FULL/LONG TITLE OF THE STUDY

Improving Hospital Opioid Substitution Therapy (iHOST): evaluation of an intervention to reduce late presentations, discharge against medical advice and repeat admissions among people who use opioids.

SHORT STUDY TITLE / ACRONYM

iHOST (Improving Hospital Opioid Substitution Therapy)

PROTOCOL VERSION NUMBER AND DATE

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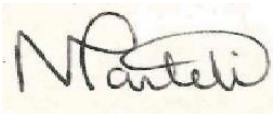
SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

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

I also confirm that I will make the findings of the study publically 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 planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: 

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1. Summary of Research

Evidence of need: People who use illicit opioids (PWUO), such as heroin, are over-represented in urgent and emergency admissions. Late presentation with complications from injecting-related infections and injuries is common, yet retention in hospital care is low. This is a serious problem, associated with: reliance on ambulatory care, complex admissions, unplanned hospitalisation, discharge against medical advice (DAMA), readmission, surgical intervention and high NHS costs.

Our research [1-3], engagement with affected groups, and international evidence [4-9] show that poor management of opioid substitution treatment (OST) in hospital emergency, acute admissions and high burden wards is a primary barrier to timely and effective care for PWUO. Experiences of OST delay or omission can cause severe physical and psychological distress and result in treatment interruption or DAMA to obtain illicit drugs. PWUO experiencing opioid withdrawal can be challenging to manage; improving their experience and feelings of safety in the hospital setting is beneficial for both patients and providers.

Intervention overview: This research will optimise, test and evaluate the iHOST toolkit to scale nationally. The toolkit will support hospitals to implement and embed evidence-based practice for optimal management of PWUO in collaboration with community drug treatment services.

iHOST comprises: 1) A 'My Meds' card. A prototype card has been developed with PWUO. This provides information for hospital staff to prioritise and expedite medicines reconciliation, including blank fields for OST prescriber and pharmacy contacts. 2) A helpline for patients and providers run by the charity Release. 3) An online training module for staff in hospital Accident and Emergency (A&E,), acute admissions, and high burden hospital wards. 4) A 'best practice' hospital policy template. 5) An iHOST 'champion' to support sustainability post intervention.

Aim: To optimise OST management in hospital settings to reduce delayed presentation, self-discharge and emergency readmission among PWUO.

Research question: Does the iHOST toolkit reduce delays in OST prescription in two hospitals compared to historical local data, and does this lead to reduced DAMA and emergency readmission of PWUO compared to historical local rates and a national comparator cohort?

Objectives:

1. Optimise iHOST components and test feasibility in a London hospital.
2. Evaluate intervention acceptability, fidelity, reach, costs and impact in a rural and urban hospital.
3. Develop and disseminate toolkits for national implementation.

Primary outcome measures:
1. Discharge against medical advice (DAMA)
2. Emergency hospital readmission within 28 days of discharge

Design: Quasi-experimental design. Our primary outcomes will be measured through a difference-in-difference analysis [10] of routinely collected clinical data at two iHOST evaluation sites, using comparative data from the national Hospital Episode Statistics (HES) database. A qualitative process evaluation [11] will assess iHOST acceptability and fidelity, clarify causal mechanisms, and identify contextual factors such as human resources and commissioning that might be associated with success.

Population: Hospital patients who are dependent on illicit opioids and/or who are prescribed OST.

Sites: University College London Hospital (UCLH) and local drug treatment services (Phases 1, 2 & 4); St James's University Hospital, Leeds; Royal Stoke University Hospital, Staffordshire, and local drug treatment services (Phases 3 & 4).

Delivery plan:

Phase 1 [months 1-8]: **Optimise**: Evidence review; NHS hospital policy analysis; clinical information systems review; workshops with PWUO and providers to optimise and finalise iHOST.

