patients' Week 3 visits, the following procedures will be undertaken:

- Review of current treatments: Non-pharmacological and medication therapies currently undergoing (including type, dose, frequency of use, duration of use) or stopped since last visit
- Review of adverse events since last visit
- Symptom assessments:
    - Patient-rated Maudsley visual analogue scales (MVAS) for symptoms of depression, mania and anxiety
    - Patient-rated measure of depression (PHQ-9)
    - Investigator-rated depressive symptoms scale (QIDS-C)
    - Investigator-rated Young Mania Rating Scale (YMRS)
- Assessment of patient engagement (ACE)
- Assessment of patient confidence (Health Confidence Scale)

10.2.4. Week 8

As part of patients' Week 8 visits, the following procedures will be undertaken:

- Review of current treatments: Non-pharmacological and medication therapies currently undergoing (including type, dose, frequency of use, duration of use) or stopped since last visit
- Review of adverse events since last visit
- Symptom assessments:
    - Patient-rated Maudsley visual analogue scales (MVAS) for symptoms of depression, mania and anxiety
    - Patient-rated measure of depression (PHQ-9)
    - Investigator-rated depressive symptoms scale (QIDS-C)
    - Investigator-rated Young Mania Rating Scale (YMRS)
- Assessment of patient engagement (ACE)
- Assessment of patient confidence (Health Confidence Scale)

10.2.5. Week 13

As part of patients' Week 13 visits, the following procedures will be undertaken:

- Review of current treatments: Non-pharmacological and medication therapies currently undergoing (including type, dose, frequency of use, duration of use) or stopped since last visit
- Review of adverse events since last visit
- Symptom assessments:
    - Patient-rated Maudsley visual analogue scales (MVAS) for symptoms of depression, mania and anxiety
    - Patient-rated measure of depression (PHQ-9)
    - Investigator-rated depressive symptoms scale (QIDS-C)
    - Investigator-rated Young Mania Rating Scale (YMRS)
- Assessments for health economic outcomes:
    - Health-related quality of life (EQ-5D-5L) [7]
    - Client service receipt inventory (CSRI) [8]

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- Assessment of patient engagement (ACE)
- Assessment of patient confidence (Health Confidence Scale)

In addition to the above, patients will be asked to complete an audit questionnaire assessing intervention delivery.

10.2.6. End of Study (Week 26)

At the Week 26 end-of-study visit, the following measures will then be administered to the participant:

- Review of current treatments: Non-pharmacological and medication therapies currently undergoing (including type, dose, frequency of use, duration of use) or stopped since last visit
- Review of adverse events since last visit
- Symptom assessments:
    - Patient-rated Maudsley visual analogue scales (MVAS) for symptoms of depression, mania and anxiety
    - Patient-rated measure of depression (PHQ-9)
    - Investigator-rated depressive symptoms scale (QIDS-C)
    - Investigator-rated Young Mania Rating Scale (YMRS)
- Assessments for health economic outcomes:
    - Health-related quality of life (EQ-5D-5L)
    - Client service receipt inventory (CSRI)
- Assessment of patient engagement (ACE)
- Assessment of patient confidence (Health Confidence Scale)
- Assessment of extent of shared decision-making (CollaboRATE and M-PICS)

In addition to the above, patients will be asked to complete an audit questionnaire assessing intervention delivery alongside the System Usability Scale [50]. Clinicians will complete these same measures, alongside the Mini-Z. Beyond this, a subsample of 8 patients and 8 clinicians involved in the intervention will be invited to participate in semi-structured interviews to evaluate the practicality and acceptability of the service, guided by the RE-AIM framework [53-55]. Separate interview guides will be developed for patients and clinicians, addressing key aspects such as:

- service integration
- barriers and facilitators to implementation
- perceived usability
- the intervention's impact on care delivery and team interaction

Patient interviews will also explore how different features of the Fora Health app (information, self-management, and shared decision-making tools) influenced engagement and care experience, while clinician interviews will examine workflow integration, training adequacy, and perceived patient outcomes.

Participant selection will be guided by predefined stratification criteria, with patients stratified by borough, service type, and level of app engagement, and clinicians by borough, role, and service. Additionally, the research team will aim to ensure that the subsample is demographically representative of SLaM's overall patient population and will periodically review its representativeness with oversight from an unblinded researcher.

