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The PARTNERS2 Study: Trial of Primary Care Based Collaborative Care for People with a Diagnosis of Schizophrenia, Bipolar or other types of Psychosis. Protocol version 7.3 dated 18.08.2020

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TRIAL PROTOCOL

The PARTNERS2 Study: Trial of Primary Care Based Collaborative Care for People with a Diagnosis of Schizophrenia, Bipolar or other types of Psychosis

Version Number: 7.3

Version Date: 18.08.2020

PROTOCOL AMENDMENTS

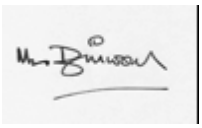
The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version

Amendment number	Date of amendment	Protocol version number	Type of amendment	Summary of amendment
Trial: 011 (Programme: 11)	27/09/2017	2.0	Substantial	Change to outcome measures, formatting, clarification on processes and procedures, changes to ensure consistent wording & referencing
Non substantial	25/01/2018	3.0	Non substantial	Change of PI - Cornwall Partnership NHS Foundation Trust. PI details added to Sites & TMG sections Addition of reference numbers Trial office contact email
Substantial Amendment AM18	22/01/2019	4.0	Substantial	Changes made throughout the protocol to reflect transfer of central trial coordination from Birmingham CTU to Peninsula CTU. Opportunity taken to make minor corrections and clarifications.
Substantial Amendment AM19	15/03/2019	5.0	Substantial	Detail added to Process Evaluation section. Clarifications made to entry criteria and recruitment processes. Minor corrections, clarifications and presentational edits made throughout.
Non substantial	18/06/2019	6.0	Non substantial	Change of PI at Birmingham and Solihull Mental Health NHS Foundation Trust. PI details added to Sites and TMG sections.
Non substantial	16/10/2019	6.1	Non substantial	Removal of Lancashire as an investigator site. Addition of Somerset as an investigator site.
Substantial Amendment AM20	06/01/2020	6.2	Substantial	Further detail added to Process Evaluation section of protocol and Appendix 3. New PE interviews for secondary care practitioners and researchers. Updates to PE participant-facing documents.

Substantial Amendment AM21	12/02/2020	7.0		1. Halting participant recruitment at the end of February 2020 to stay within study funding envelope. It is anticipated that sufficient numbers of participants will be recruited to achieve power of ~80% to detect the pre-specified target difference (as opposed to extending the study to achieve revised recruitment target of 270 participants, based on 90% power). 2. Addition of PE sub-study.
Substantial Amendment AM21	02/04/2020	7.1	Substantial	Addition of Covid-19 rapid realist evaluation
Substantial Amendment 22	10/06/20	7.2	Substantial	Addition of Covid-19 participant CRF questionnaire
Non-substantial (23)	18/08/20	7.3	Non substantial	Follow up at 9 months ± 30 days for participants due in December 2020

PROTOCOL SIGN OFF

CI Signature Page	
This protocol has been approved by:	
Trial Name:	The PARTNERS2 Study: Trial of Primary Care Based Collaborative Care for People With A Diagnosis Of Schizophrenia, Bipolar or other types of Psychosis
Protocol Version Number: Protocol Version Date:	7.3 18.08.20
CI Name:	Professor Max Birchwood/Professor Richard Byng

Trial Role:	Joint Chief Investigators
Signature and date:	 18.8.20  18.8.20

Sponsor statement:

By signing the IRAS form for this trial, Birmingham and Solihull Mental Health NHS Foundation Trust acting as sponsor of this trial, confirm approval of this protocol.

Reference Numbers	
EudraCT number	n/a
Sponsor number	134361
ISRCTN reference number	ISRCTN 95702682
Funder	NIHR Programme Grant of Applied Research (RP-PG-0611-20004)

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PI SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Principal Investigator agrees to conduct the trial in compliance with the approved protocol.

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

This protocol has been approved by:

Trial Name: Protocol Version Number:	Version: __. __
Protocol Version Date:	__ __ / __ __ / __ __ __ __
PI Name:	
Name of Site:	
Signature and date:	_____ __ __ / __ __ / __ __ __ __

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ABBREVIATIONS AND DEFINITIONS:

Abbreviations

Term	Description
AE	Adverse Event
CI	Chief Investigator
CMHT	Community Mental Health Team
CPN	Community Psychiatric Nurse
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
FE	Formative Evaluation
GCP	Good Clinical Practice
GP	General Practitioner
HRA	Health Research Authority
ICERs	Incremental cost effectiveness ratios
LEAP	Lived Experience Advisory Panel
NIHR	National Institute of Health Research
NRES	National Research Ethics Service
PenCTU	Peninsula Clinical Trials Unit
PPI	Patient and Public Involvement
QALY	Quality-Adjusted Life Years
QOF	Quality and Outcomes Framework
R&D	Research and Development
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
SMI	Severe Mental Illness
TMG	Trial Management Group
TMF	Trial Master File

Definitions

Term	Description
Standard Operating Procedures (SOP)	Standard Operating Procedures are detailed written instructions to achieve uniformity in the performance of a specific function. They define tasks, allocate responsibilities, detail processes, indicate documents and templates to be used and cross-reference to other work instructions and guidance documents. They are standards to which the University of Plymouth may be audited or inspected.

Adverse Event (AE)	Any untoward medical occurrence in a participant or clinical trial subject participating in the trial which does not necessarily have a causal relationship with the treatment received. Comment: An AE can therefore be any unfavourable and unintended sign (including abnormal laboratory findings), symptom or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product.
Related Event	An event which resulted from the administration of any of the research procedures.
Serious Adverse Event (SAE)	An untoward occurrence that: • Results in death • Is life-threatening* • Requires hospitalisation or prolongation of existing hospitalisation • Results in persistent or significant disability or incapacity • Consists of a congenital anomaly/ birth defect • Or is otherwise considered medically significant by the Investigator** Comments: The term severe is often used to describe the intensity (severity) of a specific event. This is not the same as serious, which is based on participants/event outcome or action criteria. * Life threatening in the definition of an SAE 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 that hypothetically might have caused death if it were more severe. ** Medical judgment should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should be considered serious
Unexpected and Related Event	An event which meets the definition of both an Unexpected Event and a Related Event
Unexpected Event	The type of event that is not listed in the protocol as an expected occurrence.
Source data	All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial
PenCTU	The co-ordinating centre for the trial.
Cluster	Unit of randomisation (GP practice)
Diagnostic cluster	A group of people with similar mental health characteristics assessed using the Mental Health Clustering Tool (MHCT)

TRIAL SUMMARY

Title PARTNERS2: trial of primary care based collaborative care for people with a diagnosis of schizophrenia, bipolar or other types of psychosis.

Trial Design Cluster randomised controlled trial (RCT) comparing primary case based collaborative care with standard care, with an internal pilot to assess feasibility.

Aims and Objectives

The overarching aim of this research is to establish the clinical and cost effectiveness of a primary care based model of collaborative care for adults with a clinical diagnosis of schizophrenia, bipolar, or other types of psychosis, with an internal pilot to assess feasibility. Specific objectives are:

1. Establish the feasibility of undertaking a full-scale cluster RCT by assessing recruitment of practices and patients, and safety of intervention within an internal pilot, and checking the sample size assumptions using the pilot data.

If the internal pilot shows that a full RCT is feasible

2. Assess the validity of the sample size assumptions

3. Establish the clinical and cost effectiveness of primary care based collaborative care for people with a clinical diagnosis of schizophrenia, bipolar, or other types of psychosis

Participant Population and Target Sample Size

Revised recruitment target of 204 participants with a diagnosis of schizophrenia, bipolar, or other types of psychosis from ~34 clusters (GP practices) each with an average of 6 participants, with an internal pilot aiming to recruit a minimum of 72 participants from 24 clusters.

Outcome Measures

Internal pilot

The primary outcome of the internal pilot is to assess the feasibility of undertaking a full-scale cluster RCT. This decision will be based on using a composite assessment of both quantitative and qualitative data, and will include assessment of the following at 6 months:
Practice recruitment rate
Practice withdrawal rates
Participant eligibility rates (via screening logs)
Participant recruitment rates
Participant withdrawal rates
Safety of intervention e.g. Crisis care (Home Treatment Teams), admissions (psychiatric)

Main RCT

The primary outcome of the full-scale cluster RCT is quality of life measured using the Manchester Short Assessment of Quality of Life (MANSA) at 10 months after unmasking of each cluster to the trial arm.

The secondary outcomes will consist of:

1. Number of hours per week spent in structured activity: Time Use Survey (TUS)
2. Recovery: Questionnaire about the Process of Recovery (QPR)
3. Mental wellbeing: Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS)
4. General health status: EuroQol (EQ-5D-5L)
5. Capability measure: ICEpop CAPability measure (ICECAP)
6. Experience of care (brief INSPIRE)

7. Safety variables:
    - Admissions (number of admissions and total days in patient)
    - Crisis care (number of episodes under home treatment team and total days under home treatment team
8. Quality Adjusted Life Years (from EQ-5D-5L)
9. Quality Adjusted Life Years (from ICECAP)
10. Quantity and cost of NHS and social care service use (records audit and economic interview)
    - Number of outpatient contacts
    - Number of inpatient stays
    - Number of GP consultations
    - Number of other primary and community physical health care contacts
    - Number of community mental health care contacts
    - Number of social service contacts
11. Healthcare monitoring:
    - Annual care check received
    - Blood pressure, weight, lipids, blood sugar, metabolic function assessed: checks recorded and any interventions made.
    - Smoking, diet, alcohol: evidence that status has been checked and evidence of intervention offered

Eligibility Criteria

GP Practices

Inclusion Criteria

- Practice filters into Birmingham and Solihull Mental Health NHS Foundation Trust, Livewell Southwest, Cornwall Partnership NHS Foundation Trust, or Somerset Partnership NHS Foundation Trust.
- Read code search list of 6 or more potentially eligible patients

Exclusion Criteria

- Practice lacks the capability and capacity to participate in the trial

Participants

Inclusion Criteria

- Registered with a participating GP practice which filters into the four site NHS Trusts; Birmingham and Solihull Mental Health Foundation Trust, Livewell South West, Cornwall Partnership NHS Foundation Trust, or Somerset Partnership NHS Foundation Trust.
- Aged 18 years and over
- A clinical diagnosis of schizophrenia, bipolar, or other types of psychosis
- Evidence for care need in relation to this diagnosis in previous two years (automatic for those in secondary care; assessed from notes for primary care only).

Exclusion Criteria

- Inability to understand English (and lack of access to translation services)
- Inability to give informed consent
- Those with more significant need requiring ongoing secondary multi-disciplinary care (such as those meeting criteria for diagnostic cluster 13, assertive outreach or early intervention functions)
- Currently receiving home crisis care or care in an inpatient or secure setting
- Those excluded at the discretion of GPs, if it is felt that inclusion in this trial is not within the best interests of their patient.
- Currently participating in a Cognitive Behavioural Therapy (CBT), psychosocial or medicinal trial for psychosis or bipolar.
- Individuals with a primary diagnosis of dementia receiving secondary care for dementia

- Individuals with a primary diagnosis of Learning Disability receiving care from secondary care for learning disability
  Individuals with ongoing significant and chaotic substance or alcohol misuse making engagement with trial and intervention problematic

Intervention

The collaborative care intervention has two main components enabled by specialist mental health workers (Care Partners):
1) Care Partners facilitation of the service interface, by providing links between primary and secondary care at the organizational level.
2) Enhancement of the relationship between the Care Partner and the participant, involving ongoing development of *shared understanding* and *coaching* to help the participant be more confident and proactive about their health.

Trial Schema in Appendix 2

TABLE OF CONTENTS

1. BACKGROUND AND RATIONALE

1.1 Background

The lifetime prevalence of schizophrenia is up to 1.4% (1) and for bipolar I is 0.24% (2). The National Survey of Psychiatric Morbidity found a population prevalence of probable psychotic disorder of 5 per 1000 in 16-74 year olds (3). Mental illness is the single largest cause of disability in the United Kingdom, contributing up to 22.8% of the total burden (4). The wider economic cost of mental illness in England has been estimated at £105.2 billion each year (5). Total service costs for people with a diagnosis of schizophrenia and bipolar were estimated to cost £3.8 billion in 2007, rising to £6.3 billion by 2026 (6) People with a diagnosis of schizophrenia or bipolar have a significantly reduced life expectancy compared to the general population (7). Two-thirds of the mortality gap can be explained by physical disorders and recent NHS England policy The Five Year Forward View for mental health has highlighted the low level of primary care engagement in this group: *"We should have fewer cases where people are unable to get physical care due to mental health problems affecting engagement and attendance (and vice versa). And we need provision of mental health support in physical health care settings - especially primary care"* (p 11, executive summary) (8). This trial is informed by our previous work, which suggests that about 70% of people with a diagnosis of schizophrenia and bipolar, have minimal and poorly coordinated primary and/or specialist care and lack a recovery focus (9). Such individuals frequently go 'under the radar', in primary and secondary services, exacerbating long-term social exclusion, inactivity and restricting opportunity for recovery.

PARTNERS2 focuses on the estimated 70% of adults with a diagnosis of schizophrenia or bipolar disorder who are currently seen and treated in primary care alone, or those currently seen in secondary care with lower levels of risk (operationalised as diagnostic clusters 11 and 12). Risk in this context refers to self-harm, self-neglect, suicide or harm to others.

Collaborative care is a system of delivering care, where a 'Care Partner' (for example a community psychiatric nurse) works within primary care forging collaboration between primary and secondary care and providing a platform for provision of high quality care to improve primary care support, access to routine healthcare and provide a cost effective way of raising recovery via improving activity levels and diminishing demoralization.

The collaborative care intervention aims to better address the emotional, social and physical needs of people with stable severe mental illness in a co-ordinated way by placing a secondary care practitioner within general practice. The Care Partner will work with patients to:

- Be more confident and proactive about their health, through the development of self-management skills
- Achieve their personal goals related to quality of life, mental health and physical health.

The PARTNERS2 collaborative care model involves:

1) Care Partners facilitation of the service interface, by providing links between primary and secondary care at the organizational level by

- working across primary and secondary care to support regular health monitoring and care;

- specifying clear roles for the GP, the psychiatrist and the Care Partner.

