
# TRIAL PROTOCOL

# PHOENIx

**P**harmacy **H**omeless **O**utreach **E**ngagement **N**on-medical **I**ndependent prescribing R**x** (**PHOENIx**) community pharmacy-based pilot randomised controlled trial

**This protocol has regard for the HRA guidance and is compliant with the SPIRIT guidelines (2013)**

**Version Number:** **3.0**

**Version Date:** **07-FEB-2023**

## PROTOCOL DEVELOPMENT

### 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 |
|---|---|---|---|---|
| NSA01 | **07-FEB-2023** | **3.0** | **Non-significant** | *Trident Reach* **has been added as a supporting homelessness charities changed, and references to '***third sector homelessness support organisations' added to enable support from further organisations.* **Minor grammatical/typographical changes.** |

### Funding and support in kind

| Funder(s)/Supporting Organisations | Financial and non-financial support given: |
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## PROTOCOL SIGN OFF

### Chief Investigator (CI) signature page

I, the Chief Investigator, confirm that I have read and agree with the following protocol, and that I will conduct the trial in compliance with the version of this protocol approved by the REC and any other responsible organisations.

I agree to ensure that the 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.

I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as stated in this and any subsequent approved protocol will be explained.

| | |
|---|---|
| Trial name: | PHOENIx Community Pharmacy |
| Protocol version number:<br>Protocol version date: | Version: 3.0<br>07-FEB-2023 |
| | |
| CI name: | Vibhu Paudyal |
| Signature and date: | |

### Sponsor statement

By signing the IRAS form for this trial, University of Birmingham, acting as sponsor, confirm approval of this protocol.

### Compliance statement

This protocol describes the PHOENIx Community Pharmacy (PCP) trial only. The protocol should not be used as a guide for the treatment of participants not taking part in the PCP trial.

The trial will be conducted in compliance with the approved protocol, the UK Policy Framework for Health and Social Care Research, Data Protection Act 2018 and the Principles of Good Clinical Practice (GCP) as set out in the UK Statutory Instrument (2004/1031) and subsequent amendments thereof. We will also comply to the Mental Capacity Act 2005 (England) and Section 51 of the Adults with Incapacity (Scotland) Act 2000. Every care has been taken in the drafting of this protocol, but future amendments may be necessary, which will receive the required approvals prior to implementation.

## Principal Investigator (PI) signature page

As Principal Investigator, I confirm that the following protocol has been agreed and accepted, and that I will conduct the trial in compliance with the approved protocol where this does not compromise participant safety.

I agree to ensure that the 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.

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|---|---|
| Trial name: | |
| Protocol version number: | Version: __ __ |
| Protocol version date: | __ __ / __ __ / __ __ __ __ |
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## ABBREVIATIONS

| Abbreviation | Term |
|---|---|
| ADRS | alcohol and drug recovery services |
| AE | Adverse Event |
| BCTU | Birmingham Clinical Trials Unit |
| DCF | Data Clarification Form |
| CI | Chief Investigator |
| COPD | Chronic Obstructive Pulmonary Disease |
| CRF | Case Report Form |
| DSA | Data Sharing Agreement |
| FEV1 | Forced Expiratory Volume |
| GCP | Good Clinical Practice |
| GP | General Practitioner |
| HRA | Health Research Authority |
| ICF | Informed Consent Form |
| ICS | Integrated Care System |
| ISD | Information Service Division |
| ISF | Investigator Site File |
| NHS | National Health Service |
| NHS GG&C | NHS Greater Glasgow & Clyde |
| NICE | National Institute for Health and Care Excellence |
| NIHR | National Institute for Health Research |
| NRS | National Records Scotland |
| OC | Oversight Committee |
| PEH | Persons experiencing Homelessness |
| PI | Principal Investigator |
| PCP | Phoenix Community Pharmacy |
| PIS | Participant Information Sheet |

| | |
|---|---|
| PPI | Patient and Public Engagement |
| QALYs | Quality Adjusted Life Years |
| RCT | Randomised Controlled Trial |
| REC | Research Ethics Committee |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SIGN | Scottish Intercollegiate Guidelines Network |
| TMF | Trial Master File |
| TMG | Trial Management Group |
| TOC | Trial Oversight Committee |
| UoB | University of Birmingham |
| VOI | Value of Information |

## TRIAL SUMMARY

**Title**

**P**harmacy **H**omeless **O**utreach **E**ngagement **N**on-medical **I**ndependent prescribing R**x** (**PHOENIx**) community pharmacy-based pilot randomised controlled trial

**Design**

Randomised, multicentre, open, parallel group external pilot trial with parallel economic and qualitative process evaluation.

**Objectives**

To undertake a pilot randomised controlled trial (RCT) to assess the feasibility of conducting a larger, definitive trial assessing an integrated clinical pharmacist / homeless third sector intervention (PHOENIx) delivered in a community pharmacy setting. The pilot RCT will test recruitment, retention, acceptability, trial procedures and potential future implementability and scalability of the intervention.

**Participant population and sample size**

100 adults ≥18 years experiencing current homelessness. 15-20 of these participants will be included in a qualitative substudy, plus 7-10 health care professionals and 7-10 stakeholders.

**Setting**

Glasgow and Birmingham city centre community pharmacies. Participating pharmacies will be located in parts of Glasgow and Birmingham city centre and immediate surrounding areas, where People Experiencing Homelessness (PEH) are known to frequent. This limits our selection of pharmacies but both cities are big enough to offer a choice of locations, independent or multiple chain ownership pharmacies. Initially two pharmacies in Glasgow and two in Birmingham will be recruited. Backup sites (other community pharmacies) will be asked to participate in the event that recruitment is slow in each of the four main community pharmacies, during the first 2 weeks.

**Eligibility criteria**

Inclusion:

- Adults ≥18 years and experiencing homelessness, who are attending or service users of one of the designated community pharmacies.
  Homelessness will cover:
  - rooflessness
  - houselessness
  - insecure or inadequate housing as per the ETHOS typology
  - people staying in homeless shelters
  - rough sleepers
  - people staying in temporary accommodation such as bed and breakfasts (B&Bs), hostels, squats; or those sofa surfing between family and friends' houses

Exclusion:

- Living in accommodation with 24-hour support which includes in house medical care
- Intoxicated or (in the opinion of the researcher) posing a safety risk to staff and lacking capacity to consent

**Interventions**

**Intervention group:** In addition to usual care, the PHOENIx team (pharmacist independent prescriber in partnership with a third sector charity worker) will assess the participants' physical, mental and addictions health, housing, benefits and social activities during a consultation in the community pharmacy. Taking approximately one hour, face to face (with full personal protective equipment), the PHOENIx team will record the participant's priorities, and going at the participant's pace, will assess, treat, prescribe, and refer to other health and social care teams. The team will offer 'sticky' follow up, flexible, weekly (more or less often as required) consultations in the pharmacy or outreach in temporary residence, homelessness support hub or community shelters as preferred by the participant, for six months. Our aim is to have intervention staff available in Glasgow and Birmingham, on four days per week, working two days in each pharmacy. Uptake of health and social care interventions will be maximised, and dropout minimised, through assertive outreach by the third sector charity worker to find participants in case of non-attendance at the pharmacy.

**Control Group:** Usual care. Participants allocated to usual care will not receive consultations from the PHOENIx team in the pharmacy or in any other venue, throughout the duration of the intervention phase. If allocated to usual care, the researcher will signpost or refer the participant should they identify urgent health care needs e.g. overdose.

In both intervention and usual care groups, participants can continue to obtain and seek care, treatment or help as usual. Bias is possible, although unavoidable, through signposting the usual care group to Emergency Department by the researcher (after assessments) or to other health and social care staff. Consultations (frequency, location) with health and social care for all participants, will be collected by researchers.

**Outcome measures**

**Primary:** The primary outcome is the feasibility of a subsequent phase III trial RCT according to pre-specified progression criteria. We are primarily interested in whether:

- the trial is appealing to participants (assessed by the recruitment rate)
- the PHOENIx intervention is acceptable (measured by adherence)
- we are able to collect routine data required to evaluate the effectiveness of the intervention

We will also evaluate:

- the recruitment and randomisation processes
- the effect of the intervention on outcomes listed

The data collected will be used to review the sample size assumptions for the definitive trial to be conducted in the future.

**Process outcome measures**

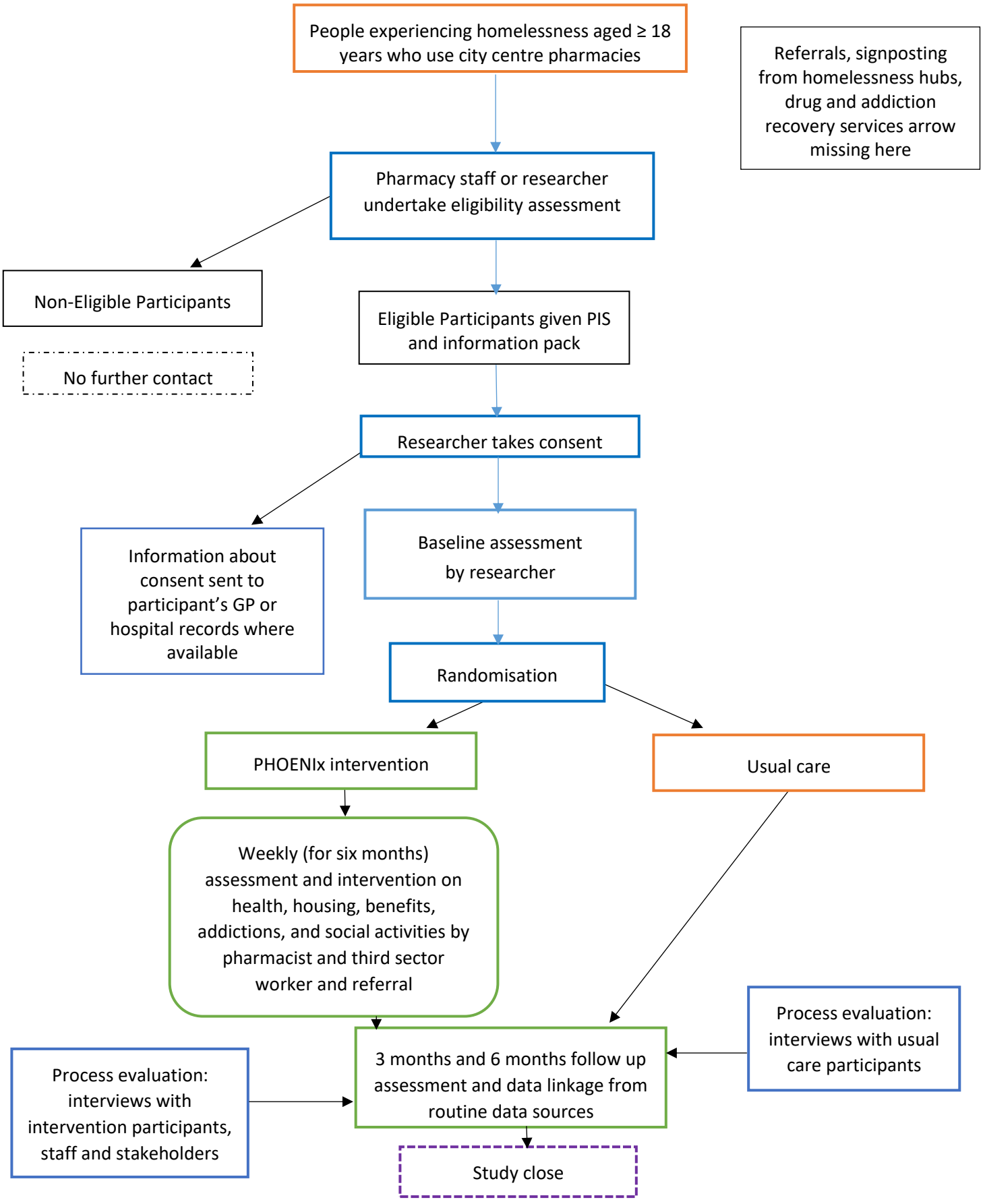
Data will be collected on outcome measures that would be collected in a definitive RCT to ensure that there are no issues with the completion of these measures in preparation for the main trial. We will objectively assess the following:

- Recruitment
- Retention
- Intervention adherence
- Routine data collection
- Proportion of patient reported outcomes collected
- Proportion of economic data collected

Data in relation to clinical, social and patient reported outcomes will also be collected. These will include:

- health services utilisation
- social care outcomes (such as housing and level of debt)
- patient reported measures (including intervention acceptability and quality of life)

- **TRIAL SCHEMA**



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# 1. BACKGROUND AND RATIONALE

## 1.1 Background

Persons experiencing homelessness (PEH), including rooflessness, houselessness, insecure or inadequate housing, face up to 12 times higher mortality rates than the general population. Most PEH tend to be in their late 30s, but on average, they have seven different health problems, on a par with people aged 85 years living in their own homes. They die at an average age of 45 years. PEH have complex health needs including acute and long-term physical ill health, mental ill health and problem poly-substance use. Social care needs include stable and safe housing, purposeful daily work related activity, and help in navigating the complex benefits system to secure means for daily living. PEH can be overwhelmed by such multiple, complex health and social care needs and may have few trusting and supportive relationships. PEH often do not find services configured to cope with their complex needs, requiring multiple visits over time to different services often in different locations. They can also have fluctuating motivation (drug use, mental health and physical health problems, prioritising safety and housing are contributory), and low health literacy, making it difficult to navigate different services in primary care. PEH therefore often have more frequent attendance at hospital Emergency Departments.

Assertive outreach is a recognised way to engage and support PEH rather than offering services in traditional health service settings. The importance of assertive outreach has been further recognised as a result of the COVID-19 pandemic and the approach is known to engage, assess, address and improve the complex health and social care problems of PEH. Within this context, we have mapped and modelled a complex intervention for PEH utilising pharmacist prescribers undertaking assertive outreach services, in partnership with third sector homelessness charity outreach workers.

This study is informed by delivering care to PEH as part of the **P**harmacy **H**omeless **O**utreach **E**ngagement **N**on-medical **I**ndependent prescriber R**x**: PHOENIx service, currently operating in Glasgow, where it is funded in the short term. The study is also built on our previous descriptive studies [1-3], and our qualitative studies incorporating the views of PEH [4-8] and stakeholders, including service commissioners, healthcare professionals and public health bodies [9]. It is well known that good health requires a multidimensional approach including safe housing, purposeful activity, and money, in addition to nutrition, and accessible comprehensive, co-ordinated health care [10]. Supportive relationships are also important. PEH unfortunately often have few, if any of these pre-requisites. This research provides the opportunity to consider health and social inequalities through an innovative outreach intervention.

Prescribing remains an important component of the PHOENIx service, as many PEH benefit from medical treatment on the spot. If prescribing is undertaken, PEH are most likely to take the first dose of their medicine in the pharmacy (and this is particularly true for antibiotics or inhalers for breathing problems). Our previous qualitative studies suggest that the process of collecting a prescription can also be challenging for PEH [7]. Follow up consultations help build therapeutic relationships and provide continuity of care until the patient is ready to trust and engage with mainstream care. Follow up is facilitated as patients tend to visit the pharmacy for repeat supplies. If they do not return, the pharmacist (and third sector worker who has extended networks on the street) can outreach the patient and ask them to return, with the aim of minimising dropout.

**Previous relevant studies by the research team**

In our exploratory study of 124 PEH in Glasgow in 2015/6, 43% had a new medicine prescribed, 8% had a medicine discontinued and 28% had other changes to their prescribing, with one third having

tests or other diagnostic workup, and one third of PEH were referred onto other services [2]. In another study involving 52 PEH in 2017, the PHOENIx intervention team visited PEH in streets and low threshold venues e.g. homeless shelters, soup kitchens [1]. Pharmacists provided pop-up, drop-in (no appointment needed) health clinics to various homeless support venues in Glasgow City Centre. The intervention led to medications being prescribed by pharmacists in 62% of all PEH, of which over 60% were new medications. New clinical issues were identified in 69% of PEH. More importantly, this exploratory study showed improvement in PEH engagement, with 85% subsequently attending either a follow-up appointment with the pharmacist or another referred service [1].

Qualitative evaluation of the PHOENIx service demonstrated that participants appreciated the time taken by the pharmacist and the third sector Homelessness Charity (Simon Community Scotland) worker [11,12]. Participants described that the service was able to help them overcome many of the barriers to accessing healthcare they experience, including stigma, discrimination and impaired mobility, and increased motivation for self-care and health seeking behaviour [11,12]. The PHOENIx service enabled immediate diagnosis and prescription of medication, and improvements in health outcomes were described by participants. Improvement in knowledge and understanding of their health issues, impact of illicit drug use on long-term health, and the side effects of prescribed medication were also described.

We found more evidence for the merits of the PHOENIx approach through our qualitative studies with participants and staff involved in the frontline delivery of services [11-13] and from stakeholder engagement events held in Birmingham [10]. Qualitative findings suggested that the interventions facilitated PEH access to healthcare, enabled immediate diagnosis and treatment and motivated participants to address their healthcare needs.

A further feasibility study using a non-randomised design comparing the PHOENIx intervention to a control group, was undertaken in Glasgow. [14] The PHOENIx intervention included pharmacist and a third sector homeless charity workers undertaking assessment of physical/mental health, addictions, housing, benefits and social activities followed by pharmacist prescribing with referral to other health service specialities as necessary Participants were PEH referred to the PHOENIx team at the point of hospital discharge. Findings of the PHOENIx feasibility study were comparable to previous results [1, 2], with new clinical issues being identified and offered treatment. The intervention was able to promote engagement with services with 67% of intervention group participants and 25% of the usual care group attending scheduled outpatient appointments. Findings led to the current planned multicentre RCT.

**Why test the intervention in community pharmacy?**

Participants in public engagement and previous research have suggested that interaction in community pharmacies is limited to medicines/items supply. Within the planned formal local care pathway framework, the PHOENIx intervention will better utilise an untapped NHS resource, given workforce shortages among doctors and nurses.

Accessing healthcare in a venue located in the city centre, sometimes a few steps away from where PEH live and sleep, without the need for an appointment; or to complete registration documents (often difficult for many PEH because of low levels of literacy), often without the need to wait, is something that PEH value. Currently, most General Practitioner (GP) and Nurse Consultations in

general practices are by appointment, on the telephone or via videoconferencing. This community pharmacy-based PHOENIx intervention aims to address PEH barriers to accessing health services as community pharmacies are used routinely by PEH. If this pilot study shows a signal in improvement in health outcomes, community pharmacists (who have the skills and knowledge to deliver the stated roles) with third sector input, can deliver the intervention.

**Wider literature**

Findings from our feasibility studies described above resonated with a study in the US involving a clinical pharmacist intervention on PEH health education [15]. Two other studies, from the Republic of Ireland [16] and North America [17], included pharmacist led clinical review of PEH residents in temporary accommodation which identified under- and potentially inappropriate prescribing, particularly in those with diagnosed mental illnesses. In these studies, referrals for social care input had to be frequently made by pharmacists as they were unavailable on site contrary to the structure of the proposed PHOENIx model which includes third sector homelessness support organisation workers who undertake these roles on the spot. A retrospective pre-post quasi-experimental study conducted in the US [18] evaluated the impact of clinical pharmacy services on health outcomes and medication adherence (focussing on hypertension and diabetes in PEH). Intervention led to an increase in the number of PEH meeting blood pressure and HbA1c goals. No comparator group was used, and the intervention was not delivered in a community pharmacy [18].

### 1.2. Trial rationale

The policy, practice and previous research identified through literature review informed the design of the proposed pilot trial. Our search of the research databases (Medline, PubMed, EMBASE and PyschInfo) using Medical Subject Headings and keywords such as ‘homelessness’, ‘homeless’, rough sleepers’, ‘street dwellers’, ‘pharmacy’, ‘pharmacist’, ‘clinical pharmacy services’, ‘community pharmacy’, and ‘social worker’ identified no published or unpublished RCTs which considered pharmacist-led support for PEH in a community pharmacy setting. Non-randomised studies assessing interventions targeted at PEH that included a main or supporting role of pharmacists as part of a multidisciplinary care team in non-community pharmacy primary care settings were identified. Of these, two studies included joint participation of a pharmacist and social worker in the intervention delivery [19,20]. Community pharmacists have shown readiness to take on further roles in supporting the health needs of PEH; 90% (n=321) of respondents in our survey undertaken in 2016/17 of community pharmacy from across England and Scotland would prefer to have further involvement in supporting PEH with health and social issues, if an evidenced-based local care pathway was available to support their input, such as the system of care we aim to test in this study [21].

The inclusion of clinical pharmacists in the primary care team is embedded in the NHS primary care framework and practice models [22], and has been shown to improve: appointment access; medication adherence; patients’ understanding of long term conditions; minimising illicit opioid use; and establishment of good quality networks with community pharmacy [23]. A systematic review of international literature corroborates these findings [24]. Approximately 7500 (of 56,000) pharmacists in the UK are qualified independent prescribers allowing them to diagnose medical conditions, prescribe medicines and make referrals. While many pharmacists in general practices have been undertaking prescribing roles, currently there is a lack of opportunities in community

pharmacy for pharmacist independent prescribers to utilise their skills. Innovative service models targeting patient groups in need of support, who can access community pharmacies, are needed to utilise their skills further. Previously in the UK, interventions have involved homeless healthcare teams based in hospitals [25]. Our previous systematic review supports the model of integrated health and social care service provision for PEH [26]. These published reviews, however, demonstrate lack of interventions based in community pharmacy.

National policy documents underscore the need for innovation in health care delivery for PEH and many of the principles are part of the PHOENIx intervention [27,28]. The proposed PHOENIx model supports current strategic priorities for inclusion of health and health equity in the NHS and local government, including further prioritisation of the health of PEH and co-occurring disorders in the context of the current pandemic [29] and the crucial role community pharmacy has to play in promoting health, wellbeing and prevention, given their broad expertise, accessibility and knowledge of their communities [30]. The research also promotes the important principle of personalisation and personalised care which enables people to have choice and control over the way their care is planned and delivered based on 'what matters' to them and their individual strengths and needs [31]. The methods advocated here also complement social prescribing, a key component of universal personalised care [32]. In social prescribing, link workers give people time, focusing on 'what matters to them' and taking a holistic approach to people's health and wellbeing. They connect people to community groups and statutory services for practical and emotional support. Link workers also support existing community groups to be accessible and sustainable, and help people to start new groups, working collaboratively with all local partners [33].

*Problem drug use and mortality in context*

In Glasgow, the number of drug related deaths among PEH compared with those for people in mainstream Scottish society, are very high in comparison with the rest of the UK and other high income countries [34]. In England and Wales, there were an estimated 778 deaths of PEH in 2019, an increase of 7.2% from the previous years; approximately two thirds of these deaths were attributed to drug poisoning [35]. The root causes of drug related deaths are most strongly correlated with poverty and deprivation; with homelessness being an indicator of the most severe and multiple disadvantage [35]. Ninety four percent of overdose deaths in Scotland [34] and over 50% in England [36] were in people who had taken more than one substance with opioids contributing to the majority of the deaths. However, many of these deaths are preventable if people with problem substance use are engaged in care and started on treatment using a wide range of engagement settings. Other important causes of deaths amongst PEH include accidents, respiratory infections, suicides / self-harm [37] much of which are preventable if PEH can access appropriate care when needed.