Interviewers will be provided with contextual data (e.g. app usage logs, RE-AIM audit survey responses, System Usability Scale scores) to inform their understanding of each participant's experience, though this information will not influence the structure of the interviews themselves. Interviews will be audio recorded, transcribed, and analysed using a codebook, developed by the research team, using a priori and emergent codes. The research team will code the data and audit to ensure intercoder reliability. Analysis will draw on grounded theory and constant comparative methods to identify themes relevant to implementation and sustainability [56, 57].

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10.3. Laboratory Tests

N/A

11. Assessment of Safety

11.1. Assessment of Therapy Safety

While safety is not an outcome of this study, the risk of the intervention for this patient population will be analysed as part of pre-trial development and used to inform the decision to start this study itself. As with previous deployments of Fora Health with other indications such as Major Depressive Disorder (MDD) and in Adolescent Polypharmacy, clinical team input into the design or the intervention, will inform the assessment of risk and the mediation of any safety concerns. The welfare of our participants is paramount, and we will closely monitor information obtained from participants to ensure their safety. Specifically, this includes monitoring of clinical wellbeing measures (as soon as information is available to the research team). If any wellbeing concerns arise in general, participants will be contacted within one working day by a study researcher for a wellbeing discussion and to provide support (i.e., study-related actions, signposting e.g., to support or healthcare services).

11.2. Specification, Timing and Recording of Safety Parameters

The study researcher will be responsible for checking with the participant verbally that there are no current negative effects and will record any injuries, notable events or other phenomena that might be of concern. These will be treated as any adverse event in any trial (see section 11.3). Any concerns will be communicated to the Lead Investigator (AHY).

11.3. Procedures for Recording and Reporting Adverse Events

Any adverse events will be recorded by a researcher at each visit asking participants if they have had any troubles and record these systematically. Even though Fora Health has been assessed internally as **not qualifying** as a Medical Device in the UK and is therefore not subject to regulation by the MHRA, this assessment has been validated the MHRA prior to the trial initiation. The standard definitions provided by The Medicines for Human Use (Clinical Trials) Regulations 2004 and Amended Regulations 2006 with regards to adverse events will be used, as follows:

- **Adverse Event (AE):** Any untoward medical occurrence in a subject to whom an intervention has been administered including occurrences which are not necessarily caused by or related to that intervention.
- **Adverse Reaction (AR):** Any untoward and unintended response in a subject to an intervention which is related to the intervention administration to that subject.
- **Unexpected Adverse Reaction (UAR):** An adverse reaction the nature and severity of which is not consistent with the information about the intervention in question.
- **Serious Adverse Event (SAE), Serious Adverse Reaction (SAR) or Suspected Unexpected Serious Adverse Reaction (SUSAR):** Any adverse event, adverse reaction or unexpected adverse reaction, respectively, that: results in death; is life-threatening; required hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability or incapacity; consists of a congenital anomaly or birth defect.
- **Important Medical Events (IME):** Events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require an intervention to prevent one of the other outcomes listed in the definition above should also be considered serious.

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Any AEs (excepting those specified in this protocol as not requiring reporting; see below section 11.4) that occur throughout the duration of the study will be recorded in the participant case report form. Investigators will assess whether the AE may be related to study participation and will also assess the severity of the event. Documented AEs reported after a participant signs the consent form will be included in the primary study report.

All AEs classified as ARs and UARs will be recorded and immediately addressed with the Chief Investigator (certainly no later than 24 hours), as well as be considered in Steering Group Meetings. All SAEs and SARs will be reported immediately (certainly no later than 24 hours) by the Chief Investigator to the Sponsor and the R&D office using a SAE report form. In accordance with the Health Research Authority procedures, only SUSARs will be reported by the Chief Investigator to the Research Ethics Committee for review (sent within seven days of the reaction for fatal or life-threatening events and 15 days of the reaction for not fatal or life-threatening events).

Although we do not anticipate any SARs or SUSARs, participants presenting any such reactions will be withdrawn from Fora Health and, if not already done by the participant, these reactions will be brought to the attention of their named healthcare professional. Non-serious ARs may also warrant a referral back to the named healthcare professional, but withdrawal from the study will depend on risk assessment, circumstances and participant's wishes.