Phase 2 [months 9-14]: **Test feasibility**: Test iHOST at UCLH and linked drug treatment services. Conduct feasibility evaluation of outcome measures and assess iHOST acceptability through interviews. Workshop findings with PWUO and providers to further refine iHOST prior to implementation.

Phase 3 [months 15-29]: **Evaluate:** Embed iHOST at St James and Royal Stoke Hospitals and linked services for 3 months prior to evaluation. Measure primary outcomes locally through difference-in-difference analysis of routinely collected clinical data, and nationally through controlled analysis using HES. These data will inform economic analysis. Conduct qualitative interviews, focus groups and observations at the hospitals and linked drug treatment services for process evaluation.

Phase 4: **Disseminate**: Co-produce final iHOST toolkit (standardised OST policy for NHS hospitals, online training promotion and links; iHOST champion training and resources; My Meds card template and purchasing information) and slide sets for findings and toolkit dissemination to diverse audiences. Target acute NHS trusts including local Medication Safety Officers, Local Authorities, Integrated Care System Commissioners, Drug and Alcohol providers, patient/service user groups and other key stakeholders for research updates, tailored policy briefings and presentations. Peer-review publication will prioritise multi-disciplinary dissemination. Findings will be published in Drink and Drugs News (DDN), a magazine aimed at drug treatment providers and Black Poppy, a magazine for people who use drugs.

Conceptual framework: Cultural safety principles aim to reduce health care practices that cause marginalised patients to feel unsafe and powerless [12]. Developed by nurse academics working with Maori patients in New Zealand [13], cultural safety has been successfully adapted in North America to reduce stigma and enhance equity of care for substance dependence in hospital settings [7, 14]. Our research will be the first to translate this evidenced approach to inform care for PWUO in the UK.

Patient and Public Involvement (PPI): Formative work with PWUO, hospital and drug treatment providers inform this research: iHOST components were co-produced through PPI workshops in response to findings from MH's NIHR fellowship award. Two team members (MH and AN) have lived experience of opioid dependency and will deliver a substantive peer-research component. PPI workshops are built into each phase to obtain feedback on emerging findings, iteratively co-develop a cultural safety framework and co-produce outputs for dissemination.

Impact: Led by a team of multidisciplinary researchers (combining clinical, social science, epidemiological, economic and substance dependence health expertise) this research will deliver value for money to patients and the NHS by contributing towards improving patient experience and care during hospital admissions; care that will have a significant health, economic and social impact.

2. Background and Rationale

The World Health Organization recommends that opioid substitution therapy (OST) be globally available for people who are dependent on illicit opioids (PWUO)[15]. OST is a medication-assisted intervention where patients are prescribed opioids such as methadone to alleviate symptoms of withdrawal, reduce drug use and help provide stability. The effectiveness of OST for opioid dependence has been well documented, with positive health, societal and economic impacts evidenced such as reduced morbidity, mortality and acquisitive crime [16-19]. There are over 260,000 PWUO in England [20], of whom 140,000 receive OST [21]. This is an ageing population, vulnerable to premature death, illness and infectious disease [22, 23], who are over-represented in urgent and emergency admissions [24-27]. Late presentation with injecting-related complications is common and retention in hospital care is low [24, 28-30]. This is a serious problem, associated with: reliance on ambulatory care, complex admissions, DAMA, emergency readmission, surgical intervention and high NHS costs [9, 28, 30-40].

PWUO experience high levels of stigma, which can prevent them from help-seeking and contribute to health inequities [2, 26, 31, 41]. Our recent research with PWUO in the UK [42] has found that fear of drug withdrawal due to delayed OST provision in hospital settings is also a primary barrier to treatment access and completion [2, 3]. Experiences of OST delay or omission can cause severe physical and psychological

distress for inpatients and result in DAMA, also ward absences and disruption to obtain illicit drugs [8, 9, 28, 31, 43, 44]. The focus of this proposal is on improving continuity of OST provision in hospital settings with the aim of improving the patient experience, reducing presentation delay, DAMA and emergency readmission.