*Prevalence of homelessness*

PEH have poor health and 12 times higher mortality rates than the general population [38]. There are an estimated 250,000 [39] and 29,000 [40] PEH in England and Scotland respectively; with a sharp rise in rough sleeping over recent years [41]. While housing PEH has been a high priority at Government and local authority level during the COVID-19 pandemic, Government departments expect homelessness to be an important societal challenge for the foreseeable future [42].

*Unmet, escalating health needs*

Our previous epidemiological studies with PEH [42-44] and published systematic review [38] show a high prevalence of long-term health conditions, infections and multi-morbidity (presence of 2 or more chronic conditions) in PEH. Severe and untreated mental health problems and substance and alcohol misuse can be a cause and a consequence of homelessness.

*Low engagement in current care pathways*

Our work shows PEH experience difficulty registering at a general practice [26, 27], find services inflexible to their requirements [4-7], and hence are known to visit Emergency Departments six times more often than mainstream populations; drug and alcohol related problems are amongst the leading causes of attendance. In the Emergency Department, PEH are 12 times more likely to die compared to the general population [45]. Non-attendance at appointments is common among PEH, and 'missingness' is associated with higher mortality [46].

*Potential for community pharmacy-based intervention*

PEH regularly visit pharmacies in city centres for care and treatment e.g. acute and repeat prescription collection, needle exchange, opioid substitution therapy, and more could be done to utilise this window of opportunity [11, 21].

A community pharmacy-based model therefore offers PEH the opportunity to access low threshold enhanced care including prescribing from a PHOENIx pharmacist working in their community pharmacy, located in the city centre streets well known to PEH, without an appointment. Work to date shows that the PHOENIx intervention offers help with care that lies outside the main health domain e.g. benefits maximisation, social prescribing leading to volunteering roles in the community such as fixing bikes, but nevertheless is important to enable PEH to function, feel safe and recover. These pre-requisites to better health include adequate housing, benefits, and a wide range of opportunities for meaningful activity. Health interventions can include immediate referral to mental health teams for suicide prevention and follow up. Having a range of local experts on speed dial, for immediate advice, and including the participant's GP is important.

*Assertive 'sticky' follow up to maximise engagement*

One challenge with PEH is engagement in their care because many PEH find that services are not designed to meet their needs. Frontline service providers report that PEH often find it difficult to navigate services and appointment systems. Frontline third sector agencies offer assertive outreach to drop-in services and visit temporary homeless accommodation. Third sector homeless staff often have strong working relationships with PEH, providing housing, food, clothing support, advocacy, benefits and advice. Unlike previous interventions that have been delivered by healthcare professionals and/or included step down accommodation [25, 47] targeting patients discharged from hospital, this intervention will be based in the community, and aims to prevent deterioration in health to the point of Emergency Department visits. However, third sector staff operate separately and cannot readily share records with the health service, therefore, opportunities to capitalise on 'windows of opportunity' for PEH who have fluctuating motivation to engage, are missed. In the health service, assertive outreach to assess and comprehensively address multiple complex health and social care needs, is patchy. Therefore, we have partnered third sector charity staff teams with

NHS pharmacists to offer a one stop shop for health and social care needs, in city centre community pharmacies, to have those joined up health conversations and make every contact count [48].

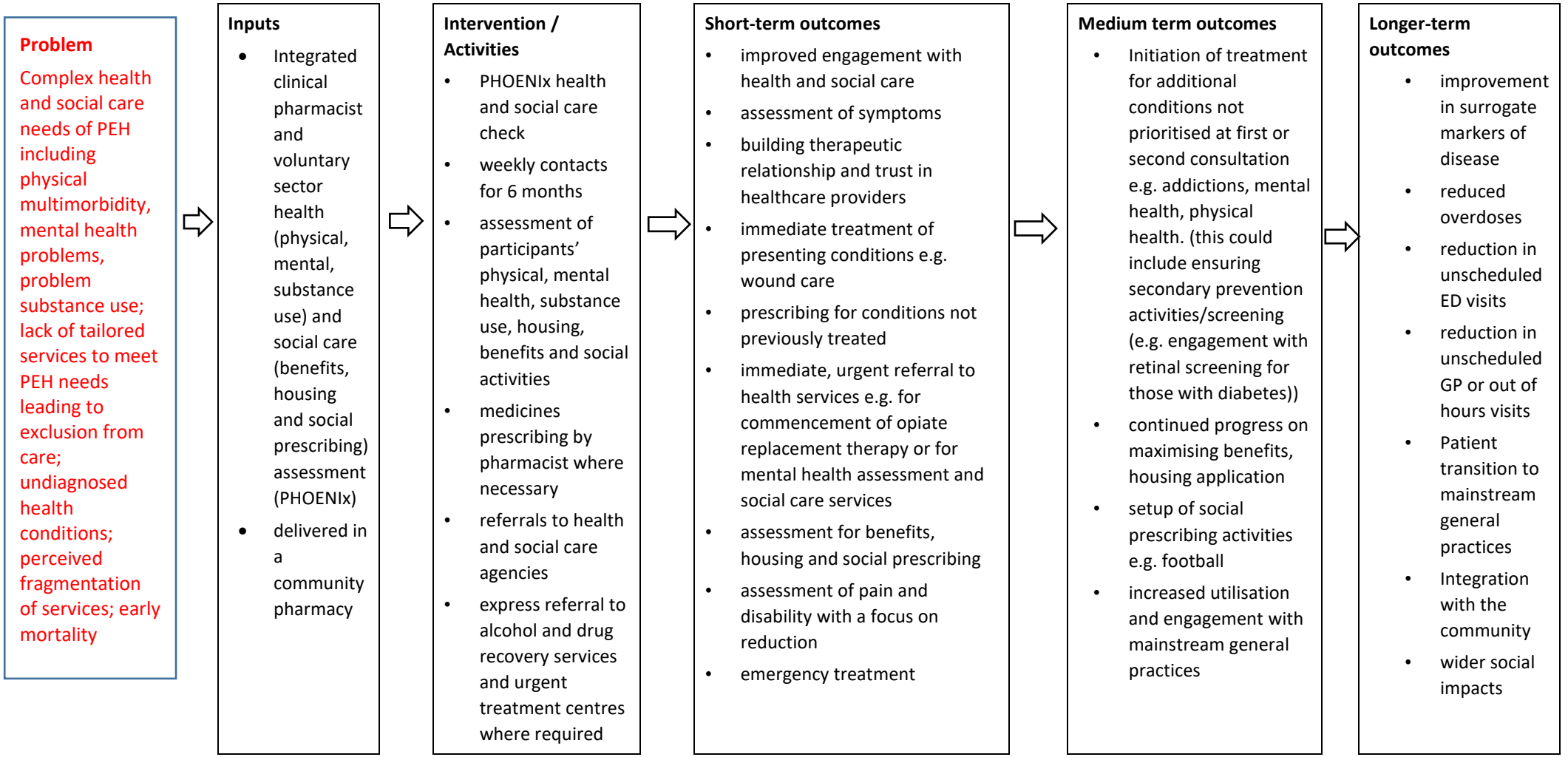
*Clinical governance*

Support is fully integrated with existing NHS care providers, the PHOENIx team are connected through remote access, to the respective Homelessness Services, GP practices (which provides the clinical governance framework) and to alcohol and drug recovery teams and hospital records, to enable co-ordinated care. Governance arrangements with the respective GP practices enable shared clinical records, participation in monthly clinical meetings and checking in with GPs for clinical queries ensures clinical oversight and safe prescribing.

There is a paucity of robustly designed prospective evaluations of models of care to address the health needs of PEH in any setting. Previous research has explored clinically and housing-led services for homeless people being discharged from hospital (including step-down accommodation) [47], but the effects of routine, community-based interventions may even help prevent admissions in the first place. This proposed pilot study will test a community pharmacy-based intervention involving clinical pharmacists and third sector homelessness charity workers.

Logic model describing the problem, inputs, proposed intervention and activities and outcomes are shown in figure 1.

**Figure 1: Logic model: PHOENIx community pharmacy based randomised controlled pilot trial**



**Potential moderators of intervention effect:** social circumstances, age, gender, underlying health conditions including problem substance use/mental health conditions.

**Potential mediators of effect:** intervention fidelity, Normalization Process Theory constructs (Coherence (sense making); cognitive participation (engagement with intervention), collective action (confidence/acceptability of intervention/workability)); reflexive monitoring (appraisal/individual specification and reconfiguration).
**ED:** Emergency department; **GP:** General practitioners; **PEH**: Persons experiencing homelessness; **PHOENIx**: Pharmacy Homeless Outreach Engagement Non-medical Independent prescribing Rx

### 1.2.1. Justification for participant population

PEH have complex health and social care needs. They have seven different health problems on average and most die in their early 40s. PEH readily access community pharmacies, but community pharmacies are not formally integrated in care pathways involving case finding, assessment, treatment, or referral.

### 1.2.2. Justification for design

Randomised controlled trials generate results that are considered to be the most valued data in the era of evidence-based practice. The underlying clinical service need driving this research project is to find out whether the proposed complex PHOENIx intervention improves outcomes in addition to usual primary health and social care. The clinical and economic impact, and the acceptability of complex interventions in comparison to usual care are best tested through a definitive RCT, with embedded economic and process evaluation, that has been preceded by a feasibility trial and then a pilot trial.

Therefore we propose a multicentre pilot RCT in advance of a definitive trial.

### 1.2.3. Justification for choice of intervention(s)

The active group intervention will be a composite of health (pharmacist) and third sector (homeless outreach worker) assertive outreach to people who are homeless and present to a community pharmacy. Given the requirement to evaluate whether this intervention in addition to usual care is beneficial, and as the comparator group cannot be denied usual care, the preferred comparator group intervention is usual care. Usual care is characterised by the range of services accessed and offered to participants who are homeless in Glasgow and Birmingham respectively.

### 1.2.4. Justification of choice of primary outcome(s)

Given this is a pilot study of a complex intervention, we have clinical, process, economic and health service utilisations, and social care outcomes. Our primary outcome is guided by established recommendations on the stages of complex intervention testing in particular (MRC guidance). Selection strategy for the primary outcome for a definitive trial will be informed by our answers to the objectives: patient/professional perceptions of the trial procedures including the outcomes; effect and sample sizes needed for possible outcomes e.g. Emergency Department visits; and estimates of outcome variability. Patient and Public Involvement (PPI) representatives will also be asked for their view on the choice of primary outcome for the main trial.

# 2. AIMS AND OBJECTIVES

## 2.1. Aim

To test the hypothesis that a pilot study of the PHOENIx intervention shows merit in progression to a definitive randomised controlled trial.

### 2.2. Trial objectives

Our objective is to undertake a pilot RCT to assess the feasibility of conducting a larger, definitive trial assessing an integrated clinical pharmacist / homeless third sector intervention (PHOENIx) delivered in a community pharmacy setting.

We aim to:

1. Determine recruitment and retention rates across community pharmacy sites

2. Measure intervention fidelity by PHOENIx team (weekly contacts with participants; assessment and intervention for health including mental health, physical health and problem substance use; housing; benefits and social activities) and intervention adherence by participants (uptake of recommendations).

3. Determine the event rates for outcomes proposed for the main trial (number of, and time to scheduled and unscheduled health care contacts; uptake and retention of treatment for problem substance use and other conditions; non-fatal overdoses; evidence-based treatment of physical health and mental health problems), and estimates of their variability.

#### 2.2.1. Economic objectives

4. To explore whether relevant resource use and health state utility data (as a proxy for quality of life) can be identified, measured and valued appropriately for the purposes of conducting a full economic evaluation in a definitive trial.