All SAEs that have not resolved by the end of the study, or that have not resolved upon discontinuation of the subject's participation in the study, will be followed until: the event resolves, the event stabilises, the event returns to baseline (if a baseline value is available), the event can be attributed to agents other than the study participation or to factors unrelated to the study, when it becomes unlikely that any additional information can be obtained. All follow-up information for SAEs that have not resolved by the end of the study or by the time of participant withdrawal will be reported to the Sponsor.

11.4. Adverse events that do not require reporting

No SAEs are expected in this study. Therefore, any SAEs will be reported as will ARs, UARs, SARs or SUSARs or IMEs. AEs that do not meet the above criteria but require intervention (e.g., safety concerns communicated to patients' healthcare professional or incidence of acute episode requiring changes to treatment regime) will be reported. Other AEs do not require reporting (e.g., mild distress disclosed by participants where no further action is required or unrelated to the study/intervention).

11.5. Stopping Rules

Other than plans noted above, no stopping rules are planned for the study. The study may be prematurely discontinued by the Sponsor or Lead Investigator based on new safety information arising during the conduct of the study, in the case of AEs associated with the intervention, or for other reasons given by the Research Ethics Committee. The study may also be prematurely discontinued due to lack of recruitment or high attrition from the study, as advised by the Study Steering Committee (SSC). If the study is prematurely discontinued, active participants will be informed, and no further participant data will be collected. The Research Ethics Committee will be informed within 15 days of the early termination of the study. Participants may discontinue treatment at any time they choose or as recommended by study researchers (section 9.6).

12. Statistics

This protocol will be published to ensure transparency of study analyses and outcome reporting following the study.

12.1. Sample Size

As an initial proof-of-concept study, a sample size calculation is not warranted. However, it has been determined that, if 60 participants are randomised to the intervention group, we will be able to estimate an adoption rate of

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50% with a margin of error of 8.89% at 95% confidence level. [58] The inclusion of a control group of the same size will allow estimation of retention and other feasibility parameters along with effect size and 95% CI in our clinical outcomes, representing putative future primary outcomes.

12.2. Analysis

A comprehensive Statistical Analysis Plan (SAP) will be developed before the first SSC meeting and finalised prior to database lock and before any analysis is undertaken. The SAP will provide detailed specifications of analysis methods, model choices, covariate adjustments, handling of missing data, and sensitivity analyses. In the event of any discrepancy between the protocol and the SAP, the SAP will take precedence.

All analyses will be conducted on an intention-to-treat (ITT) basis, with participants analysed according to their randomized allocation. As this is a feasibility study, the emphasis will be on descriptive analyses with estimates of variability and precision. No formal hypothesis testing will be conducted for effectiveness outcomes. A CONSORT flow diagram will be used to report the flow of participants through each stage of the trial. This will include the numbers screened for eligibility, numbers eligible, numbers consented and randomised, allocation to each arm, numbers completing follow-up at 26 weeks, and numbers included in the analysis. Reasons for exclusion, withdrawal, and loss to follow-up will be documented where available. Baseline demographic and clinical characteristics of participants will be summarised by trial arm. Categorical variables will be presented as counts and percentages, while continuous variables will be summarised using means and standard deviations if normally distributed, or medians and interquartile ranges if not. These summaries will describe comparability of groups at baseline but will not be subject to statistical testing.

Feasibility outcomes will be summarised descriptively with the 95% confidence intervals.

13. Study Steering Committee

The Study Steering Committee (SSC) will comprise the Lead Investigator (Prof Allan Young) in addition to other study researchers, health economist, Fora Health expert and PPI expert, as well as one individual with current/past lived experience of a mood disorder. The SSC will meet usually every 6 months, except more frequently to ensure a meeting is held at key times of the study (just before recruitment, early stages of recruitment, end of project) and 6 months at other times. The SSC will aim to provide oversight of the project, ensuring that it is conducted to a rigorous standard in line with Good Clinical Practice guidelines and other best practice conduct and reporting standards. These include pre-registration of this protocol, comprehensive and transparent reporting, and study progress and participant welfare.