We undertook a scoping review to inform our proposal and choice of primary outcome measures (DAMA, emergency readmission), searching MEDLINE and EMBASE (via Ovid) on 31/09/2020. We used search terms relating to three domains: OST; health care facility; and outcomes ["delay* OR readmission* OR discharge], excluding sources reporting on neonates [NOT neonat*]. We searched from 1/01/2000 and only reviewed sources presenting empirical data. This resulted in less than 250 unique sources. Timely OST provision for hospital inpatients and at emergency and acute admissions was evidenced to reduce rates of self-discharge and emergency readmission [5, 6, 36, 40, 44-46]. Qualitative data highlighted how the distress of opioid withdrawal could result in self-discharge [2, 8, 9, 30] with case reports cautioning of “the potential morbidity of methadone treatment interruption in the hospital setting” [47]. This evidence strongly suggests that interventions to improve OST provision in hospitals will have an important impact on reducing DAMA.

Systematic review data indicate that 25-30% of PWUO leave hospital prior to completing medical treatment [40]. Patients who leave hospital prematurely are 12 times more likely to be readmitted with a related diagnosis within 14 days, and twice as likely to die [40, 48, 49]. This exacerbates health inequalities among a marginalised population, increases health care system burden and contributes to escalating economic costs [32, 33, 50]. Economic analysis show that the average costs associated with a readmission within 30-days of DAMA are estimated as 56% higher than the costs associated with completing the initial hospitalization [33].

3. Evidence explaining why this research is needed now

Although problems associated with OST delay or omission in hospitals are documented [2, 7-9], this literature has not been systematically reviewed or led to UK intervention development. NHS hospitalisations for serious injecting-related infections have increased annually since 2012 [51] with PWUO having longer hospital admissions than other patients admitted with similar infections, more likely to have unplanned admissions, and to DAMA [32, 40]. Covid-19 has increased pressure on NHS hospitals and exacerbated health inequity among the most marginalised. There is an urgent need for evidence-based, cost-effective interventions for people with complex health conditions, who struggle to complete treatment and are at high risk of emergency readmission.

The NHS Long Term Plan proposes a new service model, comprising redesigned hospital support to relieve pressure on A&Es and free up hospital beds. This includes extensive action to reduce delayed hospital discharges, but self-discharge/DAMA does not feature in the report [52]. This is a key area for intervention. A recent NIHR-funded evaluation of specialist homeless hospital discharge schemes from 2015-2019, also focused on delayed discharge, but found instead that DAMA among the homeless (many of whom are PWUO) was a primary concern [53, 54]. Poor management of substance dependence, including delayed OST provision, on hospital wards was noted as a contributory factor. This also impacted the willingness of hostel residents to seek medical care. Findings highlighted the need for NHS hospital protocols to prioritise stabilisation of drug withdrawal through access to NICE recommended OST.

Our research supports the NHS People Plan of improving workforce culture and training, particularly for nurses [55]. We will work with hospital training and education teams to support continuing professional development (CPD) for nurses who work with a patient population often considered challenging. Our approach is supported by North American research findings showing that inpatient substance dependence assessment and OST provision is associated with improved treatment completion and reduced readmission [6]. Our training component is supported by evidence that training for A&E and urgent admissions staff in substance use management reduces stigma and improves knowledge, attitudes and care for PWUO [56-59].

FORMATIVE RESEARCH

Among 455 PWUO in London, we found that care delay was common and associated with bacterial infection severity and hospitalisation [1-3]. Inpatient hospitalisation for preventable bacterial infection was reported by 30% (137), of whom 40% (55) developed septicaemia and/or endocarditis [3]. A cycle of DAMA and emergency readmission was common. Primary reasons for DAMA were stigma and drug withdrawal due to delayed OST provision [2]. These are modifiable risk factors. Building on these findings, we requested substance dependence policies from all NHS hospital trusts (118 replied) and conducted workshops with PWUO, drug treatment service and hospital staff, to further understand this problem and identify solutions. We found:

- Poor information and care pathways between hospitals and community drug services.
- Inefficiencies in medicines reconciliation leading to delayed or omitted OST dosing.
- Limited knowledge among hospital staff about opioid withdrawal identification and management.
- Inconsistent substance dependency guidelines across hospital trusts: 59 (50%) stated they had no policy.
- A disempowered patient population, who report feeling unsafe in hospitals and lack advocacy support.