2) Enhancement of the relationship between the Care Partner and the participant by

- seeing participants in primary care and being involved in their ongoing development;

- developing a *shared understanding* and providing *coaching* to help the participants be more confident and proactive about their health and to meet personal goals.

Two Care Partners in each site (one in each in Plymouth and Cornwall) will work within the participating Trusts, and their role will involve:

- Initial engagement of the participant in primary care partnership working and building a shared understanding of unmet needs and goals;
- Active maintenance of that working relationship by following up/outreach and motivational work;
- Co-ordinating care between participants, health practitioners (particularly GP and practice nurse), other statutory and third sector services and family and linking to community resources;
- Coaching for individually agreed goals;
- Undertaking a systematic review of progress towards goals, including regular measures for mental and physical health and wellbeing;
- Ensuring that the participants are engaged with primary care and in receipt of optimal physical health care in line with the Quality and Outcomes Framework (QOF).

The vast majority of work on collaborative care has been developed and evaluated in the United States, where the nature of service user populations and of service use differ from the way we fund, structure and use the NHS in England. Whilst there is considerable evidence for its effectiveness, this research has largely been carried out with populations with non-psychotic disorders of mild to moderate severity and less functional impairment than experienced by people with schizophrenia or bipolar.

We have completed 2.5 years of preparatory work to understand the nature, strengths and limitations of the current status of primary-secondary care collaboration and, side-by-side with service users, have developed and piloted a primary care based collaborative care model for people with psychosis. PARTNERS2 is the first trial of that model to be carried out in the UK.

In summary: collaborative care is a system that offers a new way of supporting people with ongoing mental health needs, that may improve primary care engagement and healthcare access impacting on physical health, mental health and social recovery, for example, returning to vocational and social roles. This trial will put this to the test.

1.2 Trial Rationale

1.2.1 Rationale for the internal pilot trial

The aim is to carry out preliminary work for, and to test the feasibility of, a randomised controlled trial (RCT). The ultimate purpose of the RCT is to determine whether this intervention can improve outcomes for participants with a diagnosis of schizophrenia, bipolar or other psychosis. However, prior to undertaking the RCT, the acceptability of the trial needs to be assessed, specifically:

- **GP practice recruitment rates -** What proportion of practices approached are willing to participate?
- **GP practice withdrawal rates -** What proportion of recruited GP practices withdraw from the trial and at what time points?
- **Participant eligibility rates -** Participants are invited through GP practices. In order to determine the feasibility of a definitive trial, we need to know how many people will be potentially eligible for the trial. It will also help us to estimate how many GP practices would be needed for a full RCT.
- **Participant recruitment rates -** What proportion of eligible participants are willing to participate?
- **Participant withdrawal rates -** What proportion of recruited participants withdraw from the trial and at what time points?

- **Safety of intervention -** e.g. Crisis care (Home Treatment Teams), admissions (psychiatric)

The safety of the intervention will also be monitored by the independent Data Monitoring Committee (DMC) in particular whether patients experience any deterioration in their mental health.

The primary aim of the internal pilot is acceptability of the intervention to patients and GP practices. Retention rates will not be assessed in the internal pilot since the follow-up time point of 10 months will unnecessarily prolong the duration of the trial, and any interim follow-up measurement will compromise the delivery of the control group intervention. Retention will be monitored closely by the DMC if the internal pilot trial is successful and is converted to a full trial. The DMC will also check the sample size assumptions if the internal pilot is successful.

1.2.2 Justification for participant population

Our preparatory work- PARTNERS1- included a cross sectional epidemiological study of 1150 people with severe mental health illness (SMI) in England including data recorded in primary care (9). The study found that 31% (n=354) were seen only in primary care and of those seen in secondary care (n=796), 61% had at most two secondary care contacts recorded in primary care over the course of one year. For almost a third of new referrals to mental health services, the primary care record contained no information on the referral outcome, suggesting poor information continuity across the interface. We concluded that further research was needed to assess whether the mental health services contact data in primary care notes underrepresented actual contacts with secondary care. As part of the first phase of PARTNERS2 we conducted a retrospective notes review study (n=297) of patients on caseloads in secondary care in our three original recruitment sites (Birmingham, Devon and Lancashire). We found that patients had indeed received large amounts of input from secondary mental health care teams. However, this is recorded on different systems so may be invisible to primary care teams. A high proportion of patients (12.5%) had been discharged from and referred back into the mental health teams during the two year period of our data extraction. We also found that a high proportion of patients seen in secondary care were most recently recorded as being categorized within cluster 11 (ongoing / recurrent psychosis with low symptoms) (41%) and cluster 12 (ongoing / recurrent psychosis with high disability) (25%). We propose to target our intervention on individuals with lower levels of risk (operationalised as diagnostic clusters 11 and 12) along with those seen in only in primary care. We estimate this to represent approximately 75% of people with SMI in the targeted locations.

1.2.3 Justification for design

A cluster design is required as a significant component of the intervention operates at the practice level and we need to assume that some level of contamination would be likely with individual randomisation. Cluster randomisation would avoid contamination within GP practices among participants in the control arm. We do not expect any contamination within secondary care services as the locus of care is to be transferred to primary care services.

Furthermore, in the context of a) being able to recruit 336 of those potentially eligible and b) being able to implement the intervention within a trial setting, a randomised design is the most valid way to attribute a generalizable effect when evaluating the intervention.

1.2.4 Choice of intervention

Our Cochrane systematic review assessed the effectiveness of collaborative care compared to 'usual care' for people with a diagnosis of schizophrenia or bipolar living in the community, and identified 308 citations (10). However only one trial (N= 306) was included in the review; a study conducted in the United States with veterans with a diagnosis of bipolar (11). Collaborative care significantly reduced psychiatric admissions in year 2 and other non-psychiatric admissions in year 3 and improved quality of life (mental health component). There were no significant differences in overall intervention costs, mortality and attrition rates. However the review, which is currently being updated with 5 newly identified trials (from India (12), Pakistan (13) , US (14) (15), and the Netherlands (16)), is still unable to make any reliable and generalizable conclusions about the effectiveness of collaborative care for people with schizophrenia or bipolar receiving care in England. Trials of collaborative care implemented in NHS England for people with schizophrenia or

bipolar or other types of psychosis are therefore required. This underscores the need expressed by the recent NHS England Five Year Forward View for an effective model of collaboration with primary care (8).

2. AIMS AND OBJECTIVES

Aim: To determine the clinical and cost-effectiveness of a primary care based model of collaborative care for adults with a clinical diagnosis of schizophrenia, bipolar, or other types of psychosis, with an internal pilot to assess feasibility

1. Establish the feasibility of undertaking a full-scale cluster RCT by assessing recruitment of practices and patients, and safety of intervention within an internal pilot, and checking the sample size assumptions using the pilot data.

If the internal pilot shows that a full RCT is feasible.

2. Assess the sample size assumptions.

3. Establish the clinical value and cost-effectiveness of primary care based collaborative care for people with a clinical diagnosis of schizophrenia, bipolar, or other types of psychosis.

3. TRIAL DESIGN AND SETTING

3.1 Trial Design

This is a cluster RCT comparing collaborative care with care as usual, with an internal pilot to assess feasibility. The unit of randomisation is the GP practice. GP practices will be recruited across four NHS mental health providers; Birmingham and Solihull Mental Health Foundation Trust, Livewell Southwest, Cornwall Partnership NHS Foundation Trust, and Somerset Partnership NHS Foundation Trust. In total, 56 practices will be randomised on a 1-1 basis, stratified by region and practice size ('small' and 'large'). The size of practice has been determined by the number of adults registered on the practice Quality and Outcomes Framework (QOF) register, specifically classified under MH001 (adults with schizophrenia, bipolar affective disorder and other psychoses and other patients on lithium therapy). After undertaking a review of practice size across the three sites, the distribution across both arms was assessed and the median practice size used to categorise the practices. The size of practice has therefore been classified as a "small practice" if there are under 70 adults in this category and a "large practice" if there are 70 adults or over. This cut-off was considered relevant by the study investigators as e.g. a higher number of small practices in the intervention arm could affect Care Partner caseload size.

The internal pilot trial will recruit over 6 months, with stop-go rules set prior to the trial onset, in conjunction with the Trial Steering Committee (TSC) and agreed with the NIHR. These are based on minimum practice and participant recruitment rates. After 6 months, we aim to have recruited 8 GP practices and approximately 24 participants per region (24 GP practices, 72 participants in total) to the trial.

At 6 months, the recruitment target of 24 GP practices and 72 participants in total and no detrimental effect on safety of participants is expected. If these criteria are not reached and the intervention is shown to detrimentally affect the safety of the participants compared to usual care, the TSC and funders will meet in order to decide whether to proceed with the trial as designed or halt the trial. Recruitment will continue for the remaining patients until this decision is made. The sample size assumptions will be checked after at least 30 participants have reached the 10 month follow up period in order to provide robust estimates to re-estimate the sample size (if needed) for the full trial using upper 90% confidence limits of primary outcome related variability and intra-cluster correlation.

3.2 Trial Setting

The setting will be primary care (GP practices as research sites) within four trial recruitment areas: Birmingham and Solihull, Cornwall, Plymouth and Somerset each linked with a local Principal Investigator (PI) and research team.

Working with GP practices is a key feature of the PARTNERS2 collaborative care model. GP practices will be subject to a feasibility assessment to ensure they have the capacity and capability to deliver the trial. This includes: willingness to meet with Care Partner, rooms to meet with participants, computer access, can meet data collection requirements, any competing studies, assessment of number of eligible participants that meet the criteria and ability to meet Trust Research Governance Office targets of first recruit within 30 days of sign up.

4. ELIGIBILITY

4.1 Screening for eligibility and contact process

Screening for potential participants will take place within Community Mental Health Teams (CMHTs) and GP practices. CMHTs are generic area teams linked to a predefined set of GP practices, where secondary care services are provided. Trial researchers/CRN staff will facilitate CMHT staff and GP Practice staff to run patient searches. GPs and delegated staff (including CRN staff) within the practice/trusts will carry out initial screening for suitability or eligibility of patients. Consideration will be given to scheduling of searches that may coincide with extended public holidays to ensure that eligibility checking and posting of patient invitations is completed within the specified timeframes. In summary, the process will be:

1. Secondary care staff in each region will be requested to search for eligible participants within participating GP practices. List to be assessed for suitability by secondary care practitioners (or CRN staff) in CMHTs, and assigned as suitable or not.
2. Primary care lists to be determined from practice electronic medical records by searching for specific diagnostic read codes. This will be conducted by the GP practice, CRN or other NHS staff. All potential participants for the trial will be assigned a unique study ID on the screening list.
3. The full secondary care list to be transferred to GP Practice via secure NHS.net email. This will be cross-checked with practice register and primary care list. Any patients not on the primary care search will be added to it and duplicates removed by GP Practice CRN, or other NHS staff as specified on the site delegation log. Those suitable according to secondary care will be noted as reaching diagnostic criteria and do not require screening from primary care records and information packs for these individuals can be sent out immediately without further eligibility check. For those under secondary care the individual's current worker or other delegated NHS staff will then be asked to make contact with the individual to explain the reason for their selection and outline of the study. This will only be done if the worker agrees it is likely to be helpful for the individual to make an informed choice. The individual will be advised to attend an appointment and may agree to share contact details and for researchers to make contact personally.
4. This revised primary care list (or a sample if large numbers) will be assessed for eligibility by GP practice, CRN or other NHS staff and this will be signed off by the GP. Those deemed not suitable by secondary care (1. above) will also not be checked for eligibility.
5. Information packs will be sent to all (or in practices with large numbers identified, a sample) of eligible participants as soon as possible after eligibility is confirmed. The invitation letter will be signed by the GP practice or jointly signed by the GP practice and Local Principal Investigator for the Trust (for patients that receive care from the CMHT), see section 5 on consent. The research team will update the screening list to indicate the information pack has been sent.
6. 'Rapid invite' letters will be sent by the practice to those not returning expression of interest forms from two weeks after being sent an information pack. GP or delegated practice or CRN or other NHS staff will check patient list once more in order to confirm suitability for patients to be sent a rapid invite letter. The research team will update the screening list to indicate the rapid invite letter has been sent, and the practice, CRN or other NHS staff will call the patient to remind them of their appointment (a maximum of three attempts will be made to contact the patient. A scripted answerphone message may be left for patients after third attempt 'to contact the practice about a study' but no further details will be left. Alternatively, practices will be able

to send text reminders to patients about appointment times but without details regarding the study, and stating that they are to contact a member of the research team for more information

7. If the initial invitations do not yield sufficient patients in practices with large numbers of patients further information packs will be sent.

Potential participants will initially receive an information pack which contains:

i) Invitation letter signed by the GP Practice or jointly with the Local Principal Investigator for the Trust (for patients receiving care from a CMHT)
ii) Short participant information sheet (PIS)
iii) Recruitment Flyer
iv) Expression of interest form (EOIF)
v) Stamped addressed envelope

This will be sent as promptly as possible after eligibility is confirmed. The short participant information sheet and flyer describes collaborative care and briefly outlines what will happen in the trial. This has been designed with members of our Lived Experience Advisory Panels (LEAPs, see section 19) based on the amount and type of content considered appropriate for an initial approach.

If the patient is interested in participating they will be required to sign and date the EOIF which is returned to their local research team (see Administrative Information) in the stamped addressed envelope provided or call the research team on the contact details provided. One of the local researchers as listed on the delegation log will then speak to the patient to describe the trial in more detail, via telephone or email, dependent on participant preference, to clarify any points not understood, to answer questions and if they are still interested in participating to arrange a face to face meeting. The researcher will also ask whether the potential participant would like to receive a copy of the participant information sheet (PIS) in advance of meeting with the researcher (a short, long and audio version are available).

If a patient does not respond to the initial information pack, GP Practice or CRN staff will send out a rapid invite letter after two weeks. The rapid invite letter will be signed by the GP practice. The research team will update the screening list to indicate the rapid invite letter has been sent. This letter will give patients a time and date to meet with the researchers, and ask that they call their local researcher in order to reschedule or cancel this appointment.

Contact details provided to the researcher by the patient will be stored by the researcher either in a locked filing cabinet in a secure location or on a password protected document on a password protected, encrypted computer and used solely in relation to this purpose. All details will be destroyed if the patient does not consent into the trial by the date GP practice is randomised into the study.