14. Data Monitoring

There is no evidence of a potential lack of safety of the intervention, which also does not replace any usual clinical treatment or responsibility for participants. Also, as a feasibility study, considered to be low risk and where the purpose is not to assess safety or efficacy as outcomes and therefore a formal independent Data Monitoring and Ethics Committee (DMEC) is not considered to be warranted [59]. As part of the study, the following information will also be captured from the patients in the intervention arm:

- Health data:
    - Health conditions and diagnosis
    - Prescribed treatments,
    - Treatment plans
    - Treatment preferences

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- Symptoms and side-effects
- Responses to PROMs

- Personally identifiable data:
  - Basic details and contact information, such as name, address, email address, date of birth, phone number.
  - NHS number
- App usage data:
  - Analytics information about the usage of the app such as features used and engagement.

This information will be used to both support the intervention experience for the patient alongside informing product development decisions and validation of product performance.

Patient data collected by Fora Health to be stored on secure servers hosted by Fly.io Inc, and Very Good Security Inc. as sub-processors. Further details of Fora Health Ltd privacy policy can be found online [62].

15. Direct Access to Source Data and Documents

The study investigators will permit study-related monitoring, audits, and REC review by providing the Sponsor and REC direct access to source data and other documents (e.g., case report forms, test reports, etc.) when required.

16. Ethics & Regulatory Approvals

The study will be conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework and the Mental Capacity Act 2005. This protocol and related documents will be submitted for review to a local Research Ethics Committee (REC) [to be confirmed] in [TBD]. The Chief Investigator will submit a final report at conclusion of the study to the funder, the REC and the Sponsor.

17. Quality Assurance

Monitoring of this study will ensure compliance with Good Clinical Practice and scientific integrity will be managed by the study team and overseen from the SSC. Our procedures ensure that study researchers are trained and supported in conducting assessments, liaising and informing participants, and handling data. The Lead Investigator maintains overall study responsibilities, working closely with other members of the team to ensure the study is conducted according to the protocol, best practice SOPs and GCP. During the planning of the project, the proposal was reviewed by experienced academics, statisticians, and clinicians. The proposal was also reviewed by people affected by cognitive concerns and/or lived experience of caring for individuals with dementia, who were consulted using various approaches. The full proposal was formally peer reviewed via the NIHR i4i Product Development Awards Committee (ref NIHR206433).

18. Data Handling

The Lead Investigator will act as custodian for the study data. Patient data will be anonymised as far as possible (see below for detail). All study data will be stored in line with the Data Protection Act and archived in line with Sponsor requirements. The electronic database will be hosted securely on a dedicated server within KCL, with database access strictly restricted through user-specific passwords to authorised research team members

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(including researchers supporting intervention development), with passwords not to be shared and ensuring that only those authorised to access the system are allowed to do so. If new staff members join the study, a user-specific username and password must be requested from the Lead Investigator. Database and other study document access will be revoked for any staff members leaving the project.

19. Data Management

The source data for the study will be collected on paper case report forms. Participants' data will be stored using a coded identifier, e.g. SDM001, SDM002 and paper forms of participant data will be stored securely within the recruiting site in locked filing cabinets (in offices locked while empty). This source data will then be entered by recruiting site staff, typically within 14 days of data collection by authorised staff onto the study databases (see above). Participant initials and month/year of birth will be entered on the database, however identifiable information such as NHS number, email addresses, participant names and addresses and full postcodes will not be entered. No data will be entered onto the EDC system unless a participant has signed a consent form to participate in the study.

The study team will undertake appropriate reviews of the entered data where appropriate for the purpose of data cleaning and will request amendments as required. Following checks of data correctness and completeness, all data can be formally locked for analysis.

We will adhere to NHS confidentiality practices, and to the Research Governance Framework in monitoring and managing the research. Professor Young will undertake overall responsibility for management of the project. Data collected by Fora Health will be stored on secure servers hosted by Fly.io Inc, and Very Good Security Inc. as sub-processors. This data will be retained for a period of 10 years. Data will be anonymized and only be used for the purposes of unplanned data analyses pending other evidence emerging.

20. Publication Policy

It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals as well as a variety of routes and forms accessible to the general public. We intend to publish the study protocol before the end of recruitment. A primary publication will include all primary and secondary outcomes as per the protocol.

21. Insurance / Indemnity

Indemnity and insurance are provided through KCL/SlaM schemes.

22. Financial Aspects

This project is funded by the NIHR i4i Product Development Award (ref NIHR206433). The views expressed in this publication are those of the authors and not necessarily those of the funder or the Department of Health and Social Care.

23. Signatures

Professor Allan Young _____

Chief Investigator Date TBC

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