This proposal builds on these findings and aims to address the problems we have identified.

4. Aims and objectives

Aim: To optimise OST management in hospital settings nationally to reduce delayed presentation, DAMA and emergency readmission among PWUO.

Research Question: Does the iHOST toolkit reduce delays in OST prescription in two hospitals compared to historical local data, and does this lead to reduced DAMA and emergency readmission of PWUO compared to historical local rates and a national comparator cohort?

Objectives:
1. Optimise iHOST components and test feasibility in a London hospital and associated local drug services.
2. Evaluate intervention acceptability, fidelity, reach, costs and impact in rural and urban settings.
3. Develop and disseminate toolkits for national implementation.

5. Research Plan

This is a four-phase research plan. Phase 1: Optimisation (months 1-8); Phase 2: Feasibility testing (months 9-14); Phase 3: Evaluation (months 15-29) and Phase 4: Dissemination (months 30-36). [see Figure 1]

SITES: Systematic iHOST optimisation and feasibility testing in collaboration with University College London Hospital and linked drug treatment services. Mixed-method iHOST evaluation will be at St James's University Hospital, Leeds, and Royal Stoke University Hospital, Staffordshire and associated drug treatment services.

POPULATION: Hospital patients who are dependent on illicit opioids and/or receive an OST prescription.

OUTCOME MEASURES

Primary: 1. Discharge against medical advice (DAMA)
2. Emergency hospital readmission within 28 days of discharge.

Secondary: 3. Reported inpatient illicit drug use
4. Time between admission, prescription of OST and receipt of OST.
5. OST dose
6. Provider knowledge and attitudinal change.

DESIGN

We employ a quasi-experimental design. Our primary outcomes will be measured through a difference-in-difference analysis [10] of routinely collected clinical data at two iHOST evaluation sites. We will measure the

difference in primary outcomes at iHOST sites compared to the difference at other hospitals in the national database, controlling for patient-level and hospital-level confounders. In-depth qualitative interviews and focus groups will be conducted with staff and PWUO exposed to the intervention for a process evaluation of iHOST acceptability, barriers, and enablers.

Following consideration of a number of experimental designs, including cluster randomised designs, step-wedge trials, and individually randomised trials, we do not plan to conduct a randomised controlled trial of iHOST. This is because we aim to understand the best way to improve access to an evidence-based intervention (OST) in hospitals, and are seeking to generate practical (or 'realist') information about programme design rather than the most robust possible estimate of the effect of the intervention on patient outcomes. Additionally, after discussion with partners, we felt an individually-randomised trial would be unfeasible as the intervention works at hospital-level, and cluster-randomised designs would require substantially more hospital sites to achieve reasonable power.