The practice, CRN or other NHS staff will call the patient to remind them of their appointment, at which stage they can also decline the appointment and no further contact will be made. The researcher will update the screening list should they be notified that no further contact is to be made.

The reasons for excluding someone based on suitability will be collected on the screening lists.

4.2 Inclusion Criteria

- Registered with a participating GP practice which filters into the four site NHS Trusts; Birmingham and Solihull Mental Health Foundation Trust, Livewell South West, Cornwall Partnership NHS Foundation Trust, or Somerset Partnership NHS Foundation Trust.
- Aged 18 years and over
- A clinical diagnosis of schizophrenia, bipolar, or other types of psychosis.
- Evidence for care need in relation to this diagnosis in previous two years (automatic for those in secondary care; assessed from notes for primary care only).

4.3 Exclusion Criteria

- Inability to understand English (or access to translation services)
- Inability to give informed consent
- Those with more significant need requiring ongoing secondary multi-disciplinary care (such as those meeting criteria for diagnostic cluster 13, assertive outreach or early intervention functions) Currently receiving home crisis care or care in an inpatient or secure setting
- Those excluded at the discretion of GPs, if it is felt that inclusion in this trial is not within the best interests of their patient.

- Currently participating in a CBT, psychosocial or medicinal trial for psychosis or bipolar.
- Individuals with a primary diagnosis of dementia receiving secondary care for dementia
- Individuals with a primary diagnosis of Learning Disability receiving care from secondary care for learning disability
- Individuals with ongoing significant and chaotic substance or alcohol misuse making engagement with trial and intervention problematic.

Co-enrolment

- Patients may not be currently participating in a CBT, psychosocial or medicinal trial for psychosis or bipolar.

5. CONSENT

At the face to face meeting the researcher will provide a full explanation of the trial covering all of the essential elements: the aim, the intervention, anticipated benefits and potential disadvantages of taking part. They will also stress that participation is voluntary and that the participant is free to refuse to take part and may withdraw from the trial at any time. The potential participant will be allowed to consent immediately or may take the opportunity to reflect on the decision and/or discuss their participation with others outside of the site research team. If the potential participant requests more time to decide, the researcher will follow-up using the participant's preferred method of contact within two weeks. If the potential participant agrees to participate, a face to face meeting will be arranged for consent and baseline data to be collected.

It will be the responsibility of the Principal Investigator or delegate(s) (as captured on the Site Signature and Delegation Log and in accordance with Good Clinical Practice) to obtain informed consent for each participant prior to baseline data collection. The Investigator or delegate(s) will then sign and date the form. A copy of the informed consent form (ICF) and the full participant information sheet will be given to the participant. The original informed consent form will be placed in the Investigator Site File (ISF), a copy will be added to their medical records and a copy will be sent to the PenCTU for monitoring purposes.

Details of the informed consent discussions will documented by the research team. This will include date of discussions (there are likely to be more than one), the name of the trial, summary of discussions, version number/date of the PIS given to participant (and whether paper or audio version was accessed) and version number/date of ICF signed and date consent received.

At each visit the participant's willingness to continue in the trial will be ascertained and documented. Throughout the trial the participant will have the opportunity to ask questions about the trial. Any new information that may be relevant to the participant's continued participation will be made available on the study website. Where new information becomes available which may affect the participants' decision to continue, participants will be given time to consider and if happy to continue will be re-consented. Re-consent will be documented. The participant's right to withdraw from the trial will remain. Participants will be advised that they are to contact the researcher or their GP practice should they wish to withdraw from the study. Details of how to withdraw will also be found on the study website: www.partners2.net

Electronic copies of the PIS and ICF will be available from the CTU and will be printed or photocopied with the study logo and logo of the local institution. Details of all participants approached about the trial will be recorded on the Participant Screening database.

Process Evaluation

The consent process for the Process Evaluation is described in the Process Evaluation section of the protocol. Participation is entirely voluntary and trial participants will be free to withdraw at any time, without giving any reason. Any data derived from this evaluation will follow the same data protection policies as the main trial.

Disclosure Study

The disclosure study is a related, nested, study, which explores the role of personal disclosure in how researchers build rapport in recruitment, engagement and data collection conversations with participants of the PARTNERS2 trial.

COVID-19 STUDY

Participants who experienced COVID-19 restrictions during their involvement in the study will be asked additional questions about the impact of the pandemic on their lives The questionnaire will be completed by researchers during follow up interviews with both intervention and control participants. All data will be recorded directly into the main trial database.

6. ENROLMENT AND RANDOMISATION

6.1 Enrolment

This process is outlined in Appendix 2: Trial flow diagram with patient recruitment.
Anyone with responsibility for discussing the project with patients and taking consent will be detailed in the delegation log. All participant information and procedures have been developed in collaboration with our Lived Experience Advisory Panels (LEAPS) to ensure that those with a range of mental health symptoms, functional problems and disabilities have an optimum opportunity to join the trial. Our proposed flexible system of recruitment has been developed through an iterative series of adaptations during the feasibility study supported and endorsed by our LEAPs. It balances the requirement to provide opportunity to participate with privacy, confidentiality and autonomy.

NB. As part of the pre-trial public involvement work, a ranking exercise was conducted with the LEAPs to determine the preferred terminology for describing randomisation.

6.2 Randomisation

Randomisation will be provided by PenCTU. The unit of randomisation is the GP practice to avoid contamination of the intervention. Practices will be randomised on a 1:1 basis either to collaborative care or usual care, stratified by site and practice size defined in Section 3.1 Trial design.

6.3 Masking

PenCTU will be responsible for the randomisation procedure and only the Trial Statistician will know the outcome of randomisation until allocation is revealed. To avoid selection bias, each GP practice and the associated Care Partners will be notified of the outcome of randomisation (unmasked) once researchers have recruited to target at the GP practice and it has been confirmed that all participants have been consented and baseline assessments are complete.

The process is detailed in Appendix 2: Trial flow diagram with patient recruitment.

7. TRIAL INTERVENTION

7.1 Trial intervention

The collaborative care intervention works by:

1. Care Partners facilitation of the service interface, by providing links between primary and secondary care at the organizational level

2. Enhancement of the relationship between the Care Partner and the participant, involving ongoing development of *shared understanding* and *coaching* to help the participant be more confident and proactive about their health.

The Care Partner role is carried out primarily through four activities*: engagement and retention, coaching, coordination of care* and *review.* The sessions between the Care Partner and participants will take place within the GP practice or other convenient place.

- **Engagement and retention**: Care Partners will take time to establish rapport with participants; it is necessary to establish a trusting relationship before coaching can take place. One way this may develop is by working towards a shared understanding in the first few sessions between the Care Partner and the participant about the participants' strengths, interests, values and preferences for their lives and towards treatment. This will involve the Care Partner listening to the participant's experiences in life to the extent that they want to talk about them.

  Engagement and retention is likely to be an ongoing process and a key feature of collaborative care which will be achieved by *pro-actively following up* participants if they fall out of contact (e.g. by failing to attend a meeting or appointment), rather than making any assumptions about whether the participant wants to continue working with the Care Partner.

- **Coordination of care**: Care Partners have a key responsibility for coordinating care and maintaining focus around individuals' goals. This involves regular case review with a senior secondary care practitioner, interaction with primary care practitioners and carers, liaison as appropriate with third sector and community sector organisations, and systematic documentation of these interactions on the participant's primary and secondary care records.

- **Coaching**: Care Partners will continue to develop a *shared understanding* with participants based on their current life situation, and will coach service users to achieve their own goals. This will be achieved through an ongoing process of developing self-understanding and knowledge of strategies; and then to take action based on individual goals. The intervention aims to support individuals to feel more confident of their health, as much as their capacity allows.

- **Review**: The Care Partner and participant will regularly review the participants' mental and physical health and wellbeing. They will work together to move toward self-goals over time, using data routinely collected at each meeting and in more formal 'review' sessions. Participants' varied and varying needs are met by a clear protocol for stepping up/down in intensity of care, according to their progress and situation. This involves three levels, 1. Least intense: involving at least 3 meetings a year (plus annual review with GP and/or psychiatrist); 2. Standard: meetings every 1-3 months according to participant needs, with the potential for more intensive contact during short-lived crises; and 3. Intensive: stepping up to secondary care in response to sustained crisis.

  It is anticipated that for the first two months, face to face meetings will occur approximately every other week, and then be reduced to once a month or every other month, unless the individual requires further stepping up. After ten months, there will be a two month transition period back to normal care. This is in place to ensure the participant and relevant practitioners decide together the nature of ongoing care after the trial. During this period, discussions will be held between the Care Partner, participant and secondary care supervisor. A 10-15 minute discussion with the GP and Care Partner will take place to inform GP of future care plan.

The design of the intervention has been informed by a review of the literature, discussions with the Lived Experience Advisory Panels (LEAPs) and through conduct of a formative evaluation.

Participants will receive the collaborative care intervention for up to 12 months, which includes a 2 month transition period back to usual care.

7.2 Usual care

After randomisation, participants in the Usual Care arm of the trial and will be reminded of when the 10 month follow-up appointment will be due. Their care will be managed solely by their own GP and primary care practice staff and with secondary care specialist mental health services (if required). Crucially, they will not receive any contact with the PARTNERS2 Care Partner.

8. OUTCOME MEASURES AND TRIAL PROCEDURES

8.1 Outcomes for Internal Pilot

The primary outcome of the internal pilot is to assess the feasibility of undertaking a full-scale cluster RCT. This decision will be based on using a composite assessment of both quantitative and qualitative data, and will include assessment of the following at 6 months:
Practice recruitment rate
Practice withdrawal rates
Participant recruitment rates
Participant withdrawal rates
Safety of intervention e.g. Crisis care (Home Treatment Teams), admissions (psychiatric)

8.2 Outcome measures for Main Trial

8.2.1 Primary Outcome

The primary outcome of the full-scale cluster RCT is a quality of life measure, the Manchester Short Assessment of Quality of Life (MANSA) measured at baseline and 10 months after randomisation to trial arm.

Researchers and CRN staff have been trained in the use of the Manchester Short Assessment of Quality of Life (MANSA) for the trial. In summary, the MANSA is a self-complete short assessment form comprising four objective questions to be answered with yes or no and other questions that are strictly subjective focusing on satisfaction with life as a whole and with different life domains, namely work and education, personal finances, leisure activities, social life, living situation, family life, personal safety and health. Satisfaction is rated on 7-point Likert scales (1 = negative extreme, 7 = positive extreme). Objective items are analysed separately. Subjective scorings are analysed to provide three different types of results: domain ratings; an overall Quality of Life score; and a general Quality of Life rating.

8.2.2 Secondary Outcomes

Secondary outcomes:	Timepoint*
Time use: ONS Time Use Survey (TUS)	Baseline and 10 months
Recovery: Questionnaire about the Process of Recovery (QPR)	Baseline and 10 months
General health status: EuroQol (EQ-5D-5L)	Baseline and 10 months
Mental wellbeing: Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS)	Baseline and 10 months
Capability measure: ICEpop CAPability measure (ICECAP)	Baseline and 10 months
NHS and social care service use (records audit and economic interview) • Outpatient contacts • Inpatient stays • GP consultations	10 months
Experience of care (brief INSPIRE)	Baseline and 10 months
Healthcare monitoring Annual health check received Blood pressure, lipids and metabolic functions assessed, treatments for any administered.	10 months

Lifestyle interventions (Smoking and diet) delivered	
Costs of NHS and social care service use	Economic evaluation
Quality Adjusted Life Years (from EQ-5D-5L)	Baseline and 10 months
Quality Adjusted Life Years (from ICECAP)	Baseline and 10 months
Safety variables: 1. Admissions 2. Crisis care	10 months
Impact of COVID-19	**10 months**

*Follow-up will be completed at 9 months for those participants due in the final study month (December 2020)

8.3 Schedule of assessment

Activity	***Pre-baseline***	***Baseline***	***Pilot Phase 6 month***	***Month 10* + or – 30 days***
Eligibility check	*x*			
Valid informed consent	*x*	*x*		*x*
Data to inform if full-scale RCT is feasible				
Practice recruitment rates	*x*	*x*	*x*	*x*
Practice withdrawal rates			*x*	*x*
Patient eligibility rates	*x*	*x*	*x*	*X*
Patient recruitment rates		*x*	*x*	
Participant withdrawal rates			*x*	*X*
Outcome Measures				
MANSA		*x*		*X*
QPR		*x*		*X*
EQ-5D-5L		*x*		*X*
WEMWBS		*x*		*X*
ICECAP		*x*		*X*
NHS resource use: Records audit and economic interview				*X*
Brief INSPIRE		*x*		*X*
Healthcare Monitoring				*X*
Safety variables				
Admissions (psychiatric)				*X*
Crisis care (home treatment)				*X*
Process evaluation		*x*		*X*

Impact of COVID-19				*X*

*Follow-up will be completed at 9 months for those participants due in the final study month (December 2020)

Baseline data collection

The Manchester Short Assessment of Quality of Life scale is a participant completed questionnaire, which will be accompanied by other questionnaires and an interview based Time Use Survey (TUS). A more detailed outline of the questionnaire is described in section 8.2.1. Data will be recorded in the Baseline Case Report Form (CRF). The baseline and consent appointment is expected to last between one to two hours, dependent on the participant. This is due to the nature of the TUS, and because of how mental health symptoms vary and may impact upon participant time needed to complete this. If not completed at the first appointment, arrangements will be made for the visit to be completed as soon as possible at a suitable venue. This may be carried out by the researcher or CRN staff. The researcher will discuss the 10-month follow-up in detail and agree the best way to contact the participant for that appointment, depending on a range of scenarios. The participants will receive a £10 high street voucher as a gesture of thanks.

In the time period between enrolment, baseline data collection and the 10 month final follow-up we will test strategies, co-produced with the LEAPs, to promote participant retention.

Follow Up

The follow up data collection will take place at 10 months from the point of unmasking the randomisation allocation of each practice. This time point was informed by a previous stream of work in PARTNERS2 research programme. It is expected the intervention will work towards improving participant's quality of life, and therefore the optimum time to measure this will be while participants are still in receipt of the intervention. It will also help reduce the number of participants who may be lost to follow up if it were carried out later. The follow up data collection appointment is expected to last approximately 45 minutes. For a subgroup of participants due follow-up in the final study month (December 2020), follow-up will be brought forward to 9 months days to reduce the possibility of delays in data collection over the Christmas period and in the final month of data collection.