#### 2.2.2. Qualitative objectives

5. To evaluate the acceptability of randomisation and adherence with data collection procedures.

6. To explore participant and healthcare professional perceptions of the intervention and acceptability of trial procedures.

7. To explore participant, healthcare professional and stakeholder views of the likely facilitators and barriers to future implementation of the intervention as a form of routine service delivery.

## 3. TRIAL DESIGN AND SETTING

### 3.1. Trial design

A randomised, multicentre, open, parallel group external pilot trial with parallel economic and qualitative process evaluation.

### 3.2. Trial setting

Glasgow and Birmingham city centre community pharmacies. Participating pharmacies will be located in parts of Glasgow and Birmingham city centre and immediate surrounding areas, where PEH are known to frequent. This limits our selection of pharmacies but both cities are big enough to offer a choice of locations, whether independent or multiple chain ownership pharmacies. Backup sites (other community pharmacies) will be asked to participate in the event that recruitment is slow in the each of the four main community pharmacies, during the first two weeks.

### 3.3. Sub-studies

*Economic evaluation*

All health, social care and personal resource use data will be identified, measured and valued. We will explore the possibility of an economic evaluation incorporating a wider societal (or at least public service perspective) in line with the work already conducted to establish broader costs and benefits beyond the NHS [47]. We will explore the ability to use the EQ-5D-5L [49] among PEH and if necessary other outcome measures where it is not possible to use the EQ-5D-5L. Data passed to the economic analysis team (NHS Healthcare Improvement Scotland) will be anonymised.

*Qualitative evaluation*

We will undertake semi-structured interviews with a purposive sample of 15-20 participants in the trial (including both intervention and control participants), 7-10 health professionals and approximately 10 stakeholders including commissioners/senior health board/ homelessness services policy makers and representatives from volunteer sectors, in order to explore their views on the trial methods and barriers and facilitators to future implementation.

We will use Normalisation Process Theory as our underpinning theoretical framework to help us conceptualise implementation issues and the effects of the intervention on the interplay between patient capacity and self-management workload which will help us refine our preliminary logic models in relation to the intervention. Interviews will be audiotaped with participant consent and transcribed to provide data for qualitative analysis.

The qualitative researchers (employed by Glasgow University) will regularly check the information entered onto the participant's care plan/clinical record by the pharmacist and compare these data against a checklist of the components of the intervention: physical health; mental health; addictions; housing; debt; and social activities. This will be used to provide iterative feedback to the intervention team to ensure fidelity and optimise delivery of the intervention, and in addition, will address intervention fidelity.

### 3.4. Assessment of risk

All clinical trials can be considered to involve an element of risk and in accordance with the Birmingham Clinical Trials Unit (BCTU) standard operating procedures this trial has been risk assessed to clarify any risks relating uniquely to this trial beyond that associated with usual care. A Risk Assessment has been conducted and concluded that this trial corresponds to the following categorisation:

Type A = No higher than the risk of standard medical care

## 4. ELIGIBILITY

### 4.1. Inclusion criteria

Adults ≥18 years and experiencing homelessness, who are attending or service users of one of the designated community pharmacies and able to provide informed consent as per the Health Research Authority (HRA) guidance on continued capacity [51].

Homelessness will cover rooflessness, houselessness, insecure or inadequate housing as per the ETHOS typology [50].

These criteria include:

- people staying in homeless shelters;
- rough sleepers;
- people staying in temporary accommodation such as bed and breakfasts (B&Bs), hostels, squats; or those sofa surfing between family and friends' houses.

### 4.2. Exclusion Criteria

- PEH living in accommodation with 24-hour support which includes in house medical care;
- Intoxicated or (in the opinion of the researcher) posing a safety risk to staff and lacking capacity to consent

### 4.3. Co-enrolment

Co-enrolment is only allowed for non-interventional studies, such as cohort studies.

## 5. CONSENT

It is recognised that a proportion of the target population have conditions that may impair their capacity to provide informed consent e.g. severe mental illness, learning disability, intoxication or any other condition causing confusion or loss of cognitive decision-making capacity. Researchers consenting the participants will be experienced in the field of mental health, substance misuse and/or homelessness research or are likely to be experienced healthcare professionals e.g. qualified nurses, or pharmacy technicians, and will use their clinical judgement and Registered General Nurse / Technician standards of practice to adhere to The Mental Capacity Act 2005 (England) and Section 51 of the Adults with Incapacity (Scotland) Act 2000 in identifying and excluding those individuals who may lack capacity to consent for themselves or who are under the influence of illicit substances, in recruiting for this pilot trial. As per the HRA guidelines, it will be the primary responsibility of the researcher (and in consultation with the CIs or community pharmacist where necessary) to assess the capacity to consent eligible persons by considering their ability to understand the information relevant to the decision, retain the information and use or weigh the information and communicate his or her decision (by any means) [51]. Like the general population, PEH presenting to the Community Pharmacy will be there for a reason, and that reason will generally be for prescription collection, request for help with their health, or to purchase goods to improve health. This suggests PEH with the potential to participate in the study will not be likely to have a significant impairment of, or a disturbance in the functioning of their mind or brain which makes consent problematic. If a patient has managed to attend the pharmacy for collection of medicines and answers to the community pharmacist when asked to present with their name and housing status (the norm during a transaction in the pharmacy), then this will suggest capacity is intact. This is an assessment that community pharmacists are used to making in their daily interactions with this population who tend to be their regular customers.

Consent will be sought from the PEH for both the main trial and the qualitative process evaluation at the same time. Informed consent will be obtained from staff delivering the interventions and stakeholders, to record qualitative interviews. All team members taking consent will have adequate training.

Given the high overlap between homelessness and substance misuse/severe mental health, research staff will be provided with training to help them manage and diffuse any perceived untoward behaviour from prospective participants during the recruitment process in the pharmacy.

The researchers will also assess continued capacity to consent during follow up visits as we acknowledge that health conditions of those affected by substance abuse and/or severe mental health can quickly fluctuate. Researchers will assess continued capacity based on their experience and training, The Mental Capacity Act 2005 (England) and Section 51 of the Adults with Incapacity (Scotland) Act 2000. Anyone assessed as permanently lacking capacity to consent at any time point will be withdrawn from the trial, but their data collected up to that point will be retained.

It is the responsibility of the Principal Investigator (PI) to obtain written informed consent for each participant prior to performing any trial related procedures. If the patient cannot read or write or has forgotten their reading glasses, the patient information and consent materials will be read to them by the researcher or pharmacy staff in the pharmacy. The consent conversation will be documented in the participants' notes and the consent form will be annotated to confirm the researcher completed it on behalf of the patient. The form can be initialled or thumb printed. This task can be delegated by the PI to other members of the local research team, if this responsibility has been documented in the site signature and delegation log.

A Participant Information Sheet (PIS) will be provided to facilitate this process. The PI or delegate will ensure that they adequately explain the aim of the trial, the trial intervention, and the anticipated benefits of taking part in the trial to the participant. They will also explain that participation is voluntary and that the participant is free to decide whether or not to take part and may withdraw from the trial at any time. The participant will be given sufficient time to read the PIS and to discuss their participation with others outside of the site research team. If they cannot read, the researcher will verbally explain the study to them. The participant will be given the opportunity to ask questions. If the participant then expresses an interest in participating in the trial, they will be asked to sign and date the latest version of the ICF. The PI or delegate will then sign and date the ICF. A copy of the ICF will be offered to the participant along with an alternative option to securely store it at the pharmacy on their behalf if they have no secure location to store it, a copy will be filed in the participant's GP and/or other medical notes and the original placed in the Investigator Site File (ISF). Once the participant is entered into the trial, the participant's trial number will be entered on the ICF maintained in the ISF. In addition, the participant understands and acknowledges that, a copy of the signed ICF will be securely transferred to the trial team at BCTU for review and storage.

Details of the informed consent discussions will be recorded in the participant's GP's medical notes where available (some participants may not have a registered GP in which case the participants will be referred to be registered with the homelessness general practice service in Birmingham and Glasgow). In addition to all details of consent being sent to BCTU by the research team, written records of the consent conversations will also be stored in participant files at NHS Glasgow and Clyde and NHS Birmingham and Solihull Mental Health Foundations Trust. Researchers will also

communicate consent information to the patient's addictions team, and in the patient's hospital record where possible.

Written consent conversations will include date of discussion, the name of the trial, summary of discussion, version number of the PIS given to participant, version number of ICF signed and date consent received. Where consent is obtained on the same day that the trial related assessments are due to start, a note should be made in any available medical notes as to what time the consent was obtained and what time the procedures started.

At each visit by the researcher, the participant's willingness to continue in the trial will be ascertained and documented within the trial case report forms (CRFs). 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 provided. 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 they will be re-consented. Re-consent will be documented in the GP medical notes and/or alternative location as detailed above. The participant's right to withdraw from the trial will remain.

Electronic copies of the PIS and ICF will be available from the Trial Office and will be printed or photocopied onto the headed paper of the local institution. The ICF also contains additional statements for the participant to acknowledge that they understand that the Trial Office will, as part of the trial, collect participant data available in NHS routine clinical datasets, including primary care data (e.g., GP records, Scottish Ambulance Service call outs, Clinical Practice Research Datalink, The Health Improvement Network, QResearch and secondary care data through NHS Digital and other central UK NHS bodies. The participant will acknowledge that they understand that the Trial Office might send their name, any address of temporary accommodation, date of birth and NHS or Community Health Index number or any other identifier data available to the relevant national registry, and then for the national registry to link this to their data and send the information back to the Trial Office. The trial staff will have access to this data for the duration of the trial to enable data linkage. The acknowledgement by the participant will also allow access to other new central UK NHS databases that will appear in the future.

# 6. ENROLMENT, RANDOMISATION and BLINDING

## 6.1. Identification

PEH attending or who are users of participating Glasgow and Birmingham pharmacies will be approached by their care team (including but not limited to community pharmacists, addictions team), who will signpost them to the researcher in the pharmacy who can offer clients the study information or draw their attention to a poster in the pharmacy. Eligible participants will therefore meet the study researcher on site and receive the study information or if they cannot read, the researcher will verbally explain the study to them. In addition, pharmacy staff who know the patient to be homeless, can pass study information to them via an invitation pack, explain the study to them and refer any potentially eligible persons to the researchers. Posters and flyers advertising the study will be displayed in pharmacies, homeless charities, drug and alcohol services and temporary accommodations.

SIFA Fireside, Simon Community, Trident Reach or other third sector homelessness support organisations will also promote the study to their client base by speaking with patients or drawing their attention to posters displayed in the homeless hubs (located in Glasgow and Birmingham city centres respectively). Other health and social care services will disseminate the study through this same approach, and staff working in other services will be asked to signpost or refer patients to the pharmacy for consideration of participation in the study. Potential participants can return at a later date if more time is requested to decide on study participation.

### 6.2. Screening and enrolment

Information on the number of patients who enquire about the trial will be recorded on the PHOENIx Participant Screening/Enrolment Log which will be kept in the ISF, and should be available to be sent to the Trials Office upon request. The PHOENIx researcher, as delegated on the site signature and delegation log, will confirm study eligibility with potential participants after they have been signposted to the research team via the direct care team. The contractor pharmacist and researcher may work together to confirm eligibility prior to randomisation.

### 6.3. Randomisation

The local research team should add the participant to the PHOENIx Participant Recruitment and Identification Log which links participants with their Registration/Trial Number. The PHOENIx Participant Recruitment and Identification Log should be held in strict confidence. Randomisation will be provided by BCTU. The researcher will contact the randomisation line at BCTU by telephone. BCTU will ask a few questions to the researcher which they will record on the randomisation notepad. They will then confirm the participant's allocation and trial number (TNO) to the researcher over the phone and this will also be recorded on the randomisation notepad and database. A confirmation email of the allocation and TNO will be sent to the PI, CI and trial mailbox. Someone from BCTU should be available to take randomisation calls 8 hours a day, 5 days a week, apart from short periods of scheduled maintenance of the database, Monday to Friday, 09:00 to 17:00 UK time, except for bank holidays, government guided closures and University of Birmingham closed days.