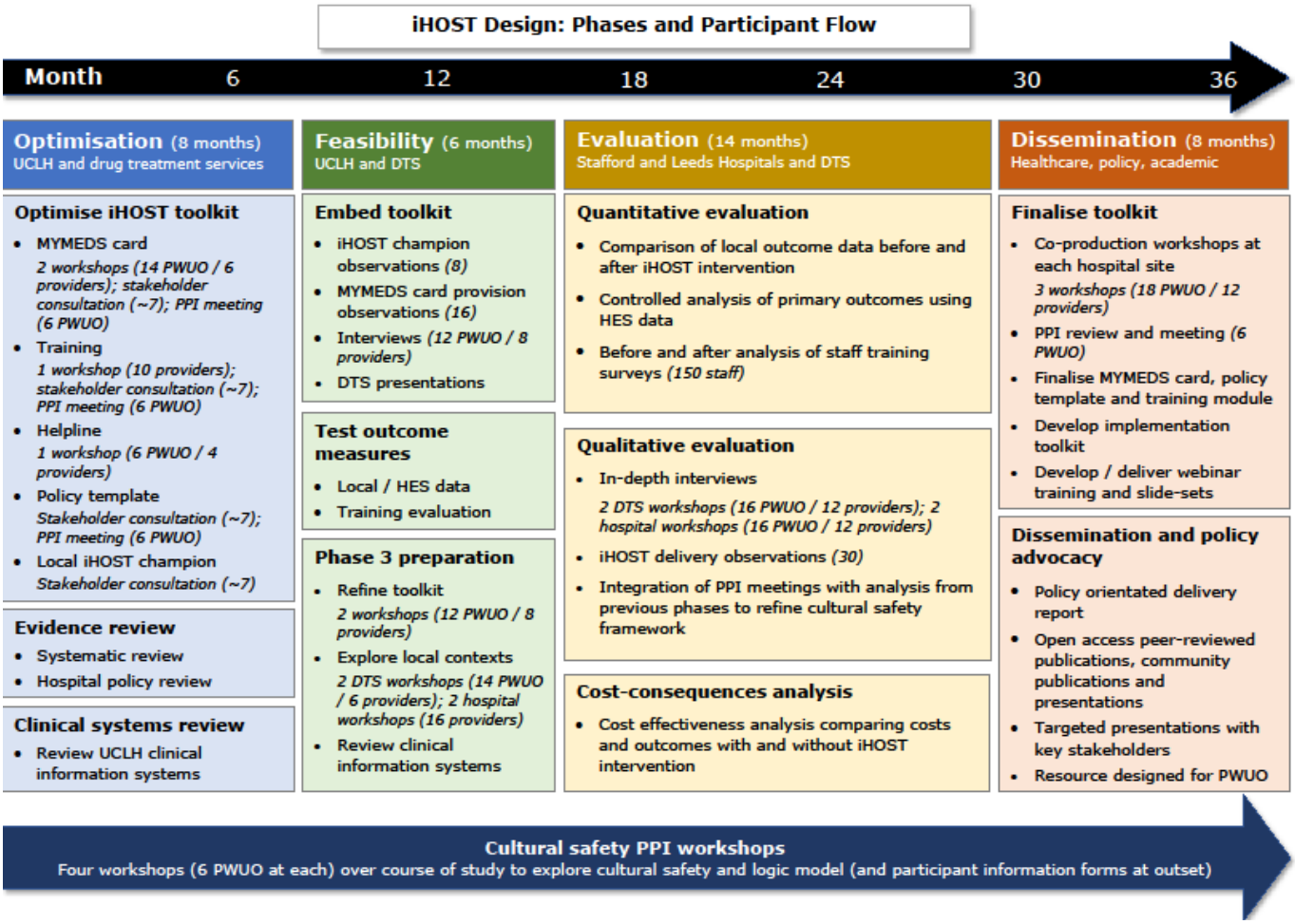

Figure 1: iHOST Phases and Participant Flow

PATIENT AND PUBLIC INVOLVEMENT

iHOST is conceptualised through collaboration of people with lived experience of OST, academic researchers, pharmacists, physicians, drug treatment providers, and public health policy makers. PWUO have been actively involved in the design of the research, and will continue to provide management oversight, with three PWUO confirmed advisory board members. Team member AN is a peer researcher and experienced PPI lead. The PI (MH), has a past history of opioid use and OST, extensive experience in community-participatory research and in training peers in qualitative research methods. We will follow NIHR best practice guidelines for PPI [60] including reimbursements for time. We have a strong track record of

meaningful PPI in research, which facilitates community trust and support as well as a diverse recruitment network to draw on. This, in turn, enables PPI sustainability and diversity.