At approximately 9 months after unmasking, the researcher will contact the participant to arrange the follow-up appointment. The 10 month follow-up can take place within a 1 month window around 10 months (i.e. ± 30 days) post unmasking, although researchers will aim to complete data collection close to the 10 month point.

The research team will follow up each participant, until the trial end date, after which those who still cannot be contacted will be recorded as 'lost to follow up'. The numbers and reasons for withdrawals and lost to follow up will be reported for each arm of the trial.

The researcher will notify the participant of any changes since their last visit and confirm the participant is happy to continue in the trial, this will be documented in the CRF and patient medical notes. The researcher will deliver the 10 month follow up interview as described previously for baseline data collection. The participant will receive a £10 high street voucher as a gesture of thanks upon completion of the outcome measures.

Each recruited participant is expected to be involved in the trial for a maximum of 12 months. A sample of participants may participate for longer if taking part in the process evaluation interview (see section 20).

After ten months, there will be a two month transition period back to normal care. This is in place to ensure the participant and relevant practitioners decide together the nature of ongoing care after the trial. During this period, discussions will be held between the Care Partner, participant and secondary care supervisor. A 10-15 minute discussion with the GP and Care Partner will take place to inform of future care plan.

After completion of 10 month follow up data researchers will review patient GP medical notes to collect healthcare monitoring data. This will include annual health check received, blood pressure,

lipids and metabolic functions assessed and any treatments administered, and lifestyle interventions (Smoking and diet etc.) delivered. In addition, researchers will review patient secondary care medical notes to collect NHS service use: number of outpatient contacts, number of inpatient stays and number of GP consultations

8.4 Participant and cluster withdrawal

8.4.1 Participant withdrawal

Informed consent is defined as the process of learning the key facts about a clinical trial before deciding whether or not to participate. It is a continuous and dynamic process and participants will be asked about their ongoing willingness to continue participation.

Participants will be made aware that they can freely withdraw (discontinue participation) from the trial (or part of) at any time. Participants will be advised that they are to contact the researcher or their GP practice should they wish to withdraw from the trial. Participants will be given researcher contact details for future contact. Local site details can also be found on the study website and participants will also be informed that they can notify us by email through the 'contact us' page on the trial website. Website address: www.partners2.net.

Participant withdrawal is defined as withdrawal from trial intervention AND all follow up contact. Participant may withdraw from the trial at any time if they choose not to continue, or the responsible clinician feels that continued participation is inappropriate. For any participants who withdraw from the trial, their data will be included in analyses up to the point of consent being revoked (when it is expected that no further data will be received).

Participants will be withdrawn from the trial if:

- Written informed consent is revoked by the participant;
- The clinician in contact with the participant feels that it is inappropriate and harmful for the participant to continue with BOTH the trial intervention AND the continuing follow up and data collection. The clinician and Local PI will decide together if complete withdrawal from the trial is in the best interest of the participant
- The participating GP practice withdraws from the trial
- If a participant consents to participate in the trial but baseline data is not collected from them before the practice is randomised

Participants who cease involvement in the intervention but who continue with ongoing follow up will NOT be classed as withdrawn. They will be followed-up in accordance with the protocol (they may attend follow up visits and outcome data will continue to be collected).

Participants withdrawing from intervention will be offered a two month transition period back to normal care in order to ensure the participant and relevant practitioners decide together the nature of ongoing care after the trial. During this period, discussions will be held between the Care Partner, participant and secondary care supervisor. A 10-15 minute discussion with the GP and Care Partner will take place to inform the participant of the future care plan.

The details of withdrawal (date, reason and type of withdrawal) will be clearly documented in the source data.

8.4.2 Cluster withdrawal

If a recruited GP practice has withdrawn from participation *prior to randomisation*, such as a result of unsuccessful participant recruitment rates (defined as less than two per cluster) they may be replaced by another practice. If a practice withdraws after randomisation, consideration will be given to replacing by another practice. The sample size calculations have allowed for some GP practice drop out. This is also an outcome measure of the pilot trial.

If a GP practice withdraws from participation, any patients registered at the practice and who have consented to the trial will be withdrawn. If the GP practice is randomised to the intervention arm of the trial, these participants will be offered a transition period back to normal care (as previously described)

9 ADVERSE EVENT REPORTING

9.1 Reporting Requirements

The collection and reporting of Adverse Events (AEs) will be in accordance with the UK policy framework for health and social care research and the requirements of the Health Research Authority (HRA). Definitions of different types of AEs are listed in the table of abbreviations and definitions. The Investigator should assess the seriousness and causality (relatedness) of all AEs experienced by the trial participant. *This assessment should be documented in the source data.* Assessment of expectedness will be performed by Chief Investigator or delegate, and deemed expected in relation to the intervention, or unexpected.

9.2 Adverse Events (AE)

The risk of harm associated with trial procedures and the intervention are considered to be very low, and therefore no non-serious adverse events will be collected for this trial.

9.3 Serious Adverse Advents (SAE)

Investigators will collect and report all SAEs that meet the following definition:
Any untoward medical occurrence or affect that:

- Results in death
- Is life threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Is a congenital abnormality/ birth defect
- Is otherwise considered medically significant by the investigator. This will include:
    - Crisis care (contact with Home Treatment Team)
    - Self-harm

SAEs will be recorded in the source data, and on the CRF and in addition will be reported to the trials office within 24 hours of being made aware of the event by completing and submitting an SAE form.

The following will not be regarded as SAEs and will not be collected or reported for this trial:

- Hospital admissions, or prolongation of existing inpatient hospitalisations, where admissions are for elective procedures determined prior trial intervention
- Hospital admissions with no overnight stay

9.4 Reporting period

AEs will not be collected for this trial however SAEs will be reported from the date of consent, up until 12 months after the point of unmasking the practice.

9.5 Reporting Procedure – At Site

9.5.1 Adverse Events

AEs will not be collected for this trial.

9.5.2 Serious Adverse Events

SAEs should be reported on an SAE Form. When completing the form, the Investigator will be asked to define the causality and the severity of the SAE. Standard categories for causality are: unrelated, unlikely to be related, possibly related, probably related or definitely related

Causal relationship	Descriptor
Unrelated = unrelated	There is no evidence of any causal relationship

Unlikely to be related = unrelated	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after receiving the trial intervention). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment).
Possibly related = related	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after receiving the trial intervention/ research procedure). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant treatments).
Probably related = related	There is evidence to suggest a causal relationship and the influence of other factors is unlikely.
Definitely related = related	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.

On becoming aware that a participant has experienced an SAE, the Investigator (or delegate) must complete, date and sign an SAE Form. The form should be faxed to the PenCTU trials team using the number listed below as soon as possible and no later than 24 hours after first becoming aware of the event:

To report an SAE, fax the SAE Form to:

01752 315254

On receipt the PenCTU trials team will allocate each SAE a unique reference number which will be forwarded to the site as proof of receipt. If confirmation of receipt is not received within one working day please contact the PenCTU trials team. The SAE reference number should be quoted on all correspondence and follow-up reports regarding the SAE and filed with the actual SAE in the Site File.

For SAE Forms completed by someone other than the Investigator, the Investigator will be required to countersign the original SAE Form to confirm agreement with the causality and severity assessments. The form should then be returned to the PenCTU trials team and a copy kept in the Investigator Site File at the GP Practice. Principal Investigators should also report SAEs to their own Trust in accordance with local practice.

9.5.3 Provision of follow-up information

Participants should be followed up until resolution or stabilisation of the event and all anonymised information provided to PenCTU with the participant trial ID and SAE reference numbers clearly marked.

9.6 Reporting Procedure

9.6.1 PenCTU procedure

On receipt, the PenCTU trials team will allocate each SAE a unique reference number which will be forwarded to the site as proof of receipt within one working day. The SAE reference number will be quoted on all correspondence and follow-up reports regarding the SAE and filed with the actual SAE in the TMF.

On receipt of an SAE Form relatedness and causality will be reviewed by the CI who will also make the expectedness assessment.

An SAE occurring to a research participant should be reported to the main REC where, in the opinion of the Chief Investigator, the event was:

- Related (that is, it resulted from administration of any of the research procedures)

AND

- Unexpected (that is, the type of event is not listed in the protocol as an expected occurrence)

9.6.2 Reporting to the main Research Ethics Committee

PenCTU will report all events categorised as Unexpected and Related to the main REC and the Research Governance Team at (RGT) at Birmingham and Solihull Mental Health NHS Foundation Trust within 15 days of becoming aware of the event.

The main REC and RGT will be notified immediately if a significant safety issue is identified during the course of the trial.

9.6.3 Investigators

Details of all Unexpected and Related SAEs and any other safety issue which arises during the course of the trial will be reported to Principal Investigators. A copy of any such correspondence should be filed in the Site File.

9.7 Data Monitoring Committee

A Data Monitoring Committee has been established. Data analyses will be supplied in confidence to an independent Data Monitoring (DMC), which will be asked to give advice on whether the accumulated data from the trial – recruitment/retention rates, data quality and safety, together with the results from other relevant research, justifies the continuing recruitment of further participants. The DMC will meet *every 6 months unless there is a specific reason (e.g. safety phase) to amend the schedule. The DMC will review all reported SAEs.*

Additional meetings may be called if recruitment is much faster than anticipated and the DMC may, at their discretion, request to meet more frequently or continue to meet following completion of recruitment. An emergency meeting may also be convened if a safety issue is identified. The DMC will report directly to the *Trial Steering Committee* who will convey the findings of the DMC to the *sponsor.* The DMC may consider recommending the discontinuation of the trial if the recruitment rate or data quality are unacceptable or if any issues are identified which may compromise participant safety. The trial would also stop early if the interim analyses showed differences between treatments that were deemed to be convincing to the clinical community.

The trial may be stopped due to poor recruitment.

The DMC will be responsible for the regular monitoring of trial data. The DMC will assess the progress of the trial and give advice on whether the accumulated data from the trial, together with the results from other relevant trials, justifies the continuing recruitment of further participants. The committee will meet in person or by teleconference prior to the trial commencing and then six months after initiation of the trial. The DMC will make confidential recommendations to the TSC as the decision–making committee for the trial.

10 DATA HANDLING AND RECORD KEEPING

10.1 Source Data

In order to allow for the accurate reconstruction of the trial and clinical management of the subject, source data will be maintained at site and kept in accordance with GCP. They will be made available for monitoring, audit and inspection.

Data variables and questionnaires may be entered directly onto the CRF and will be considered source data. For all other data items, the source data will be found in the participant medical records, including mental health diagnosis (this is an eligibility criteria*).*

Participants will have the option to give audio consent. Recordings will be stored on a password protected computer at the local site and PenCTU and destroyed in accordance with the Information Communication and Technology Policy (IG02), Version 3, July 2018 and the Confidentiality Policy

(IG01), Version 5, May 2018 (Birmingham and Solihull Mental Health NHS Foundation Trust) after a period of 10 years

10.2 CRF Completion

Data reported on each CRF will be consistent with the source data and any discrepancies will be explained. All missing and ambiguous data will be queried. RAs are trained to respond sensitively to questions participants are unwilling to answer. Staff delegated to complete CRFs will be trained to adhere to the following CRF completion guideline:

- Entries on the CRF will be made in ballpoint pen;
- Errors will be crossed out with a single stroke, the correction will be inserted and the change initialled and dated. If it is not clear why a change has been made, an explanation should be written next to the change. Correction fluid should not be used;
- Data reported on each CRF should be consistent with the source data or the discrepancies explained;
- Reasons for missing data should be documented on the CRF;
- Where information is not known or refused, this will be clearly indicated on the form;
- Where data is missing without explanation, or unclearly entered onto the CRF, a data query will be raised by the PenCTU data team and returned to site for completion following established PenCTU Standard Operating Procedures.

Data collected as part of this trial will be entered into the trial database by the research assistants at each local co-ordinating centre or by trained staff at the PenCTU. Original copies are to be sent to PenCTU for data management and storage. Copies will be held at the local co-ordinating centre within the ISF.

10.3 The Interview Measures and Participant Completed Questionnaires

Participant Completed Questionnaires and Interview Measures will be completed by the participant at a convenient location (GP practice, participant's home or appropriate community setting) at baseline and at 10 months post allocation.

Participants will ideally complete the Participant Completed Questionnaires independently, but this will be overseen by the researcher or CRN research practitioner who can answer any questions the participant may have. This will be followed by the ONS Time Use Survey, an interview based questionnaire. In some cases, Participant Completed Questionnaires will be completed by the participant with assistance from friends, family or the clinical or research team. Any assistance or proxy completion will be recorded and flagged to the trials office. On completion, the Participant Completed Questionnaires will be checked on site by a member of the research team for missing data. The participant will be given the opportunity to complete any missing data.

Staff delegated to administer Participant Completed Questionnaires will be trained to adhere to the following Participant Completed Questionnaire completion guidelines in addition to the CRF completion guidelines:

- Participant completed questionnaires to be completed in accordance with completion instructions.
- Participants will be encouraged to answer all questions when completing the CRFs and the Participant Completed Questionnaires.
- Participant Completed Questionnaires will be checked for missing data and where feasible participants will be given the opportunity to complete any missing data.

10.4 Data Management

Processes will be employed to ensure the accuracy of the data included in the final report. These processes will be detailed in the trial data management plan. Coding and validation will be agreed between the trial team, statistician, and the trial programmer. The trial database will be signed off once the implementation of these processes has been assured.

CRFs will be entered onto the database by staff (researchers and/or coordinating CTU staff) in accordance with the trial specific work instruction. A tracking system for CRFs will be used. The data management plan will detail the process for dealing with data queries which will be managed through

the use of data clarification forms. The type of self-evident corrections that can be made will be agreed with the CI.

10.4.1 Data security

PARTNERS2 data will managed in accordance with University of Plymouth Information Security Policy (EA-ISP-001). Electronic data will be kept in password protected REDCap Cloud (https://www.redcapcloud.com/) databases on highly secure servers hosted in Amazon Web Server (AWS) datacentres located in the European Union.