#### Randomisation method

Participants will be randomised at the level of the individual in a 1:1 ratio to either intervention or usual care. The randomisation list will be generated by an independent statistician at BCTU and will stratify by recruiting city (Glasgow or Birmingham), using permuted blocks of varying lengths.

### 6.4. Blinding

This will be an open trial design. It will not be possible to blind the participant or pharmacist/third sector worker due to the nature of the intervention. It will also not be possible to blind researchers at Birmingham or Glasgow delivering assessments as they will give the participant their allocation (Intervention or usual care) and the same researchers will be following up participants at 3 and 6 months.

### 6.5. Informing the participant's GP and other parties

If the participant has a GP and has agreed, then the participant's GP should be notified that they are in PHOENIx trial, using the PHOENIx GP Letter. If the participant is under the care of an addictions team then they will also be notified, via the PHOENIx Notification of participation letter.

## 7. TRIAL INTERVENTION

### 7.1. Trial intervention content

#### Intervention content

In addition to the usual care, PHOENIx intervention will involve a structured face to face health and social care check [18] involving the participant, pharmacist and SIFA Fireside, Simon Community, Trident Reach or other third sector homelessness support worker in the pharmacy or other venue. The consultation involves the pharmacist assessing physical, mental and problem drug use which includes any relevant near patient tests and/or clinical examination in a face-to-face setting. Full harm reduction interventions will be offered including: Injecting Equipment Provision, foils, Naloxone, sign posting to services to conduct a Dry Blood Spot Test for blood borne viruses, are offered as standard. The third sector homelessness support organisation worker address housing, benefits, advocacy and social prescribing.

Homelessness support worker asks about benefits, debt, accommodation and social activities. Following completion of the health and social check, the participant identifies their priorities for action, and the team work through these one at a time. Actions arising from the consultation are implemented over the subsequent weeks, again during face-to-face consultations. Prescribing is one component of our intervention undertaken where needed after a full health assessment. Any prescribing activities by the pharmacist will follow established clinical guidelines from National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN) or local clinical guidelines or professional societies as appropriate. Referral to other services follows established, immediate referral pathways for conditions requiring specialist input, e.g. for mental health crisis presentations.

Both the pharmacist and support worker will be working in line with their normal practice and guidelines. Pharmacist independent prescribers will prescribe as normal within standard care.

Where it is legally required to do so, all potential participants will be required to complete a COVID screen at all visits prior to the visit commencing. If the screen is failed, the visit can be rescheduled for a future date. The following questions will be asked;

- do you or any person in your accommodation have a recent onset of: a new continuous cough or fever or loss of/change in taste or smell

- do you have any of these other symptoms; fatigue; sputum; shortness of breath; muscle aches; sore throat;

headache; chills; nasal congestion; nausea; diarrhoea;

- have you been in contact with anyone else who has symptoms of covid-19 or have you been self isolating over the last 7 days

- is anyone in your accommodation in the vulnerable covid-19 group and/or shielding

- are you in agreement that we should go ahead with face to face consultation

Uptake of health and social care interventions will be maximised, and dropout minimised, through assertive outreach by the third sector charity worker to find participants in case of non- attendance at the pharmacy.

#### Duration

Based on our experience in the feasibility work, it will take approximately one hour for each consultation. The intervention period begins with the first consultation and will continue weekly during the study for up to 6 months if the participant and PHOENIx team think it is beneficial. Throughout the intervention the patient will continue to engage with mainstream care. When the

intervention period finishes, the participant will return to receiving usual care alone. It will be stressed to the patient at recruitment, and during the intervention, that the PHOENIx input is fixed term, temporary, in addition to usual care, and is not a substitute for usual care.

### Frequency

The participant will agree a flexible schedule of visits at the first consultation with the pharmacist and the third sector homelessness support worker, but will re-present as and when they feel able, aiming for weekly (more or less often as required) contacts. While each patient will be offered 6 months of support, the frequency and duration of intervention will be tailored to the participant's needs.

After each researcher visit, the participant will receive a £10 shopping voucher as a token of appreciation for their participation.

### Location

In the pharmacy's private consultation room. Based on the participant's preferences and ability to visit pharmacies, some visits can also happen as outreach in temporary accommodations, homeless hubs or community centres.

### Staff delivering the intervention

Pharmacists working on this trial will be employed by their respective NHS trust. Staff will be experienced pharmacist independent prescribers employed by NHS Greater Glasgow and Clyde, and Birmingham and Solihull Mental Health Foundations Trust; and experienced SIFA Fireside, Simon Community, Trident Reach or other third sector homelessness workers from respective organisations. Where legally required to do so, personal protective equipment (PPE) will be worn by all research staff interacting with participants during their time in the trial. The intervention will always be delivered by the Pharmacist and third sector outreach worker in pairs, so that there is no lone working.

### Usual care

Participants allocated to usual care will not receive consultations from the PHOENIx team in the pharmacy or in any other venue, throughout the duration of the intervention phase. If allocated to usual care, the researcher will signpost or refer the participant should they identify urgent health care needs e.g. overdose, or likely infected venous leg ulcer needing dressing, during assessment. Consultations (frequency, location) with health and social care for usual care participants will be collected by researchers.

In both intervention and usual care groups, participants continue to obtain and seek care, treatment or help as usual. Both groups will have the same assessments. Bias is possible, although unavoidable, through signposting the usual care group to Emergency Department by the researcher (after conducting follow up assessments) or to other health and social care staff.

## 7.2. Continuation of intervention after the trial

It is likely that there will be no continuation of the intervention in Birmingham after the trial has ended. In Glasgow, the intervention may be continued, delivered by another NHS pharmacist working with a third sector support worker as other PHOENIx projects may be ongoing. In Glasgow,

participants allocated to the usual care group will be offered the intervention if participants think they would benefit from it and if the intervention is available once their participation in the trial has ended.

The participants GP will be informed of any medications prescribed by the pharmacist independent prescribers to ensure the medication is continued if needed.

# 8. OUTCOME MEASURES

## 8.1. Feasibility (process) outcomes

The pilot trial outcomes are related to the feasibility of a subsequent substantive RCT.

We are primarily interested in whether:

- the trial is appealing to participants (assessed by the recruitment rate)
- the PHOENIx intervention is acceptable (measured by adherence)
- we are able to collect routine data required to evaluate the effectiveness of the intervention

We will also evaluate:

the recruitment and randomisation processes. Specific feasibility outcomes related to these are listed in the first column of Table 1 below. These outcomes along with progression criteria will be considered by the Trial Oversight Committee (TOC), to determine whether we should proceed to a subsequent definitive trial:

Table 1: Criteria for progression to substantive trial at the end of the pilot

| | Red (discuss with Oversight Committee and consider substantial changes before proceeding to the definitive trial) | Amber (discuss with Oversight Committee strategies for improvement and consider changes to processes before deciding whether to proceed to full trial) | Green (go ahead) |
|---|---|---|---|
| **Recruitment** | | | |
| Proportion of PEH (as assessed by the researchers) meeting eligibility criteria and agreeing to participate | <40% | 40-50% | >50% |
| **Retention** | | | |
| Proportion of participants remaining in the study at 6 months | <50% | 50-60% | >60% |
| **Intervention adherence** | | | |
| Proportion of participants attending >50% of intervention visits as planned (flexible schedule agreed at consultation) | <50% | 50-60% | >60% |
| **Outcome data** | | | |
| Proportion of participants with Emergency Department visits and mortality data available at 6 months | <60% | 60-70% | >70% |
| Proportion of patients with questionnaire booklets completed at 6 months | <50% | 50-60% | >60% |

The data collected in this pilot will help inform the sample size calculation for the definitive trial. We anticipate the primary outcome for the definitive RCT to be a composite outcome of Emergency Department visits and mortality.

### 8.2. Clinical outcomes

The following will be measured at 3 and 6 months post-randomisation:

- Number, time to and cause of Emergency Department /primary care general practice visits
- Number of Emergency Department /general practice visits
- Mortality
- Medication changes (prescribed) and taken (in the case of opioid substitution therapy where supervised)

- Number, time to, duration and cause of hospitalisations
- Intervention acceptability (qualitative process evaluation)
- Generic health related quality of life score and health thermometer score (EQ-5D-5L)
- Fried's adapted frailty phenotype
- Peak Expiratory Flow Rate, MRC Dyspnoea scale
- Chronic Obstructive Pulmonary Disease (COPD) Assessment Test
- Blood pressure
- Temperature
- Pulse/heart rate

Social Care outcomes:

- Housing tenure including night shelters, emergency accommodation provided by the council or third sector, or care home
- Level of debt
- Criminal justice encounters

Addictions specific:

- Number of participants experiencing drug overdoses not requiring Emergency Department visit and number of overdoses
- Number of participants (and number of times) referred to drug and alcohol services, rehab, mental health and GP, and numbers attending subsequently
- Numbers and time to commencement on OST/Benzodiazepine/heroin assisted treatment and collecting ≥ 80% of daily doses
- Number of participants treated with and time to minimum therapeutic opioid substitution therapy dose
- Dose of opioid substitution therapy
- Number of missed appointments (with any team, including irregular discharges) and number of participants with missed appointments
- Number of people and days in prison/criminal justice encounters
- Number of threatening incidents involving pharmacy staff or other service users of pharmacy

### 8.3. Economic evaluation

The items of resource use will include measures of drug/alcohol treatment uptake and treatment retention; overdose rates; mortality rates and time to death; number of missed appointments (with any team, including irregular discharges); number of people and days in prison/criminal justice encounters (self-reported); number, time to and cause of ED/primary care general practice visits; medication changes (prescribed and used); housing tenure; level of debt; number and duration of hospitalisations; patient reported measures and intervention acceptability.

We will explore the possibility of an evaluation incorporating a wider societal (or at least public service perspective) in line with the work already conducted to establish broader costs and benefits beyond the NHS [47]. The main measure of benefit explored will be the EQ-5D-5L, cross-walked to the EQ-5D-3L. We will also consider the impact of using the EQ-5D-5L value set.

If unanticipated issues arise in data collection that lead to it not being possible to use both the EQ-5D-5L data or the resource use data, the results of the economics work would simply summarise narratively where there have been successes in data collection for economic-relevant outcomes, compared to where this was less successful, in order to inform methods of data collection that are more likely to facilitate good response rates among PEH for future RCTs in this area.

### 8.4. Qualitative evaluation

#### Process evaluation and associated outcomes

The main outcome from the qualitative interviews will be whether the intervention and trial procedures are acceptable.

## 9. TRIAL PROCEDURES

A researcher will meet all participants at baseline (pre-randomisation) and then at 3- and 6-months post-randomisation to collect data on:

1. Medicines prescribed, dispensed and taken (in the case of opioid substitution therapy).
2. Co-morbidities.
3. Health related quality of life using EQ-5D-5L.
4. Peak Expiratory Flow Rate (PEFR) respiratory rate; modified MRC Dyspnoea scale.
5. Hand grip strength
6. COPD Assessment Test,
7. Blood pressure, temperature, heart rate/pulse oximeter
8. Resource use data: Frequency of GP visits, nurse visits, addictions and mental health team and other primary healthcare contacts; un/scheduled secondary healthcare contacts including missed appointments.
9. Adapted frailty phenotype.
10. Criminal justice encounters.
11. All changes to prescribing, treatments given, and referrals made by PHOENIx team during intervention.
12. All referrals made by researcher during baseline and follow up assessments, as a result of the researcher noticing acute health problems.
13. Height and weight

Through directly accessing patient records, and through data linkage (to inform whether this can be done on time in the context of a future RCT), we will request healthcare utilisation data including Emergency Department and in-patient hospitalisation data from National Records Scotland (Data Intelligence Division), NHS Digital (England), any other NHS database portals or local NHS Trusts and Clinical Commissioning Groups. We will access local healthcare Trusts and general practices to record GP data, Alcohol and Drug Recovery Services recording systems to collect consultations and prescribing for problem drug use. Due to the often chaotic nature of consultations with PEH, the PHOENIx team and researchers will enter data onto paper clinical recording forms, which will then be sent to Birmingham Clinical Trials Unit to enter onto the database.