Qualitative interviews will be primarily conducted by peer researchers – both MH and AN disclose, where appropriate, their personal history to participants: we have found this aids rapport and dispels fear of judgement among highly marginalised PWUO. In 2019 AN attended qualitative methods workshops taught by MH and was supported by her to conduct ten interviews with PWUO in the UCLH hospital setting. These interviews were instigated by the UCLH 'Drug Users Group' of which AN, MH and CIs AS and MB are members. The group was set up in response to problems encountered by ward nurses, such as discharge against medical advice and illicit drug use on the wards. Members of this group have been involved in iHOST conceptualisation and support its implementation at UCLH.

Four PPI meetings are embedded into the project design [Figure 1], in addition to the data generation workshops and focus groups with PWUO. The aim is to provide feedback on each phase progress and findings, discuss future steps and progress co development of the 'cultural safety' conceptual framework. We will ensure the PPI meetings are inclusive, including women, people who are unstably housed and from non-white backgrounds. We have extensive networks in which to do so, including those developed by the PI in her UK-wide work with PWUO since 2009. Output production will follow the model used by the PI to develop previous resources, in that they will be led by, and co-produced with, members of the affected community. Meaningful engagement of all parties will ensure project relevance and acceptability to the affected population, also enhancing the relevance, reach, and transformative potential of outputs.

CONCEPTUAL FRAMEWORK

This research is conceptually informed by 'cultural safety' principles. These focus attention on the way in which dominant cultural expectations of care seeking and systems of health care can be experienced as unsafe by marginalised populations and how providers and systems can change to facilitate equitable care [12, 13]. Cultural safety informed training aims to foster practitioner reflection on the impact of power imbalance and inequitable social relationships in health care, including in relation to personal attitudes and beliefs [14]. A simple visual conceptualisation of cultural risk and safety in health care [61] can be seen in our logic model (Figure 2) whereby the "3 Rs" (recognise, respect, rights) represent safety, as opposed to the "3 Ds" (demean, diminish, disempower). We will use this model as a starting point in study workshops to develop a cultural safety framework with PWUO, to inform practical and theoretical innovations in the field.

THE INTERVENTION

We regard iHOST as a structural intervention. That is, an intervention that promotes the availability, accessibility or acceptability of specific resources needed to improve health outcomes [62]. iHOST is purposefully designed to be pragmatic and practical within the real-world settings of hospital and drug treatment centres. The five iHOST components (My Meds card, hospital provider training, advocacy helpline, policy template and iHOST champion) have been co-produced. Their proposed relationship to short, medium- and long-term outcomes (figure 2) is informed by the team's research, PPI consultation and evidence review.

Our scoping review identified procedural and attitudinal barriers to the effective management of opioid withdrawal in hospital, with medical professionals often displaying negative attitudes towards PWUO, which may impact the care they provide [31, 41]. In the short term, we anticipate the iHOST **training module** and **champion** will help to increase awareness of the importance of managing withdrawal and challenge stigmatising preconceptions held about PWUO, while the information fields on the **MY MEDS Card (**supplemented by **Helpline** guidance if required) will help remove procedural barriers to timely OST medicines reconciliation. Qualitative work has demonstrated that drug withdrawal, and fear of withdrawal is a key factor leading DAMA [2, 63, 64], which is associated with hospital readmission and increased mortality risk related to delays in treatment [[38, 65-68].