The PARTNERS2 REDCap Cloud data system will be managed by PenCTU development and data management staff.

Storage of personal data on manual files; paper copies of questionnaires, consent forms and CRFs will be held in secure data storage such as lockable filing cabinets in a restricted access environment. Storage of data on university computer and NHS desktop computers will be kept in password protected, access limited electronic format. The trial information including CRF will be entered into the online PARTNERS2 REDCap Cloud database and will be anonymised at point of entry.

Manual files containing personal information and allocated identifiers will be kept in a separate location to the anonymised data. When identifiable data are no longer required for linking, quality checking or after the follow up period is complete, they will be destroyed. Data will be collected and stored in accordance with Data Protection Legislation, comprising all applicable laws, statutes, regulations and directives applicable to the performance of this trial, including but not limited to the EU General Data Protection Regulations ('GDPR') and the Data Protection Act of 2018, and in accordance with the NHS Code of Confidentiality. All data analyses will be done on fully anonymised data.

10.4.2 Data Management

A Data Management Working Procedure Document will be provided that will detail the process of data entry, data management and data clarification queries. This working procedure will provide full detail about the data entry, coding, checks and resolution of queries, including required timelines.

It is the responsibility of the Principal Investigator to ensure all essential trial documentation and source documents (e.g. signed Informed Consent Forms, Investigator Site Files, participants' hospital notes, copies of CRFs etc.) at their site are securely retained for at least 10 years.

The PenCTU trials team will be responsible for preparing the Trial Master File (TMF) and centrally held data for archive. Archiving will be undertaken by the Sponsor. No documents will be destroyed without prior approval from the Sponsor.

11. QUALITY CONTROL AND QUALITY ASSURANCE

11.1 Site Set-up and Initiation

A tripartite agreement between the CI, Sponsor and CTU will document the delegation of trial-related duties between the parties.

All participating Investigators will be asked to sign the necessary agreements and supply a current CV and GCP certificate to PenCTU. All members of the regional research team will also be required to sign a Site Signature and Delegation Log. Prior to commencing recruitment all sites will undergo a process of initiation. Key members of the regional research team will be required to attend either a meeting or a teleconference covering aspects of the trial design, protocol procedures, Adverse Event reporting, collection and reporting of data and record keeping. Sites will be provided with an Investigator Site File containing essential documentation, instructions, and other documentation required for the conduct of the trial. The PenCTU trials team must be informed immediately of any change in the site research team.

11.2 Monitoring

11.2.1 Onsite Monitoring

On-site monitoring visits may be triggered, for example by poor CRF return, poor data quality, low SAE reporting rates, excessive number of participant withdrawals or deviations. If a monitoring visit is

required the PenCTU trials team will contact the site to arrange a date for the proposed visit and will provide the site with written confirmation. Investigators will allow the PARTNERS2 trial staff access to source documents as requested. The monitoring will be conducted by PenCTU trial management staff.

11.2.2 Central Monitoring

PenCTU staff will be in regular contact with the site research team to check on progress and address any queries that they may have. PenCTU staff will check incoming CRFs for compliance with the protocol, data consistency, missing data and timing. Monitoring will include ensuring timely CRF input, and review of SAE reports and return rates. Sites will be sent Data Clarification Forms requesting missing data or clarification of inconsistencies or discrepancies. The outcome of central monitoring will be discussed at Trial Management Group (TMG) meetings.

11.2.3 Audit and Inspection

Investigators and Institutions will permit trial-related monitoring, audits, ethical review, and regulatory inspection(s) at their site, providing direct access to source data/documents. The investigator will comply with these visits and any required follow up, as outlined in the delegation log.

11.3 Notification of Serious Breaches

The sponsor is responsible for notifying the REC of any serious breach of the conditions and principles of GCP in connection with that trial or the protocol relating to that trial. Sites are therefore requested to notify the PenCTU of any suspected trial-related serious breach of GCP and/or the trial protocol. Where the Trials Office is investigating whether or not a serious breach has occurred sites are also requested to cooperate with the PenCTU in providing sufficient information to report the breach to the REC where required and in undertaking any corrective and/or preventive action.

Sites may be suspended from further recruitment in the event of serious and persistent non-compliance with the protocol and/or GCP, and/or poor recruitment. Any major problems identified during monitoring may be reported to the TMG, Trial Steering Committee, and the REC. This includes reporting serious breaches of GCP and/or the trial protocol to the REC. A copy is sent to Birmingham and Solihull Mental Health NHS Foundation Trust at the time of reporting to the REC.

12. END OF TRIAL DEFINITION

Once the final participant has reached 12 months post unmasking the follow up measures collected and entered on the database, a data cleaning period will commence. We expect this to take approximately 6 months at which point the database will be locked. This will signify the end of the trial. The PARTNERS2 trial team will notify the main REC and sponsor that the trial has ended *within 90 days of the end of trial* and a summary of the clinical trial report will be provided within 12 months of the end of trial.

A copy of the end of trial notification as well as the summary report is sent to the Birmingham and Solihull Mental Health NHS Foundation Trust Research Governance Department at the same time these are sent to the REC.

13. STATISTICAL CONSIDERATIONS

13.1. Sample Size

The sample size for the full trial is based on detecting a mean difference of 0.45 points on the MANSA quality of life domain measure using the MANSA. Assuming a standard deviation (SD) of 0.9, this is equivalent to detecting half a standard deviation. The MANSA is seen as clinically relevant to the target population and to the intervention under investigation by the research team and LEAP, and measures individuals' quality of life across a range of domains. There is evidence that it is amenable to change by the intervention because it aggregates outcomes across the range of causal pathways the intervention is designed to affect. For example the MANSA will change if relationships, mental wellbeing or creative activity are improved, each of which can be affected by the intervention. Our effect size is consistent with what was found in the Priebe paper. This corresponds to a medium to large effect.

To detect the target difference of 0.45 points, and assuming a standard deviation (SD) of 0.9, coefficient of variation of cluster size of 0.74 and intra-cluster correlation of 0.05, the recruitment target for the full trial was originally 336 participants across ~56 GP clusters, assuming an average of 6 participants per cluster and 20% drop out at the individual participant level and 10% drop out at the cluster level following randomisation.

The internal pilot will plan to recruit 72 participants across approximately 24 clusters, assuming a minimum target of 3 participants per cluster over a 6 month period.

13.1.1
Interim blinded review of assumptions underpinning the original sample size calculation and revised recruitment target
This pre-specified review was based on data from 39 participants with complete baseline and follow-up primary outcome data and explored the *a priori* assumption of a correlation of 0.5 between baseline and follow-up MANSA scores. The point estimate of this correlation was 0.69 (80% confidence interval: 0.56 to 0.79) and as such, it was deemed appropriate to conservatively allow for a correlation of 0.5 in a revised sample size calculation. Retaining the other original underpinning assumptions of the sample size calculation indicates a recruitment target of 270 participants from ~45 GP practices, to achieve 90% power or 204 participants from ~34 GP practices to achieve 80% power, to detect the pre-specified between-group difference of 0.45 units. In December 2019, both the Data Monitoring and Trial Steering Committees approved a revised recruitment target of 270 participants.

In January 2020, the study funder mandated that trial recruitment be terminated at the end of February 2020, regardless of recruitment figures. By mid-January 2020, 170 participants had been recruited to the trial. Following the funder's decision, the aim is to recruit 204 participants, from ~34 GP practices, to achieve 80% power to detect the pre-specified target difference of 0.45 units, based on the underpinning assumptions of SD of 0.9, mean cluster size of 6 participants, coefficient of variation of 0.74, intra-cluster correlation of 0.05 and correlation between baseline and follow-up MANSA scores of 0.5 and allowing for 20% drop out at the individual participant level and 10% drop out at the cluster level following randomisation.

13.2. Analysis of Outcome Measures

A separate Statistical Analysis Plan will be produced and will provide a more comprehensive description of the planned statistical analyses. A brief outline of these analyses is given below. The primary comparison groups will be composed of those treated with collaborative care versus those treated with usual care. In the first instance, all analyses will be based on the intention to treat principle, i.e. all clusters and participants will be analysed in the treatment group to which they were randomised irrespective of protocol deviations. The data analysis for the internal pilot will be descriptive and mainly focus on confidence interval estimation, with no hypothesis testing performed.

13.2.1. Internal Pilot

The recruitment rate of clusters and participants will be presented as a proportion of those eligible and assessed against the stop-go criteria (see section 13.3.1) to examine the validity of progressing to a full RCT.

13.2.2. Primary Outcome Measure

The primary outcome measure proposed for the full RCT is quality of life assessed using the MANSA. The adjusted mean difference at 10 months between treatment groups will be presented with 95% confidence intervals and p-values from two-sided tests also given. Linear mixed models will be used to compare the MANSA data between groups at 10 months, with adjustment for baseline values and the size of practice (stratification variable) as fixed effects and cluster and centre as random effects. No adjustment for multiple comparisons will be made.

13.2.3. Secondary Outcome Measures

The secondary outcome measures for the full RCT will be analysed in the same way as the primary outcome.

13.2.4. Subgroup Analyses

Subgroup analyses will include effect of intervention on different diagnostic groups, different sites and whether primary care only or secondary care

13.2.5. Missing Data and Sensitivity Analyses

Every attempt will be made to collect full follow-up data on all trial participants; it is thus anticipated that missing data will be minimal. Participants with missing primary outcome data will not be included in the primary analysis in the first instance. This presents a risk of bias, and sensitivity analyses will be undertaken to assess the possible impact of the risk. In brief, this will include multiple imputation methods. Full details will be included in the Statistical Analysis Plan

13.3. Planned Interim Analysis

There will be an interim analysis at the end of the internal pilot phase to assess whether to continue to the full trial.

13.3.1 Decision to continue to a definitive trial

The decision to continue to a full trial will be decided by pre-defined stop-go criteria as agreed by the TSC. A traffic light system based on recruitment and drop-out rates will be designed that will guide the decision process on whether to progress to the full RCT.

The Trial Steering Committee will take into consideration statistical uncertainty around the rates using 95% confidence intervals.

The sample size assumptions will also be checked after a minimum of 30 participants have reached the 10 month follow up period, using available follow up data, and if needed the sample size will be re-calculated based on estimates from the pilot data. The sample size for the full trial will be re-estimated using upper 90% confidence limits of primary outcome related variability and ICC. The assumption of a baseline measurement correlation of 0.5 will also be explored and appropriately adjusted.

13.3.2. Interim analyses for full RCT

If the trial progresses to the full RCT, interim analyses of safety and efficacy for presentation to the independent DMC will take place during the trial. The manner and timing of such analyses will be agreed with the DMC following the end of the internal pilot phase, but is likely to include the analysis of the primary and major secondary outcomes and full assessment of safety (serious adverse events) at least at annual intervals. Criteria for stopping or modifying the trial based on this information will be ratified by the DMC. Details of the agreed plan will be written into the Statistical Analysis Plan. Further details of DMC arrangements are given in section 14.5.

13.4. Planned Final Analyses

The primary analysis for the trial will occur after the data has been locked. This analysis will include data items up to and including the 10 month assessment and SAE's collected up to 12 months post unmasking.

14. TRIAL ORGANISATIONAL STRUCTURE

14.1 Organisational structure

Sponsor

Birmingham and Solihull Mental Health NHS Foundation Trust are the sponsors of this trial.

Coordinating Centre

The day-to-day management of the trial will be shared by the PenCTU and the PARTNERS2 Programme Manager.

Trial Management Group

The Trial Management Group (CI/PI, trial team, members of PenCTU) will meet regularly (usually quarterly, with additional meetings as required) to ensure successful implementation of the trial. They will monitor participant recruitment; any departure from the expected recruitment rate will be dealt with according to the specific issues discovered.

The Chief Investigator (CI) takes overall responsibility for the conduct of the trial. The Principal Investigator (PI) will take responsibility for all activity conducted at site. Any delegated responsibility

will be documented on the site delegation log. It is the PI's responsibility to ensure that staff is appropriately trained to perform the tasks delegated to them, that training is documented and the delegation log completed.

The research will be managed by the PARTNERS2 Trial Management Group consisting of:

- Professor Max Birchwood (CI)
- Professor Nicky Britten (Process Evaluation lead)
- Professor Richard Byng (Southwest Site PI)
- Dr Richard Laugharne (Cornwall Partnership NHS Foundation Trust PI)
- Dr Steven Marwaha (Birmingham site PI)
- Professor Linda Gask (Intervention lead)
- Dr Vanessa Pinfold (PPI Lead)
- Dr Humera Plappert (Programme Manager)
- Dr Siobhan Reilly (Lancashire Site PI)
- Dr Nathan Maynard (Somerset Clinical Site PI)
- Professor Siobhan Creanor (PenCTU Director / Senior Statistician)
- Dr Joanne Hosking/Mr Ben Jones (PenCTU Statisticians)
- Dr Alison Jeffery (PenCTU Trial Manager)
- Dr Julia Frost (Process Evaluation/Qualitative Researcher)

This team will meet on a fortnightly basis in the initial stages of the trial; once the trial is past the development stage the timings and constitution of these meetings will be reviewed and amended as appropriate.

14.2 Trial Steering Committee

The role of the Trial Steering Committee (TSC) is to provide the overall supervision of the trial. The Committee includes an independent chair, independent members, patient and public Involvement partners and the CI. Representatives from both the Sponsor and funding organisations will be invited to trial related elements of the TSC meetings as observers.

The TSC will meet at least once a year and minutes of the meetings will be sent to the Sponsor. The TSC will monitor trial progress and conduct and advise on scientific credibility. The TSC will consider and act, as appropriate, upon the recommendations of the Data Monitoring Committee (DMC) or equivalent and ultimately carries the responsibility for deciding whether a trial needs to be stopped on grounds of safety or efficacy.

The existing Programme Steering Committee has formally agreed to adopt the role of Trial Steering Committee.

14.3 Data Monitoring Committee

Data analyses will be supplied in confidence to an independent Data Monitoring Committee (DMC), which will be asked to give advice on whether the accumulated data from the trial, together with the results from other relevant research, justifies the continuing recruitment of further participants. The DMC will operate in accordance with a trial specific charter based upon the template created by the Damocles Group. The DMC is scheduled to meet 6 months after the trial opens.