Full details of the sources for the clinical data are listed in table 2. Data will be collected where possible to indicate feasibility for the main trial.

**Table 2: Sources of clinical feasibility data**

| Measure | Source |
|---|---|
| Number, time to and cause of Emergency Department visit | NHS Greater Glasgow and Clyde IT services; Emergency Departments in Birmingham City; NHS Digital; Integrated Care System (ICS) data; NRS, Ambulance Services in Scotland and England |
| Number, time to and cause of primary care general practice visits | Direct access to registered GP records; ICS data |
| Mortality rates and time to death | NRS Scotland data linkage; NHS Digital; GP records |
| Medication changes (prescribed) and taken (in the case of opioid substitution therapy where supervised) | GP records and alcohol and drug recovery services (ADRS) IT systems data; Community pharmacy patient medication records. |
| Number of participants with, cause, time to and duration of hospitalisations | NHS Greater Glasgow and Clyde IT services; NRS; NHS Digital; GP records |
| Patient reported events | Completed paper questionnaire |
| Intervention acceptability | Qualitative interview transcripts |
| Generic health related quality of life (EQ-5D-5L) | Paper completed EQ5D5L |
| Number of drug overdoses not requiring ED visit and number of participants with overdoses | Self-reported by participant on CRF, ADRS or other addictions services records such as Change Grow Live; accommodation providers' testimonies; GP records; ambulance records |
| Number of people (and number of times per person) referred to ADRS or addictions services, rehab, mental health and GP, and numbers attending subsequently | ADRS or other addictions services records such as Change Grow Live, NHS GG&C IT services, data linkage; Integrated Care System (ICS) data, GP records |
| Numbers and time to commencement on OST/Benzodiazepine/heroin assisted treatment and collecting ≥ 80% of daily doses | ADRS or other addictions services records such as Change Grow Live; NHS GG&C Addictions services clinical records data linkage; community pharmacy records; GP records |
| N$^{o}$ of participants treated with and time to minimum therapeutic opioid substitution therapy dose | ADRS or other addictions services records such as Change Grow Live, NHS GG&C IT services; data linkage; community pharmacy records; GP records |

| | |
|---|---|
| Treatment retention (number and duration of missed prescriptions for treatments for problem drug use) | Community pharmacy records; ADRS or other addictions services records such as Change Grow Live |
| Dose of opioid substitution therapy | ADRS or other addictions services records such as Change Grow Live; NHS GG&C IT services; data linkage; community pharmacy records |
| N$^{o}$ of missed appointments (with any team, including irregular discharges) and number of participants with missed appointments | NHS GG&C IT services; ADRS or other addictions services such as Change Grow Live and mental health; team records; GP records |
| PEFR | Participants from paper case report forms |
| Adapted frailty phenotype | Participants from paper case report forms |
| MRC dyspnoea scale | Participants from paper case report forms |
| COPD assessment test | Participants from paper case report forms |

### Table 3: Social Care Outcomes

| **Measure** | **Source** |
|---|---|
| Criminal justice encounters | Self-reported on paper forms, Spring Housing Offenders Hub; Homelessness support hubs including third sector homelessness support organisations |
| Housing tenure including night shelters, emergency accommodation provided by the council or third sector, or care homes | Third sector homelessness support organisation, rough sleepers outreach team in Birmingham, partners like Tabor House providing night shelters; City Council Housing Officers based at third sector homelessness support organisations and temporary accommodations/ hostels |
| Level of debt (self-reported, and from social security records where possible) | Third sector homelessness support organisation records; Specialist Tenancy Worker; |
| Number of people and days in prison/criminal justice encounters | Scottish Prison Service (Prisons in GG&C only); Birmingham and Solihull Mental Health Foundations Trust |

### 9.1. Schedule of assessments

**Table 4:** Schedule of Assessments

| Visit | Screening | Baseline | Month 3 | Month 6 |
|---|---|---|---|---|
| Eligibility check | x | | | |
| Valid informed consent | x | x | x | x |
| Relevant medical history taken | | x | x | x |
| Concomitant medication | | x | x | x |
| Randomisation | | x | | |
| Baseline CRF | | x | | |
| 3 month CRF | | | x | |
| 6 month CRF | | | | x |
| Qualitative Interviews* | | | x | x |

**15-20 intervention participants will be selected. Interviews will be conducted after baseline but before month 6*

### 9.2. Withdrawal and changes in levels of participation

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 should be asked about their ongoing willingness to continue participation at all visits. Capacity of the participant to continue in the trial will be assessed by the study researcher during follow up for the duration of the participant's time in the trial. If a participant is assessed to have permanently lost capacity, then they will be withdrawn from the trial. Data collected until withdrawal will be kept. This will be noted in their trial case report forms and on any records available (as per the consent section). Participants should be aware from the beginning that they can freely withdraw (cease to participate) from the trial at any time. A participant may wish to cease to participate in a particular aspect of the trial.

Participants found to be ineligible post randomisation should be followed up according to all trial processes and will still have their data analysed unless they explicitly change their level of participation.

The changes in levels of participation within the trial are categorised in the following ways:

**No trial intervention:** The participant would no longer like to receive the trial intervention, but is willing to be followed up in accordance with the schedule of assessments and if applicable using any central UK NHS bodies for long-term outcomes (i.e., the participant has agreed that data can be collected and used in the trial analysis).

**No trial related follow-up:** The participant does not wish to attend trial visits in accordance with the schedule of assessments, but is willing to be followed up at standard clinic visits and if applicable using any central UK NHS bodies for long-term outcomes (i.e., the participant has agreed that data can be collected at standard clinic visits and used in the trial analysis, including data collected as part of long-term outcomes).

**No further data collection:** The participant is not willing to be followed up in any way for the purposes of the trial AND does not wish for any further data to be collected (i.e., only data collected prior to any changes of levels in participation can be used in the trial analysis).

The details of changes of levels in participation within trial (date, reason and category of status change) should be clearly documented on the change of status CRF.

For the qualitative process evaluation, participants will have 5 days to request their interview data is removed.

**Switch from usual care to intervention group**: see above, with example given of case where patient needs emergency treatment at follow up or any time thereafter in pharmacy. In these circumstances, patient will be withdrawn from the trial.

# 10. ADVERSE EVENT REPORTING

We do not anticipate any safety concerns arising as a result of this intervention and as such we do not need to monitor AEs to assess the interventions safety. There is no reason to assume that this trial will lead to any AEs related to the intervention. AEs are being collected as part of outcome measures and hence monitoring of AE due to the intervention is not anticipated. AEs collected as part of outcome measures will include:

- Overdose incidents
- Hospital admissions for less than 24 hours
- Alcohol withdrawal symptoms
- Any serious adverse drug reactions resulting from the medicines prescribed*

During follow-up, we will systematically collect self-reported data as part of the clinical outcomes, from participants regarding admissions to hospital requiring an overnight admission and the reasons for this. We will also capture whether there have been any deaths and cause of death. These will be reviewed by the Trial Oversight Committee at regular intervals.

Safety issues are expected to be no different from those experienced in routine care, when medicines are prescribed by the participant's GP. Pharmacist independent prescribers are required to follow National clinical guidelines from NICE, SIGN or local clinical guidelines or professional society guidelines as appropriate and use the same treatment algorithms, and ask the participants to attend for the same schedule of monitoring e.g. 6 monthly blood tests for liver function in the case of antipsychotics. Any medication prescribed will be reviewed and monitored by the usual care team. The decision to continue any medications will be the responsibility of the usual care team.

# 11. DATA HANDLING AND RECORD KEEPING

## 11.1.Source data

Source data is defined as 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. In order to allow for the accurate reconstruction of the trial and clinical management of participants, source data will be accessible and maintained.

Some data variables may be entered directly onto the CRF, these are clearly identified and detailed below in Table 6:

**Table 6**: Source data in PHOENIx (excluding clinical feasibility data)

| **Data** | **Source** |
|---|---|
| Participant Reported Outcomes | The original participant-completed CRF is the source and will be kept with the participant's trial record at site, whilst copies will be provided to the trial office. |

| | |
|---|---|
| Blood pressure | The routine clinic blood pressures of trial participants at various time points will be available through blood pressure checks undertaken by the PHOENIx research team. |
| Temperature | Thermometer, from case record form, undertaken by the PHOENIx research team. |
| Heart Rate/pulse | Pulse oximeter, undertaken by the PHOENIx research team. |
| Respiratory rate | Manual count and clock, undertaken by the PHOENIx research team. |
| Peak Flow rate | Peak Flow Meter, undertaken by the PHOENIx research team. |
| Health economics data | Obtained by discussions directly with the participants for transcription into CRF and this will constitute the source data. |
| Recruitment | The original record of the randomisation is the source. It is held on BCTU servers as part of the randomisation and data entry system. |
| Withdrawal | Where a participant expresses a wish to withdraw, the conversation must be recorded in the CRF. The CRF will be the data source. |
| Qualitative Interviews | Interviews will be recorded and transcribed clean verbatim for analysis. The recording is the source. |

### 11.2. Case Report Form (CRF) completion

The CRFs will include (but will NOT be limited to) the following forms (see Table 7: Case report forms in PHOENIx 7).

**Table 7**: Case report forms in PHOENIx

| **Form Name** | **Schedule for submission** |
|---|---|
| Consent and Randomisation CRF | At the point of randomisation |
| Baseline and follow-up CRFs including participant reported outcome measures | As soon as possible after each follow-up assessment time point |
| Change of status CRF | As soon as possible after the point of reduced participation or death |

A CRF should be completed for each individual participant.

In all cases it remains the responsibility of the PI to ensure that the CRF has been completed correctly and that the data are accurate. This will be evidenced by the signature of the PI, or delegate(s). The Site Signature & Delegation Log will identify all those personnel with responsibilities for data collection.

The delegated staff completing the CRF should ensure the accuracy, completeness and timeliness of the data reported. This will be evidenced by signing and dating the CRF.

Data reported on each CRF will be consistent with the source data and any discrepancies will be explained. Staff delegated to complete CRFs will be trained to adhere to PHOENIx Trial working instructions.

The following guidance applies to data and partial data:

- Only CRFs provided by the Trial Office should be used.
- Original completed CRFs or true copies should be sent to the Trial Office with copies filed in the ISF.
- Entries should be made in dark ink and must be legible.
- Any errors should be crossed out with a single stroke, the correction inserted and the change initialled and dated.
- Time format – all times should be in accordance with the 24hr clock
- Rounding conventions – rounding should be to the nearest whole number: If the number you are rounding is followed by 5, 6, 7, 8, or 9, round the number up. **Example**: 3.8 rounded to the nearest whole number is 4. If the number you are rounding is followed by 1, 2, 3 or 4, round the number down. **Example**: 3.4 rounded to the nearest whole number is 3
- Trial-specific interpretation of data fields – where guidance is needed additional information will be supplied
- Entry requirements for concomitant medications (generic or brand names) – generic names should be used where possible
- Missing/incomplete data – should be clearly indicated – all blank fields will be queried by the Trial Office
- Repeat laboratory tests – the data used to inform clinical decisions should always be supplied. If a test is repeated it is either to confirm or clarify a previous reading. Confirmatory tests should use the original test values.
- Protocol and GCP non-compliances should be reported to the Trial Office on discovery.