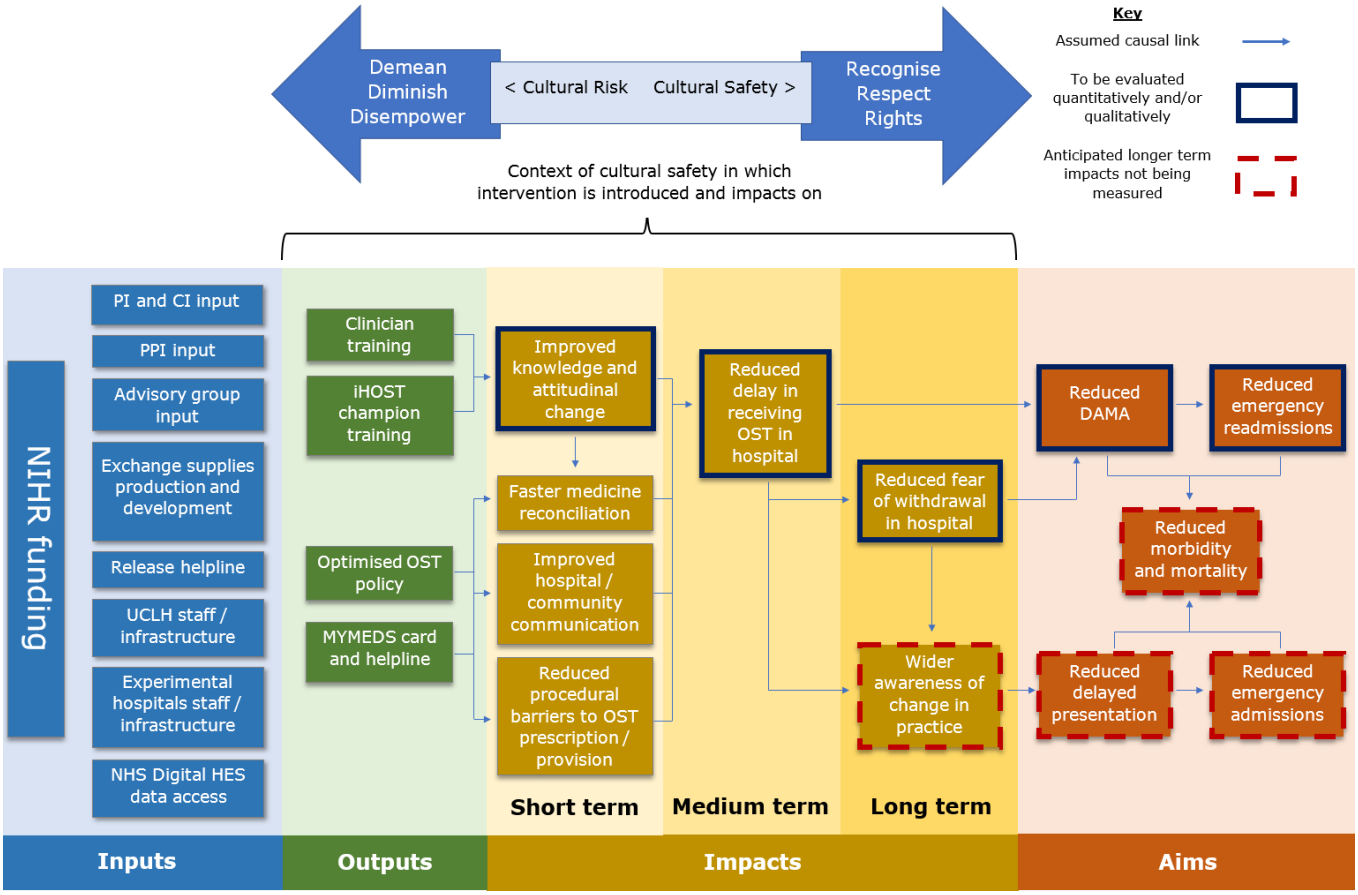

Figure 2: Working logic model

By improving the management of withdrawal and reducing delays in the prescription of OST we anticipate a reduction in DAMA, which will lead to decreasing re-admissions, morbidity, and mortality. Our London-based research with PWUO highlighted how fear of withdrawal informed delayed care seeking, leading to severe complications and hospitalisation [2, 3]. The **MY MEDS Card** and the **Advocacy Helpline** are informed by PPI and cultural safety principles [69, 70] with the aim of helping PWUO feel safer and more confident to seek timely medical care. In the longer term, we envisage that increasing awareness of changes in practice among the wider PWUO community related to iHOST will encourage patients to seek care earlier, leading to improved medical outcomes.