Additional meetings may be called if recruitment is much faster than anticipated and the DMC may, at their discretion, request to meet more frequently or continue to meet following completion of recruitment. An emergency meeting may also be convened if a safety issue is identified. The DMC will report directly to the Trial Management Group (TMG) who will convey the findings of the DMC to the Trial Steering Committee, funders, and/or sponsors as applicable. The DMC may consider recommending the discontinuation of the trial if the recruitment rate or data quality are unacceptable or if any issues are identified which may compromise participant safety. The trial would also stop early if the interim analyses showed differences between treatments that were deemed to be convincing to the clinical community.

14.4 Finance

This is a clinician-initiated and clinician-led trial funded by the NIHR as part of a Programme Grant of Applied Research (RP-PG-0611-20004). This programme of research has been previously adopted by the NIHR Clinical Research Network [portfolio number 16841, 16842 and 16843]

15. ETHICAL CONSIDERATIONS

The trial will be performed in accordance with the recommendations guiding physicians in biomedical research involving human subjects, adopted by the 18th World Medical Association General Assembly, Helsinki, Finland, 1964, amended by the 48th WMA General Assembly, Somerset West, Republic of South Africa, 1996 (website: http://www.wma.net/en/30publications/10policies/b3/index.html).

The trial will be conducted in accordance with the UK Policy Framework for Health and Social Care Research, the Data Protection Act 2018) and the Principles of Good Clinical Practice (GCP) The protocol will be submitted to and approved by the main Research Ethics Committee (REC) prior to circulation.

Before any participants are enrolled into the trial, the Principal Investigator at each site is required to obtain local R&D approval/assurance. Sites will not be permitted to enrol participants until written confirmation of R&D approval/assurance is received by the PenCTU trials team.

It is the responsibility of the Principal Investigator to ensure that all subsequent amendments gain the necessary local approval. This does not affect the individual clinicians' responsibility to take immediate action if thought necessary to protect the health and interest of individual participants.

The trial has been designed to minimise pain, discomfort, fear and any foreseeable risk in terms of the intervention. As such, we do not anticipate any major ethical issues arising during the conduct of this trial. The explicit wishes of the participant will be respected including the right to withdraw from the trial at any time and these wishes will prevail over those of science and society.

If a participant in the intervention arm withdraws from the trial they will be transferred back to usual care in accordance with Clinical Governance arrangements agreed with each site. A two month transition period back to normal care will be offered to ensure the participant and relevant practitioners decide together the nature of ongoing care after trial involvement.

16. CONFIDENTIALITY AND DATA PROTECTION

Personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored in accordance with the Data Protection Act 2018.

Participants will always be identified using only their unique trial identification number, on the Case Report Form and in correspondence between research sites and the PenCTU

The Investigator must maintain documents not for submission to PenCTU (e.g. Participant Identification Logs) in strict confidence. In the case of *specific* issues and/or queries from the regulatory authorities, it will be necessary to have access to the complete trial records, provided that participant confidentiality is protected. Patients will provide written consent for PenCTU to hold a copy of their ICF for monitoring and quality purposes.

PenCTU will maintain the confidentiality of all participants' data and will not disclose information by which participants may be identified to any third party other than those directly involved in the treatment of the participant and organisations for which the participant has given explicit consent for data transfer e.g. competent authority, sponsor. Representatives of the PARTNERS2 trial team and sponsor may be required to have access to participant's notes for quality assurance purposes but participants should be reassured that their confidentiality will be respected at all times.

17. INSURANCE AND INDEMNITY

The sponsor for the trial is Birmingham and Solihull Mental Health NHS Foundation Trust. As the sponsor is an NHS organisation, NHS indemnity will apply. This will cover all indemnity regarding the design, management and conduct of the programme, as detailed and approved by REC.

18. PUBLICATION POLICY

Results of this trial will be submitted for publication in a peer reviewed journal. The manuscript will be prepared by the PARTNERS2 team and authorship will be determined by the trial publication policy.

Any secondary publications and presentations prepared by Investigators must be reviewed and approved by the TMG. Manuscripts must be submitted to the TMG in a timely fashion and in advance of being submitted for publication, to allow time for review and resolution of any outstanding issues. Authors must acknowledge that the trial was performed with the support of Clinical Trials Units hosted by the Universities of Birmingham and Plymouth. Intellectual property rights will be addressed in the Clinical Trial Site Agreement between Sponsor and site.

Trial results will also be communicated to participants, healthcare professionals, the public, and other relevant groups using appropriate formats for the audience, for example, leaflets, short reports, and presentations. The protocol will be submitted for publication and will be accessible via the PARTNERS2 study website.

19. PATIENT AND PUBLIC INVOLVEMENT (PPI)

The PPI strategy for the trial builds on the preparatory work carried out over the past year, and is based on integrating lived experience expertise throughout PARTNERS2. This means:

- PPI input into decision-making committees.
- Three Lived Experience Advisory Panels (LEAPs), one per study site, with up to 10 members in each panel with either personal experience of ongoing mental health needs or caring for someone with ongoing mental health needs.
- An employed PPI coordinator to support all PPI activities, LEAPs and individual public contributors.
- Three service user researchers, one per study site, working within the research team drawing on their research skills as well as own lived expertise to benefit the study.

  The LEAPs have been meeting quarterly over the past two years to work with researchers to develop the intervention and to inform the design of the trial. This important work is outlined in Appendix 1.

The focus of their work will now shift as we move into the trial. All of the LEAP members will meet once a year as a combined LEAP group and maintain local meetings as needed but at a minimum twice a year. A quarterly newsletter will ensure everyone is kept up to date with progress. Meetings will be used to problem solve around local issues such as recruitment or engagement challenges and input into REC amendments including changes to recruitment materials if required, reflect on emerging findings, input into the study web site and plan dissemination activities.

20. PROCESS EVALUATION

The PARTNERS2 process evaluation will be led by Dr Ruth Gwernan-Jones and Julia Frost, at the University of Exeter Medical School.

In line with MRC guidelines (18), a comprehensive mixed methods process evaluation will be a key part of the trial and will assess fidelity to the model, behaviour change of the care partners, service users and institutions and develop an understanding of how the intervention does or does not work. This will inform further improvements and provide suggestions for implementation. The process evaluation will build on the earlier formative evaluation in work stream 3 and the preceding stages of theory development. The programme theory is represented in a logic model (see Appendix 3) and is operationalised in the PARTNERS2 manuals (for care partners, service users and carers. The process evaluation will use similar methods as the formative evaluation (19), elaborated or modified as necessary and focussed more clearly on context. One aspect of the evaluation will incorporate a Realist Evaluation approach (20) building on the programme theory. We consider context – wider (the cultures, organisational configuration, geography and policy environment) and individual (capacity/predisposition/beliefs of practitioners and service users) – within which the intervention

operates, to be an active adapting system with its own causal powers, and which has the potential to interact with the intervention. Within the realist analysis we will focus on mechanisms (reasoning or automatic responses to resources), and whether outcomes are achieved in which contexts.

The key objectives are:

1. To assess the fidelity of the intervention during delivery against the PARTNERS2 theory represented by the logic model (Appendix 3) and operationalised by the PARTNERS2 manuals.
2. In particular, to assess how any changes in the understanding and behaviour of the care partners over the duration of the trial were influenced by the initial and top up training, supervision sessions, and tape assisted recall
3. To achieve a more in depth understanding of how the intervention works or does not work in comparison to the programme theory, and how it can be implemented in different contexts; and
4. To develop implementation recommendations, especially in relation to acceptability, adoption, feasibility, fidelity and penetration.

Recruitment

Service user participants

All service user participants whose GP practice was randomised to the intervention arm of the trial will be asked to complete a fidelity questionnaire. This may be during the follow-up appointment with the researcher, or the questionnaire may be posted to them for completion at home, along with a prepaid envelope for the reply.

When completing informed consent for the trial, service user participants will consent, or not, to researchers inviting them to be involved in other related studies. Those that consent to such contact will be considered as potential process evaluation participants.

Trial researchers will have existing records of demographic details from the CRF:

- Gender
- Ethnicity
- Diagnosis
- Age at diagnosis.

These details will enable purposive sampling so that a diverse range of service users are represented. Purposive sampling will also be used to capture data from participants who are at different points in the 12 month PARTNERS2 model, and in the case of the care partners' learning.

Researchers will contact a potential participant in the way specified on their Participant Preference Information form and remind the participant that s/he previously consented to other studies and ask if they are still willing to take part in the evaluation of the trial, as described on the full Patient Information Sheet. If the participant does not agree, this will be appropriately recorded. If the participant agrees, the researcher will arrange to meet him/her, either at the GP practice or other convenient location, to discuss consent and give the participant the opportunity to ask questions. Process evaluation interviews may be carried out during the same or subsequent meetings. These participants will also be asked to consent to having one of their sessions with the care partner audio recorded and take part in a second interview in relation to extracts from that session recording. Participants will be able to consent to the main interview alone if they prefer.

Informal carer participants

When service users give informed consent, they will be asked if they have a relative or friend who is involved in their care and who may also be willing to participate in an interview. If the service user identifies a potential carer participant, s/he will be given a letter, a Family and Friends Participant Information Sheet, a Family and Friends Expression of Interest form and a prepaid envelope and asked to pass these on to their relative or friend. When an Expression of Interest form is returned, a researcher will contact the potential carer participant to arrange to meet him/her, either at the service user's GP practice or other convenient location, to take informed consent and carry out an interview.

GP or primary care practitioner participants

GP practices that are within the intervention arm of the trial will be asked to take part in the process evaluation towards the end of that practice's involvement. Researchers will then make contact with the link person identified at each practice and ask if s/he, or another member of the practice team, is

willing to take part in an interview, and send them a copy of the relevant participant information sheet. This may include, but is not limited to, the lead GP, practice manager or deputy, or research nurse. . If the participant agrees, the researcher will arrange to meet him/her at the practice, to take informed consent and carry out an interview.

Care partner participants
Researchers will contact the care partner, ask if they are willing to take part in the process evaluation, and send them a copy of the relevant participant information sheet. If the participant agrees, the researcher will arrange to meet him/her at his/her usual place of work, or other convenient location to take informed consent and carry out the first interview. The first interview will take place during the first few months of the care partner's practice. A second interview with the care partner will take place towards the end of their practice. Care partners will also be asked to audio record 2 of their supervision sessions and take part in one interview per session in relation to research-selected extracts from that recording. Care partners will be asked to audio record sessions with up to five participants and take part in one interview per recorded session in relation to extracts from that recording. Care partners will be asked to keep a written record of their contacts with service users and complete monthly reflective logs. Care partners will be able to consent to the stand alone interviews without consenting to the recording, if they wish.

Supervisor participants
Researchers will contact the supervisor, ask them if they are willing to take part in the process evaluation, and send them a copy of the relevant participant information sheet. If the participant agrees, the researcher will arrange to meet him/her at his/her usual place of work, or other convenient location to take informed consent and carry out the first interview. The first interview will take place during the first few months of the care partner's practice. A second interview with the supervisor will take place towards the end of each care partner's practice. Supervisors will be asked to keep written records of their supervision sessions. Supervisors will also be asked to consent to an audio recording of up to two supervision sessions per care partner and take part in one interview per recording in relation to researcher selected extracts from the recordings. Supervisors will be able to consent to the stand alone interviews without consenting to the recordings if they wish.

Secondary care institutions
Local trial researchers will use their records of liaising with secondary care providers to identify those in the local secondary care bodies who have been involved in delivering PARTNERS2, and invite them to be interviewed towards the end of their involvement. Potential participants will be contacted by the local team, asked to take part in a process evaluation interview, and sent a copy of the relevant participant information sheet. If the potential participants are interested a member of the research team will meet with them at a convenient location to discuss, answer questions, take consent and undertake an interview. Potential secondary care participants may include: research manager, research nurse, team leader, principle investigator, clinical lead, other PARTNERS2 instigator/champion (e.g. CEO).

Partners2 researchers
A selection of researchers involved in the recruitment of patients and GP practices (research assistants, associates, fellows and peer researchers), and secondary care providers (chief investigators, clinical investigators) to both the main trial and the process evaluation sub-samples will be invited to take part in a process evaluation interview. Researchers involved in the training of care partners and supervisors (research fellows, clinical investigators, peer researchers) will be invited to take part in a process evaluation interview. Potential participants will be contacted by the process evaluation team, asked to take part in a process evaluation interview, and sent a copy of the relevant participant information sheet. If the potential participants are interested a member of the process evaluation team will meet with them at a convenient location to discuss, answer questions, take consent and undertake an interview.

Consent

At the face to face meeting the researcher will provide a full explanation of the process evaluation covering all of the essential elements: the aim, what taking part would involve, anticipated benefits and potential disadvantages of taking part. They will also stress that participation is voluntary and that the participant is free to refuse to take part and may withdraw from the study at any time, without withdrawing from the main trial or the intervention. The participant will be asked to consent separately to all elements of data collection relevant to their role. For service users this consists of: participation in a semi-structured interview, having an intervention session recorded, participating in an interview about the recorded session and having a relative or friend who is involved in their care approached for an interview. For informal carers and GPs this consists only of a semi-structured interview. For care partners this consists of participation in two semi-structured interviews, having an intervention session recorded, participating in an interview about the recorded session, having a supervision session recorded and submitting written entries from a reflective practice log. For supervisors this consists of participation in two semi-structured interviews and having a supervision session recorded. The potential participant will be allowed to consent immediately or may take the opportunity to reflect on the decision and/or discuss their participation with others outside of the site research team. If the potential participant requests more time to decide, the researcher will follow-up within two weeks. If at follow-up the potential participant agrees to participate, a face to face meeting will be arranged for consent to be collected and a semi-structured interview to take place. Copies of the consent form will be given to the participant and placed in the investigator site file and the original signed informed consent form will be sent to the process evaluation lead at the University of Exeter.

Sample size

Following consent, we will collect data from each care partner (n=6) and their supervisor, from a selection of GP practices in the intervention arm (n=12), and from each secondary care institution involved in the trial (n=8). We will collect data from 30-36 trial participants, we anticipate this to be approximately 5 service user participants per care partner. We will interview Partners2 researchers in relation to processes of training and recruitment (n=6).