On completion, a copy or a scan of each form will be submitted to the Trial Office and the original filed in the ISF.

### 11.3.Participant completed questionnaires

Participant completed questionnaires will be completedduring pharmacy consultations or alternative locations agreed by the study researcher and the participant. These could include third sector support hub, participant accommodations or soup kitchens. The researcher or the pharmacist will oversee the completion of the questionnaire. Missing data will be identified via a check by the researcher prior to the participant leaving. If any missing data is identified at this point then the participant will be asked to complete it prior to leaving. Any missing data identified after the participant has left will remain missing.

### 11.4.Data management

Processes will be employed to facilitate the accuracy and completeness of the data included in the final report. These processes will be detailed in the trial specific Data Management Plan and include the processes of data entry, data queries and self-evident corrections on trial data.

Data entry will be completed by the sites on paper and sent to BCTU to be entered. The data capture system will conduct automatic range checks for specific data values to ensure high levels of data quality. Queries will be raised using data clarification forms (DCFs) via the trial database, with the expectation that these queries will be completed by the site within 30 days of receipt. Overdue data entry and data queries will be requested on a monthly basis.

### 11.5.Self-evident corrections

The below self-evident corrections will be permitted by the Trial Office:

**Contingent fields:** When a response to a question determines, to a degree, the response required by a second question, then conflicts in the responses can be resolved by the data entry clerk. E.g., Has the person had procedure “x”? If yes, state type. If the response to the first question is “no”, yet the type of procedure is stated, it is self-evidently true that the initial response was incorrect.

**Changes to administrative notes and reference numbers**: when new information becomes available such that a reference number does not accurately reflect the sequence of CRFs received, then it is appropriate to change the reference number provided no DCFs have been raised using the original number. Similarly, any notes relating to the participant care which have an impact on the administration process, but not the data fields themselves, can be changed as appropriate.

### 11.6.Data security

University of Birmingham, and University of Glasgow in relation to the qualitative work, have policies in place, which are designed to protect the security, accuracy, integrity and confidentiality of Personal Data. The trial will be registered with the Data Protection Officer at Birmingham. Data at both institutions will be held in accordance with the Data Protection Act (2018 and subsequent amendments). The Trial Office has arrangements in place for the secure storage and processing of the trial data which comply with data security policies at the relevant institution.

The Trial Database System incorporates the following security countermeasures:

**Physical security measures:** restricted access to the building, supervised onsite repairs and storages of back-up tapes/disks are stored in a fire-proof safe.

**Logical measures for access control and privilege management:** including restricted accessibility, access controlled servers, separate controls of non-identifiable data.

**Network security measures:** including site firewalls, antivirus software and separate secure network protected hosting.

**System management:** the system will be developed by the Programming Team at the Trial Office, and will be implemented and maintained by the Programming Team.

**System design:** the system will comprise of a database and a data entry application with firewalls, restricted access, encryption and role based security controls.

**Operational processes:** the data will be processed and stored within BCTU. Qualitative data will be held at Glasgow University and their processes will be followed for secure data storage there.

**System audit:** The system will benefit from the following internal/external audit arrangements:

- Internal audit of the system
- Periodic IT risk assessment

**Data Protection Registration:** UoB's Data Protection Registration number is Z6195856.

### 11.7.Archiving

It is the responsibility of the PI to ensure all essential trial documentation and source documents (e.g., signed ICFs, Investigator Site Files, Pharmacy Files, participants' clinical notes, copies of CRFs) at their site are securely retained for the contractual period. Archiving will be authorised by BCTU on behalf of UoB following submission of the end of trial report. No documents should be destroyed without prior approval from the BCTU Director or their delegate.

The Trial Master File (TMF) will be stored at BCTU for at least 3 years after the end of the trial. Long-term offsite data archiving facilities will be considered for storage after this time; data will be stored securely and confidentially for at least 10 years. The University of Glasgow will also store their collected data for at least 10 years. BCTU has standard processes for both hard copy and computer database legacy archiving.

## 12. QUALITY CONTROL AND QUALITY ASSURANCE

### 12.1.Site set-up and initiation

All PIs will be asked to sign the necessary agreements including a Site Signature and Delegation log between the PI and the Trial Office and provide evidence of relevant training to carry out their delegated duties. All members of the site research team are required to sign the Site Signature and Delegation Log, which details which tasks have been delegated to them by the PI. The Site Signature and Delegation Log should be kept up to date by the PI. It is the PI's responsibility to inform the Trial Office of any changes in the site research team.

Prior to commencing recruitment, each recruiting site will undergo a process of site initiation, either a meeting or a tele/video conference, at which key members of the site research team are required to attend, 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 ISF containing essential documentation, instructions, and other documentation required for the conduct of the trial.

### 12.2.Monitoring

The central and on-site monitoring requirements for this trial have been developed in conjunction with the trial specific risk assessment and are documented in the trial specific monitoring plan.

#### 12.2.1. On-site monitoring

For this trial, all sites will be monitored in accordance with the trial risk assessment and monitoring plan. Any monitoring activities will be reported to the Trial Office and any issues noted will be followed up to resolution. Additional on-site monitoring visits may be triggered. PIs and site research teams will allow the PHOENIx trial staff access to source documents as requested. The monitoring will be conducted by BCTU/UoB staff.

#### 12.2.2. Central monitoring

The Trial Office will check received ICFs and CRFs for compliance with the protocol, data consistency, missing data and timing at a frequency and intensity determined by the Data Management Plan. Sites will be sent DCFs requesting missing data or clarification of inconsistencies or discrepancies.

### 12.3.Audit and inspection

The Investigator will permit trial-related monitoring, audits, ethical review, and regulatory inspection(s) at their site and provide direct access to source data/documents. The investigator will comply with these visits and any required follow-up. Sites are also requested to notify the Trial Office of any relevant inspections or local audits.

### 12.4.Notification of Serious Breaches

The sponsor is responsible for notifying the Research Ethics Committee (REC) of any serious breach of the conditions and principles of GCP in connection with that trial or of the protocol relating to that trial. Sites are therefore requested to notify the Trial Office of any suspected trial-related serious breach of GCP and/or the trial protocol as soon as they become aware of them. Where the Trial Office is investigating whether or not a serious breach has occurred, sites are also requested to co-operate with the Trial Office 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.

## 13. END OF TRIAL DEFINITION

The end of trial will be the date of the last data capture including resolution of DCFs. This will allow sufficient time for the completion of protocol procedures, data collection and input and data cleaning. The Trial Office will notify the REC and the Sponsor within 90 days of the end of trial. Where the trial has terminated early, the Trial Office will notify the REC and sponsor within 15 days of the end of trial. The Trial Office will provide the REC and the Sponsor with a summary of the clinical trial report within 12 months of the end of trial.

## 14. STATISTICAL CONSIDERATIONS

### 14.1 Sample size

The sample size calculation is based around two of the main feasibility objectives: rate of recruitment and retention. We plan to recruit and randomise 100 participants. If the total number of eligible persons is 200, this will allow measurement of the recruitment rate with a 95% confidence interval width of approximately 14%. If 70% of those recruited are followed up in terms of measuring ED visits, this will allow measurement of the rate with 95% confidence interval width of approximately 18%.

### 14.2 Analysis of outcomes

A separate Statistical Analysis Plan will be produced and will provide a more comprehensive description of the planned statistical analyses. A brief outline of the planned analyses is given below:

Feasibility measures will be analysed using appropriate summary measures including proportions, along with 95% confidence intervals (based on a normal approximation method for one sample proportions) to describe uncertainty.

For clinical measures, the study sample size is too small to allow reliable analysis of the effect of the intervention on outcomes. No hypothesis testing will be performed and the analysis will be limited to estimates of effects size and measures of uncertainty where appropriate. The primary comparison groups will be composed of those randomised to the trial intervention (PHOENIx health and social care check) versus those randomised to the control group (usual care). In the first instance, all analyses will be based on the intention to treat principle, i.e., all participants will be analysed in the intervention group to which they were randomised irrespective of adherence to randomised intervention or protocol deviations. Appropriate summary statistics and differences between groups (e.g., mean differences, relative risks, absolute differences) will be presented, with 95% confidence intervals. A log-binomial regression model will be used for binary outcomes and a linear regression model used for continuous outcomes.

#### 14.2.1. Planned subgroup analyses

No subgroup analysis will be undertaken.

#### 14.2.2. Missing data and sensitivity analyses

There is a potential for some missing data to occur at follow-up. However, in this context, this is part of the assessment of the success of the study and imputation of missing responses is not proposed.

### 14.3.Planned final analyses

The primary analysis for the trial will occur once all participants have completed their 6 month assessment and corresponding outcome data has been entered onto the trial database and validated as being ready for analysis.

## 15. HEALTH ECONOMICS

A separate Health Economics Analysis Plan will be produced and will provide a more comprehensive description of the planned analyses. A brief outline of these analyses is given below.

### 15.1.Within-trial economic evaluation

A resource use questionnaire will identify, measure and value all health, social care and personal resource use data. The responses will cover the number of people incurring each resource and the number of times each resource was incurred by each person who experienced it, since the previous administration of the same questionnaire (except for baseline where it will be the previous month).

The items of resource use will include measures of drug/alcohol treatment uptake and treatment retention; overdose rates; mortality rates and time to death; number of missed appointments (with

any team, including irregular discharges); number of people and days in prison/criminal justice encounters (self-reported); number, time to and cause of Emergency Department/primary care general practice visits; medication changes (prescribed and used); housing tenure; level of debt; number and duration of hospitalisations; patient reported measures and intervention acceptability. We will also explore the possibility of an evaluation incorporating a wider societal (or at least public service perspective) at least in a sensitivity analysis. All resources will be quantified in Pounds Sterling, for the most recent price year available at the time of the analysis.

We will summarise total costs (i.e. health, social care and personal resource use), and also provide disaggregated costs for individual resource use items (where the resource is incurred sufficiently frequently that patient confidentiality is protected) and make clear how we have defined which costs fall within the categories of 'health', 'social care' and 'personal resource use' (and other public sector/societal costs if measurement has proved possible). We will calculate total costs for each individual in the intervention and usual care arms of the trial, in order to derive average costs for each trial arm.

We will use the EQ-5D-5L to evaluate the potential health benefits of the PHOENIx intervention. Although there are known difficulties associated with collecting this outcome among PEH, the research team have prior experience of collecting this outcome measure for this intervention.

Enhanced understanding of the acceptability and frequency of EQ-5D instrument data collection gained from this pilot trial will provide further insight as to the ability to generate Quality Adjusted Life Years (QALYs) for use alongside the cost data with PEH to give an indicative picture of cost-effectiveness. This indicative picture would require first using the cross-walk of the EQ-5D-5L data to the 3L in order to generate consistent values with previous research, as the value set for EQ-5D-5L is very new. However, we will also explore the use of the 5L value set for the UK if possible.

Should we encounter pragmatic difficulties in data collection that make it not possible to use the EQ-5D data, we will consider how benefits could be measured via a cost consequence analyses using the resource use data, in line with measuring benefits in terms of e.g. cumulative bed days avoided, as was done by Cornes et al [49]. We will explore other outcomes that may be more relevant than bed-days avoided given this is a community-based intervention, e.g. emergency department visits avoided.

It is possible that the pilot study sample data may not provide enough information for analysis, and if this occurs we are willing to explore the application of Value of Information (VOI) techniques to the data. The extent to which this is possible depends on whether or not enough information for the proposed analysis is available from the collected data, as well as additional parameters about the underlying population (e.g. accurate data on prevalence which may be underestimated by routine data sources reliant on people presenting to services).