Inclusion Criteria

Service users

1. Have received more than 4 sessions of the PARTNERS intervention.

Carers

1. Referred by a service user who has consented to take part in the process evaluation.
2. Speaks English.

GPs and primary care practitioners

1. Currently working in a primary care practice where the intervention has been delivered for at least 5 months

Care partners and supervisors

1. Has been involved in providing the PARTNERS intervention for at least 6 weeks.

Partners2 researchers. Researcher experience of recruitment and/or training during the Partner2 trial.

Exclusion Criteria

Service users or carers

1. Service users or carers of service users not currently able to give informed consent.

2. Service users or carers of service users currently managed in an acute setting.

Data collection
Qualitative data will be collected from:

90-110 semi-structured interviews
Semi-structured interviews will explore participants' experiences and perspectives of the intervention, focussing on which components of the intervention were delivered and how, whether the components were delivered as intended and the perceived effects the components had on each category of participant. The range of participants and time points will allow exploration of the changes within the care partner, service users, and institutions involved in delivering the intervention.

Approximately 36 interviews with a purposive sample of service users, with a maximum diversity in age, gender, ethnicity, diagnosis and time since diagnosis and from as wide a range of participating GP practices as possible, length of time receiving the intervention, length of experience of care partner in delivering PARTNERS2 intervention and service users that the care partner or research team perceive to be responding particularly well, or not so well, to the intervention.

Up to 16 interviews with informal carers, as referred by service users consenting to taking part in the process evaluation. We do not anticipate all service users in the process evaluation to want to/have an appropriate person to refer.

Up to 20 interviews with GPs or primary care staff. We will invite staff from practices in the intervention arm, with a purposive sample to include practices where the care partner or research team perceive the practice engagement with the intervention to be working well and not so well.

Approximately 24-30 interviews with mental health practitioners involved in delivering the intervention, either as care partners or supervisors. These participants will be interviewed twice, once at an early (approximately 6 weeks of delivery) and later stage (approximately 12 months).

Up to 12 interviews with secondary care staff involved with PARTNERS2, two interviews per secondary care institution including one with a staff member involved with PARTNERS2 at strategic level, and one with a member of staff involved at delivery level.

Up to 8 interviews with Partners2 researchers to capture implementation- and context-related information such as recruitment of and interaction with Trusts, GP surgeries, supervisors, care partners and service users.

18-24 Intervention session recordings and 36-40 follow-up interviews
Drawing from a method found to be particularly able to support evaluation of delivery of the intervention during the formative evaluation of Partners2 (4), we will be recording sessions between care partners and service users, and supervisors and care partners, to provide direct documentation of delivery of the intervention. Extracts from the session recordings will then be used to prompt discussion of specific moments during the sessions in separate follow-up interviews. The follow-up interviews will allow us to explore the intentions of supervisors and care partners during recorded sessions, and how care partners and service users experienced these.

12-16 audio-recordings of intervention sessions between care partners and service users (up to 5 per care partner)
Service users who consent to taking part in the process evaluation will also be asked to consent to one of their sessions being audio recorded. If both the care partner and service user consent then a session will be recorded. Up to five sessions will be recorded, aiming to capture a range of time points both across the care partner's experience delivering the intervention, and at different

stages of the 12 month intervention. This will capture both the care partner's development, as well as exploring how delivering different stages of the model works in practice.

24-32 follow-up interviews, using intervention session recordings as a stimulus for discussion (12-16 care partner interviews and 12-16 service user interviews)

Each audio session recording will be used to provide extracts used in two separate follow-up interviews: one with the care partner and one with the service user. Four to six extracts from the session recording will be chosen in advance by researchers because:

- The care partner and service user seem to be collaborating effectively on elements of the model (doing 'well');
- The care partner and service user are failing to collaborate.
- The extracts will be played back to the participant who will then be asked:
- Care partner: What were you trying to do there?; What do you think you were doing well? Would you have liked to do anything differently?
- Service user: What was helpful about that? Was there anything that was not helpful?
- This will allow exploration of practitioner and service user viewpoints about specific interactions, further understanding of the process of change within both the care partners and service users, and allow for deeper understanding of implementation of the model. Participants in tape assisted recall interviews will be offered the option of switching to a typed transcript if they find working with the recording too uncomfortable to proceed.

6-8 audio-recorded supervision meetings between care partners and their supervisors (2 per care partner).
One session will be recorded at an early stage in the care partner's experience of delivering the intervention (approximately 3-4 months) and one at a later stage (approximately 15? months), in order to allow exploration of developments in the care partner's and supervisor's practice over time, as well as implantation, particularly penetration of the model at supervisor and wider institution level. Audio recordings will allow direct observation of how supervision is being delivered and how the care partner is engaging with it, through the least intrusive possible means.
12-16 follow-up interviews, using supervision session recordings as a stimulus for discussion (6-8 with care partners, 6-8 with supervisors)

Each audio recorded supervision session will be used to provide extracts for two follow-up interviews: one with the care partner and one with the supervisor. Four to six extracts from the session will be chosen in advance by researchers and played back to the participant who will then be asked to reflect on what they thought was helpful and what could have been improved about the care partner or supervisor's approach at that point. This will allow exploration of practitioner's and supervisor's viewpoints about particular interactions, further understanding of the process of change within both the care partners and supervisor/related institutions, and allow for deeper understanding of implementation of the model. Participants in tape assisted recall interviews will be offered the option of switching to a typed transcript if they find working with the recording too uncomfortable to proceed.

Care partner entries in a reflective practice log, completed on a monthly basis, during the delivery of the intervention
Care partners will be asked to choose and reflect on a particular experience of delivering the intervention and record these on a monthly basis, using prompts (Appendix 9.9.1 in the Care Partner and Supervisor Manual) to guide them in considering their intentions, what had worked well, what they could have done differently and what they had learnt from the experience. These will be used to aid understanding of the process of change within the care partner, and may also be of use to understand the change in service users and/or institutions.
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Researchers' observations and field notes
During initial training and local top up training sessions for care partners and supervisors, and following semi-structured interview sessions, researchers will take field notes. These will capture the care partners' and supervisors' engagement with and response to the training provided, and to note wider context of interviews from the researcher viewpoint. This will aid understanding of the process of change within care partners and supervisors, and support interpretation of interview data.

Quantitative data

Process of care data

Process of care data will be collected by care partners, through completing the following templates in the Care Partner and Supervisor Manual (version 1.10, July 2019):
Appendix 9.4.1 Core-10
Appendix 9.4.2 Individual Goal Record
Appendix 9.8 Record of Service User contact and PARTNERS implementation
Appendix 9.10 Early contact with Service Users
Appendix 9.14 PARTNERS' Supervisor's recording sheet
Appendix 9.17 Final review with Service User
Appendix 9.18 Process of working with primary care

Fidelity survey
Following completion of Partners2, service users will be asked to complete a short scale evaluating fidelity of their experiences to the intervention theory.

Institutional context survey
Researchers will contact practice managers from participant primary and secondary care institutions to complete contextual surveys.

Outcome measures
Outcome measures at baseline and follow-up for service user participants including use of services, measures of physical health (e.g. use of primary care, admission to hospital, smoking and alcohol use), the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS), EuroQol and Manchester Short Assessment of Quality of Life (MANSA).

Patient and public involvement
Patient and public involvement has been shown to contribute to qualitative data analysis alongside healthcare trials (Frost et al. 2018). Partners2 involves a well-established thread of patient and public involvement, including a number of Lived Experience Advisory Panel (LEAP) members, some of whom have been involved from the beginning of the project, and many who understand the intervention theory well. A number of LEAP members have agreed to support the process evaluation. Three members commented on service user case study 304044; their interpretations were aligned with researcher interpretations, and they identified additional examples of the intervention theory in practice which were added to our analysis. We will continue to ask LEAP members for feedback about our interpretations around the experiences of service users, and for their perceptions about whether the Partners2 healthcare that service user participants received met the intentions of the intervention theory. LEAP members will feed back either through email or during workshops where LEAP members and researchers meet to work in more depth.

Data analysis

The analyses will follow a realist approach, with the aim of identifying demi-regularities between contexts, intervention resources, participant mechanisms and outcomes to explain how, for whom and in what contexts the Partners2 intervention works. The analyses will be structured by Partners theory developed previously using realist approaches (19; 21).
In order to encompass the complexity of the Partners2 intervention, we will be conducting longitudinal, integrated mixed-methods case studies at three levels:

- Service user level
- Care partner level
- Institutional level (22).

Qualitative and quantitative data will be integrated by individual case. For figures showing data contributing to each level, see Appendix 4 (service users), Appendix 5 (care partners) and Appendix 6 (institutions). Below we explain how we will work towards each of the process evaluation objectives. Miles et al (23) suggest that each hour of qualitative data collected requires a minimum of 8 hours data management and analyses, but emphasise that this figure is multiplied in the case for complex within- and across- case analyses. Cresswell and Plano Clark (24) have also noted that the stages of a mixed-methods analysis (including data reduction, display, transformation, correlation, consolidation, comparison and integration) take considerably longer.

Objective 1

To assess the fidelity of the intervention during delivery against the PARTNERS2 theory represented by the logic model (Appendix 3) and operationalised by the Partners2 manuals
In order to assess the fidelity of Partners2 delivery against the programme theory over time, we will conduct evaluation coding (23) focused on the presence and/or direction of intervention resources, mechanisms and outcomes relevant to each level of analysis identified on the Partners 2 logic model (Appendix 3).

Objective 2

In particular, to assess how any changes in the understanding and behaviour of the care partners over the duration of the trial were influenced by the initial and top up training, supervision sessions, and tape assisted recall
The Partners2 formative evaluation (19) identified the difficulty of creating changes to care partner practice as a potentially substantial barrier to intervention fidelity. We will therefore look in particular depth at this issue within care partner level case studies. Training field notes, longitudinal data including repeat interviews, intervention session and supervision session recordings, follow-up interviews and reflective practice journals will all contribute to documenting change. We will conduct evaluation coding on this data as described in Objective 1.

Objective 3

To achieve a more in depth understanding of how the intervention works or does not work in comparison to the programme theory, and how it can be implemented in different contexts
Where we have established fidelity in the data, we will compare and contrast these findings to context—resource—mechanism—outcome pathways identified in the Partners2 theory, looking for support for, refutation of and gaps in existing theory. This process will provide information about whom P2 works best for and how and inform our suggestions for implementation (see Objective 4). Ultimately we will adapt the Partners2 intervention theory to reflect these findings.

Objective 4

To develop implementation recommendations, especially in relation to acceptability, adoption, feasibility, fidelity and penetration.

In order to develop knowledge that is beneficial to scaling the Partners2 intervention up or out, we will adopt an implementation framework to guide our data analysis, particularly focusing on acceptability, adoption, feasibility, fidelity and penetration (25).

Confidentiality and data protection

Any data derived from this evaluation will follow the same data protection policies as the main trial. Data held at the University of Exeter will be stored securely in accordance with the university's data protection policy.

Participants will be identified by only their participant ID number on written data that is transferred to the University of Exeter, such as field notes and file names of digital audio recordings.

Informed consent forms will be stored in a locked filing cabinet in the office of the process evaluation lead within a secure area of the university.

Audio-recordings and field notes will be uploaded onto the University of Exeter OneDrive as soon as the researcher returns to their office base. Audio-recordings will be downloaded directly from OneDrive by a contracted professional transcriber, who will remove identifying details during transcribing. Transcripts will then be uploaded to OneDrive.

Quantitative data will forwarded by care partners to PenCTU for storage in the trial database.

Rapid realist evaluation during Covid-19 pandemic

In response to social distancing requirements started in March 2020, within the process evaluation a rapid realist evaluation of the ability of care partners to remotely provide the Partners service will be undertaken. This will explore:

1) Which aspects of the Partners2 intervention, and what dose, are deliverable in the context of lockdown within England due to the Covid-19 pandemic, which limits service delivery to telephone or video chat?

- What aspects of the logic model remain relevant?
- What approaches do care partners take to adapting the service?
- Are there aspects of programme theory that need to be added to the logic model in these circumstances?

2) What aspects of Partners2 are core to delivering the desired outcomes (maintaining stability of mental health, improving physical health and wellbeing)?

3) What characteristics of care partners and service users support the ability to provide/receive the Partners service during lockdown? (e.g. is there a minimum dose or a threshold of viability that can be identified).

4) What types of communication do care partners and service users use to communicate, why is each approach chosen, and how well do they work (and on what basis/whose judgement is that assessment made. Ie is this service user or care partner driven)?

The findings will inform decisions around the continuation of the Partners service during the pandemic.

21 PROCESS EVALUATION SUB-STUDY

The aim of this sub-study is to boost the number of participants in the process evaluation by allocating the last few GP practices recruited to the intervention arm of the study, in order to extend our understanding of delivery of the Partners2 intervention in the context of the new NHS policy for community mental health transformation. This will maximise our understanding of the fidelity of the intervention delivery against the programme theory over time, and further assist with recommendations for implementation (Objectives 1 and 4 above).

A sub-group of GP practices (three to six) and their eligible patients will be invited to take part in this optional sub-study towards the end of the recruitment period for the main randomised trial. Rather than being randomised to receive either collaborative care from the care partner (intervention group), or to continue with usual care (control group), these practices will all be allocated to receive the intervention. Both the intervention delivery (as described in Section 7 of this protocol) and the Process Evaluation (Section 20) will be delivered in the same manner as for the main randomised trial participants. A separate participant information sheet designed for this PE sub-study will be given to potential participants and written consent to participate in the PE sub-study will be obtained. All other study processes (for example, safety and non-compliance reporting) will continue as for participants in the randomised trial. Only some of the participants in this PE sub-study will be approached to participate in the qualitative interviews, as in the main randomised trial.

Quantitative data collected from participants in this PE sub-study will not be included in the statistical analyses of the main randomised trial, but will be used as context for the sub-study and to informally assess and describe any differences from main trial participants. Qualitative analysis of data collected during the Process Evaluation to date suggests that both practices and participants enjoy receiving the intervention and perceive this as beneficial.

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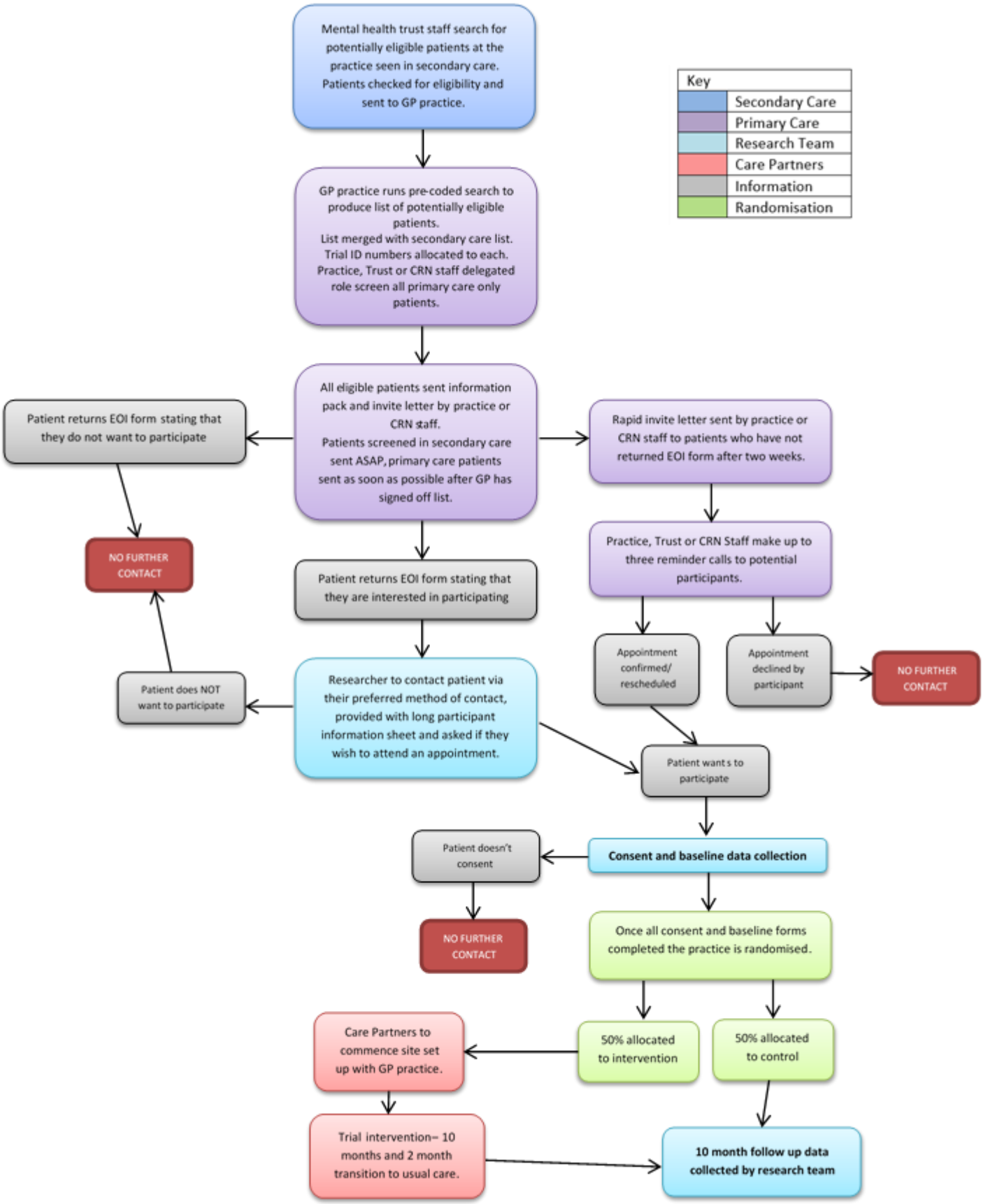
APPENDICES

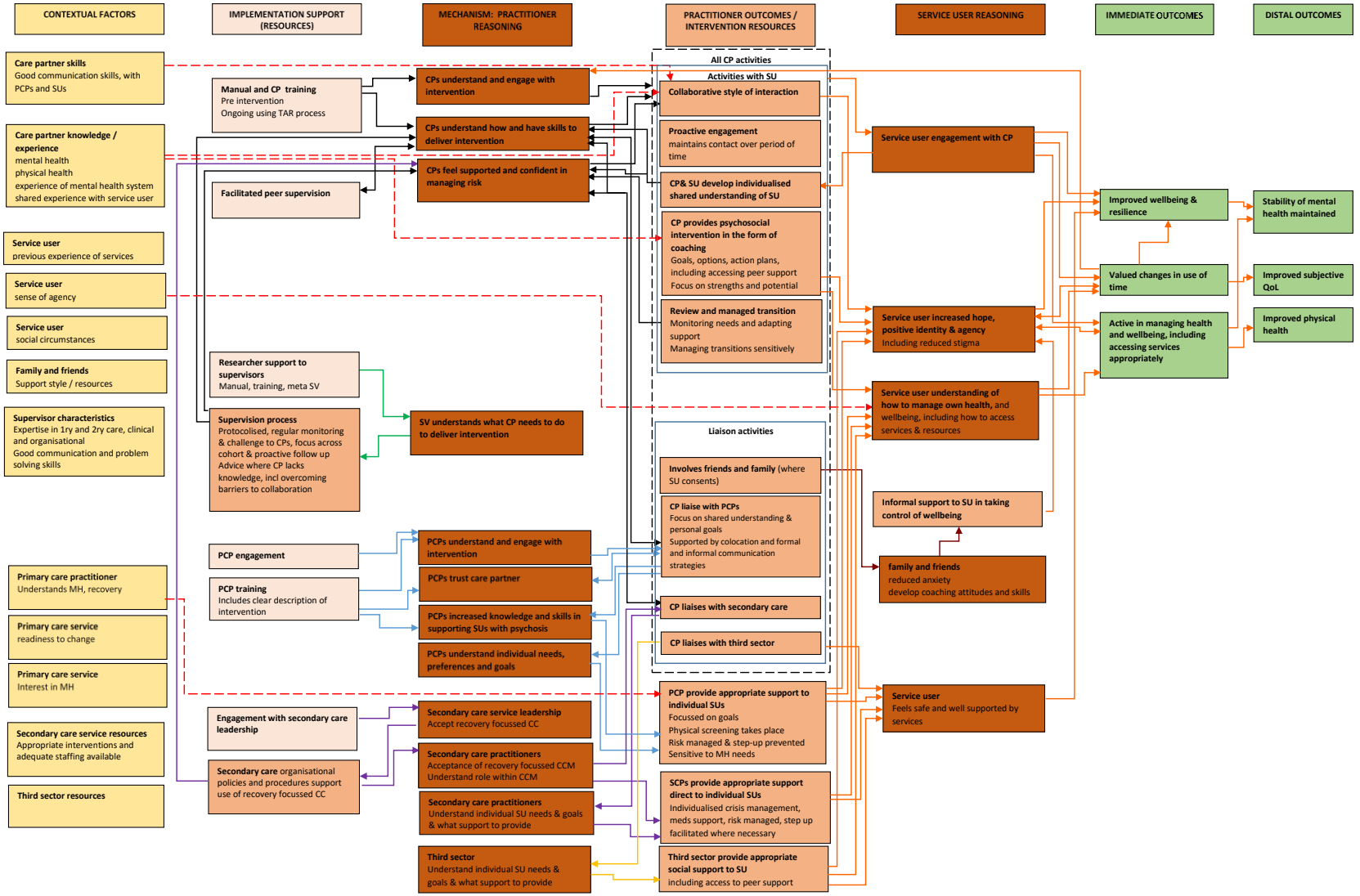
Appendix 1: activities involving the LEAPs, service user researchers, PPI coordinator and co-applicant Vanessa Pinfold

Intervention design	Formative evaluation (FE)	Trial design	Other programme-related activities
Selecting the scales used as repeated measures by the Care Partners Developing the service user guide Developing the PARTNERS2 practitioner manual Developing an information leaflet for carers about PARTNERS2	Supporting ideas for recruitment strategies during FE Development of interview schedules for the service user and carer versions Analysis and interpretation of FE data Refining aspects of the intervention in response to FE findings Developing a PARTNERS2 service evaluation survey	Developing the participant information leaflet Identifying outcomes of interest and testing measures to assess wellbeing and quality of life Developing and testing appropriate language around recruitment and strategies for overcoming recruitment barriers Developing a plan for the continuation of the LEAPs in the trial phase	Developing a Core Outcome Set for Bipolar disorder: involved in selecting the long list of domains for schizophrenia and bipolar Editing the lay summary descriptors for the final long list domains both for schizophrenia and bipolar Input into identifying the outcome measures of interest in the Cochrane review and inputting into relevant sections

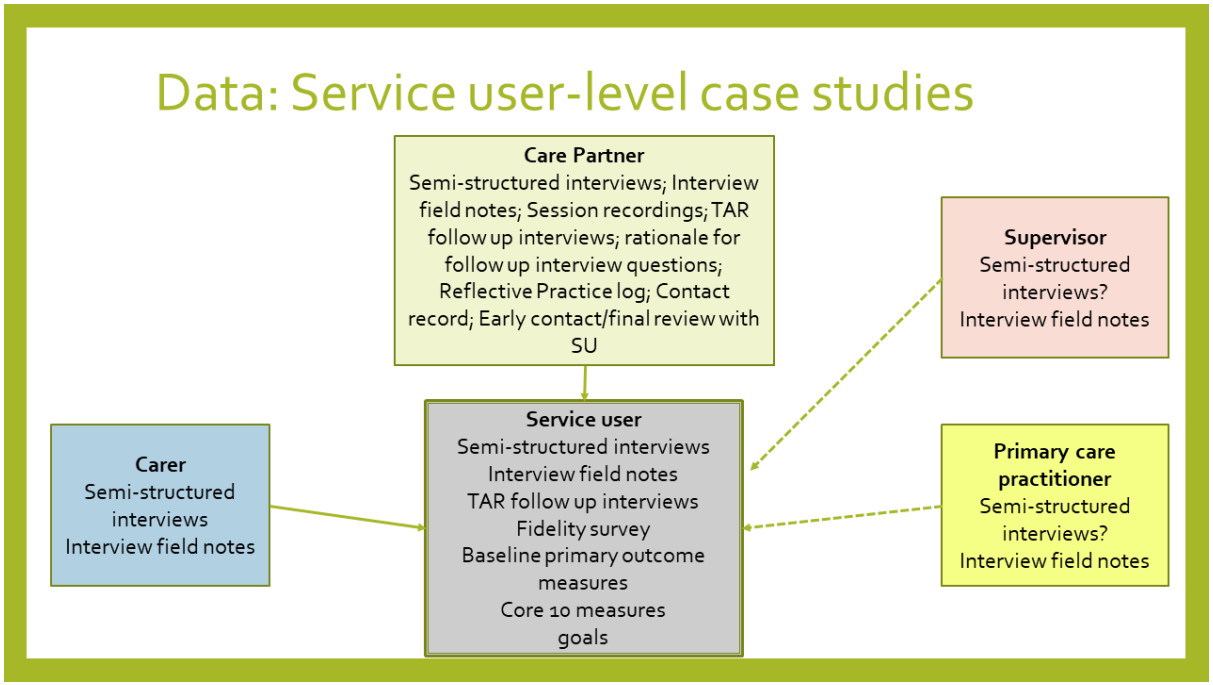
Appendix 2: Trial schema



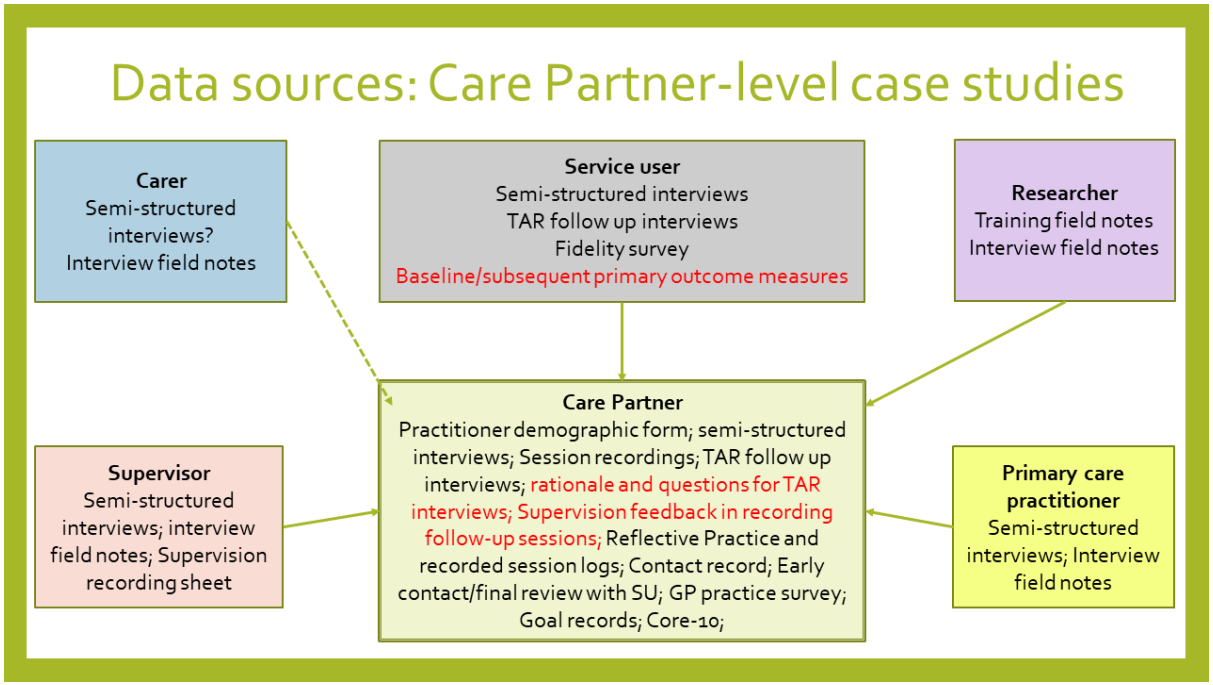
Appendix 3: Process Evaluation logic model



Appendix 4: Data contributing to service user level case studies



Appendix 5: Data contributing to care partner level case studies



Appendix 6: Data contributing to Institution level case studies