If it is not possible to conduct a value of information analysis within the capacity limits and timeframe agreed, we will still strive to use similar techniques to support decision-makers with view to future development of a full RCT. This could take the form, for example, of a threshold analysis for a particular parameter, with the results explored within the context of the existing published

evidence base for this or similar interventions in primary care settings, and/or an exploration of methods used in the wider literature to address possible confounding in RCTs undertaken among similar study populations (i.e. with complex but potentially highly variable care needs even at baseline).

### 15.2.Model-based economic evaluation

No model-based economic evaluation is proposed for this pilot RCT. However, we may utilise some of the methods used in model-based economic evaluations to supplement the within-trial analysis as described above (e.g. a more detailed exploration of the existing published evidence base in order to inform uncertainty in a particular parameters). If this occurs, we will use standard good practice methods to undertake searches.

## 16. SUB-STUDIES

There will be an economic evaluation and qualitative sub study conducted as part of this pilot study.

### Process evaluation and associated outcomes

The qualitative researchers (employed by Glasgow University) will check the information entered onto a randomly selected subset of participant's care plan/clinical record by the pharmacist by reviewing anonymised clinical care records kept by the PHOENIx team and transferred to the qualitative team. The qualitative researchers will then compare these data against a checklist of the components of the intervention: physical health; mental health; addictions; housing; debt; and social activities. This will be used to provide iterative feedback to the intervention team to ensure fidelity and optimise delivery of the intervention, and in addition, will address intervention fidelity.

We will also undertake semi-structured interviews with a purposive sample of 15-20 trial participants, 7-10 health professionals and up to approximately 10 stakeholders, including commissioners/ senior health board / homelessness services policy makers and representatives from volunteer sectors, in order to explore their views on the trial methods and barriers and facilitators to future implementability. The coinvestigators will use Interviews will be audiotaped with encrypted recorders with participant consent and transcribed to provide data for qualitative analysis.

We will use Normalisation Process Theory as our underpinning theoretical framework to help us conceptualise implementation issues and the effects of the intervention on the interplay between patient capacity and self-management workload which will help us refine our preliminary logic models in relation to the intervention. Interview transcripts will be analysed thematically and the data conceptualised through a Normalisation Process Theory, an implementation theory which consists of with four constructs: coherence (sense making); cognitive participation (engagement); collective action (operationalisation) and reflexive monitoring (appraisal) [52].

### Patient and professional interview process

A researcher will contact patients and professionals the day before the interview, to remind the time and venue for the interviews. The interviews will be held either in a patient's homeless venue if known or in the pharmacy or at a location of the interviewee's preference.

Interviews will adhere to the lone working policies of each NHS location.

At the beginning the researcher will explain the ground rules, such as:

- Explaining there are no right or wrong ideas, but that it is the interviewees perspectives that are of interest
- Everything said will be considered absolutely confidential
- Explanation of the recording and note taking and data protection
- The interview can be stopped at any time should a person request it

If they have inquiries, they will be invited to discuss with a researcher. Informed verbal consent will be taken before each interview starts and also will be recorded digitally. The interview will start with an easy and open question which will be followed by asking key questions from the topic guide. Participants can ask for a break if he or she want. Any hesitations and non-verbal communications will be noted and prompted as appropriate.

The duration of interview is likely to be 30 to 60 minutes each.

# 17. TRIAL ORGANISATIONAL STRUCTURE

## 17.1. Sponsor

The Sponsor for this trial is the University of Birmingham (UoB).

## 17.2. Coordinating centre

The trial coordinating centre (Trial Office) is Birmingham Clinical Trials Unit (BCTU), based at UoB.

## 17.3. Trial Management Group

The Trial Management Group (TMG) comprises individuals responsible for the day-to-day management of the trial: the co-CIs, statisticians, trial team leader, trial manager and data manager. The role of the group is to monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of the trial itself. The TMG will meet sufficiently frequently to fulfil its function.

## 17.4. Co-investigator group

The Co-investigator group, an extended TMG, will comprise all members of the co-applicant group and the members of the TMG to review progress, troubleshoot and plan strategically.

## 17.5. Independent Trial Oversight Committee (TOC)

Oversight of the PHOENIx trial will be provided by an independent TOC. The TOC will meet via teleconference/face-to-face approximately twice a year or as required depending on the needs of the trial.

Membership and duties/responsibilities are outlined in the TOC Terms of Reference. In summary, the TOC will provide overall oversight of the trial, including the practical aspects of the trial, as well as ensuring that the trial is run in a way which is both safe for the participants and provides appropriate feasibility data to the sponsor and investigators.

The intervention is considered low risk. This is a general population and no adverse events are expected as a result of the intervention. An emergency meeting may however be convened if a safety issue is identified.

### 17.6. Finance

The research costs of the trial are funded by NIHR HS&DR awarded to Dr Vibhu Paudyal, University of Birmingham. The trial has been designed to minimise extra 'service support' costs for participating sites as far as possible. Additional costs, service support costs and excess intervention costs associated with the trial, e.g., gaining consent, are estimated in the SoECAThave been calculated and funding identified within the relevant Trusts.

## 18. ETHICAL CONSIDERATIONS

The trial will be conducted in accordance with the UK Policy Framework for Health and Social Care Research and applicable UK Acts of Parliament and Statutory Instruments (and relevant subsequent amendments), which include the Data Protection Act 2018, the Mental Capacity Act 2005 (England) and Section 51 of the Adults with Incapacity (Scotland) Act 2000, and the Principles of GCP as set out in the UK Statutory Instrument (2004/1031; and subsequent amendments). The protocol will be submitted to and approved by the REC prior to the start of the trial.

All correspondence with the REC will be retained in the TMF/ISF, and an annual progress report will be submitted to the REC and sponsor within 30 days of the anniversary date on which the favourable opinion was given by the REC, and annually until the trial is declared ended. A trial-specific risk assessment and monitoring plan will be developed before submission to the REC and sponsor and will be reviewed regularly during the trial.

Before any participants are enrolled into the trial, the PI at each site is required to obtain the necessary local approval.

It is the responsibility of the PI 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.

## 19. DATA PROTECTION AND CONFIDENTIALITY

Personal data and sensitive 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 (and subsequent amendments) and per UoB guidance on secure password protected servers. Physical data (paper CRFs) will stored in locked filing cabinets in a secure swipe card access building.

Personal data categories that will be collected and analysed include name, date of birth, NHS number, email or postal address (if applicable). We will also collect some sensitive personal data that will include gender, ethnicity, health information, medical history and drug use. Personal data will be deleted in a timely fashion once analysis has been completed.

Participants will only be identified by their unique trial identification number in any correspondence between the site and BCTU. Participants will give their explicit consent for the movement and storage of their consent form, giving permission for BCTU to be sent a copy. Participants will provide their personal contact details to the central research team at BCTU so they are able to contact the participants for follow up questionnaires. Participants will acknowledge the transfer of their personal data to NHS Digital, NRS (National Records Scotland), or other central UK NHS bodies or NHS data portals, ambulance services, SIFA Fireside, Simon Community, Trident Reach or other third sector homelessness support organisations and University of Glasgow who will be processing data on behalf of the trial. Identifiable information will never be transported or transferred with pseudonymised data collection forms. At the end of the study all personal data will be deleted and only anonymised data will be archived.

BCTU will maintain the confidentiality of all participant's data and will not disclose information by which participants may be identified to any third party, with the exception of the transcription service, NRS, SIFA Fireside, Simon Community, Trident Reach or other third sector homelessness support organisations, ambulance services, NHS Digital and any other NHS bodies or data portals. For 3rd sector charities, information will be only what is sufficient to identify the participant. A professional transcription company that already works with the University of Glasgow will transcribe the audio files. This company will be required to sign a confidentiality agreement before any files are sent to them and we will request that audio files are deleted after the transcription is complete. A member of the research team will check the transcripts once received from the transcription company and remove any names/ identifiers from the documents. Once the accuracy of the transcriptions has been confirmed, the original recordings will be deleted. All transfers will be done securely and according to University of Glasgow's IT guidance.

NHS Digital and other third party organisations listed above will need to be sent identifiers for them to provide us with the information necessary. Details of what data will be shared with NHS Digital will be contained in the PIS and consent will be sought from the participant to allow this. Data linkage will stop once analysis has been completed.

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. Representatives of the PHOENIx trial team and sponsor may be required to have access to participants' notes for quality assurance purposes, but participants should be reassured that their confidentiality will be respected at all times. The Trial Office will maintain the confidentiality of all participant data and will not disclose information by which participants may be identified to any third party.

## 20. FINANCIAL AND OTHER COMPETING INTERESTS

There are no financial or other competing interests related to the results of this trial. Members of the TOC are required to provide declarations on potential competing interests as part of their membership of the committee. Authors are similarly required to provide declarations at the time of submission to publishers.

## 21. INSURANCE AND INDEMNITY

The University has in force a Public Liability Policy and/or Clinical Trials policy which provides cover for claims for "negligent harm" and the activities here are included within that coverage.

With respect to the conduct of the trial at Site and other clinical care of the patient, responsibility for the care of the participants remains with the NHS organisation responsible for the Clinical Site and is therefore indemnified through the NHS Litigation Authority.

## 22. POST-TRIAL CARE

The PHOENIx intervention may be able to continue in Glasgow (funded out with the trial) however there will be no intervention continuation in Birmingham.

## 23. END OF TRIAL DEFINITION

The end of trial will be six months after the last data capture (i.e. 6 months after the date at which the last participant has completed their 6 month follow up.) The BCTU trial team will notify the main REC and Sponsor that the trial has ended and a summary of the clinical trial report will be provided within 12 months of the end of trial.

## 24. ACCESS TO FINAL DATASET

The final dataset will be available to members of the Trial Management and co-applicant group who need access to the data to undertake the final analyses.

Requests for data generated during this study will be considered by BCTU. Data will typically be available six months after the primary publication unless it is not possible to share the data (for example: the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or BCTU is not the controller of the data).

Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the BCTU Data Sharing Committee in discussion with the CIs and, where appropriate (or in absence of the CIs) any of the following: the Trial Sponsor, the relevant Trial Management Group (TMG), and independent TOC.

A formal Data Sharing Agreement (DSA) may be required between respective organisations once release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers transfer of participant identifiable information. Any data transfer will use a secure and encrypted method.

## 25. DISSEMINATION AND PUBLICATION PLAN

### Dissemination

We will prepare a final study report and share this with the funder. The report will also be available on the study website. We plan to share the pilot study results with relevant stakeholders with the aim of further engagement and support for the main study.

We will also present and share our findings directly with patients in pharmacies, accommodation sites, and low threshold venues in Glasgow and Birmingham. Our research team represent local and national constituents and stakeholders in addictions, recovery groups, criminal justice, homelessness, general practice, academia and pharmacy.

### Publication

The findings will be published in medical journals, presented at national scientific meetings and made available through websites of professional societies and national charities e.g. Shelter, Crisis. Journal manuscripts will be prepared by the writing group as defined in the trial publication plan. Manuscripts should be submitted to the TMG in a timely fashion and in advance of being submitted for publication to allow time for review. The PPI representatives within our research team will help distribute our findings through their networks and homelessness and inclusion health networks in the UK and the North America. Academic networks, public health practice networks, NHS Scotland and NHS England connections will be informed of our findings. These strategies will facilitate transition to the main study and implementation of services.

Summary results will be made available for research participants upon request through the participating third sector homelessness support organisations.

It is anticipated that all co-investigators including trial team members from BCTU will contribute to the writing and editing of manuscripts for publications resulting from the trial and fulfil the International Committee of Medical Journal Editors (IJCME) criteria for authorship. If there are any disagreements, the CIs will have a final say.

In all publications, authors should acknowledge that the trial was performed with the support of NIHR and University of Birmingham, BCTU and University of Glasgow. Intellectual property rights will be addressed in the Study Site Agreement between Sponsor and site.

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## 27. APPENDIX