The iHOST intervention comprises:

1. MY MEDS CARD

"We need something like that [card] to take to the hospital to say I've got a right to be treated with dignity" (PWUO workshop participant, Care and Prevent Study, London 2019)

The 'My Meds' card prototype (Figure 3) was co-produced in three London workshops with PWUO and refined in collaboration with hospital clinicians, pharmacy and drug treatment service providers. It is designed to be given to those on OST by their prescriber or drug treatment key worker. We have consulted drug treatment providers CGL, Turning Point, Humankind and NHS addiction services regarding implementation feasibility. Most already liaise with the social enterprise Exchange Supplies who will design, produce and distribute the finalised cards (optimisation, phase 1) to intervention site drug services.

Figure 3. My Meds Card prototype

The MY Meds card is credit card sized, double sided, and generic rather than personalised. **It aims to:**

•Empower people on OST to feel safe to access hospital care and to disclose their medication requirements.

•Enable timely medicines reconciliation: prescriber and pharmacist contacts to be entered by the drug service

• Support patients and staff with specialised OST advocacy and information (Release helpline).

No hospital will prescribe OST on the basis of the card alone. PWUO can choose to take or refuse a card (not mandatory).

The card was developed at the request of service users who valued the prospect of having physical 'evidence' of the right to treatment. On consultation we found that a digital record would be difficult for many to carry or access. This would also require data-harmonisation across multiple prescribing agencies, and data protection measures difficult to agree and complete within the scope of this project. We will scope potential for future digitisation to inform project recommendations (in line with the NHS Long Term Plan).

2. HOSPITAL PROVIDER TRAINING

"People who inject drugs are afraid that when they come into hospital they will be "ignored" and will have to wait for some time before they receive OST. This leads them to "tank up" before coming into hospital - which only serves to reinforce the often negative view that staff have of this vulnerable patient group". (Infectious Disease Consultant, St James's University Hospital, Leeds)

Our consultations with healthcare professionals align with the international literature: PWUO are perceived as a challenging population to manage in the hospital setting. Limited training or skills in working with substance dependent patients can exacerbate tensions and workplace stress. There is a clear need for a dedicated training package that can support development of de-escalation strategies and improve patient-centred care and communication as well as provide education on the specifics of OST dosing and management. We have two specialist addiction pharmacists in our team (JS, RG). JS will lead training development, in collaboration with Exchange Supplies who will host it on their training site. This will be a similar format to their NICE accredited Needle and Syringe Provision training (developed with JS) (Figure 4).

iHOST training will be offered to healthcare professionals and administrative staff in: A&E, Medical Assessment Unit, ITU/HDU, medical and surgical and all Pharmacy staff. The training will be compulsory for the iHOST champions; voluntary for all other inpatient and pharmacy staff. We have sought leadership support by engaging with relevant medical consultants, chief pharmacists and senior leadership teams, which we will continue to engage with during the optimisation phase, to enable maximum participation.

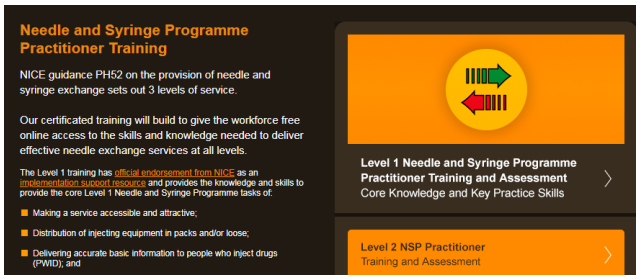

Figure 4. NSP Practitioner Training
https://training.exchangesupplies.org/nsp_training

Our module will follow the NSSCT e-learning format, which includes a mandatory pre- and post-assessment measure of knowledge and attitudes drawing on validated questionnaires. We will monitor how long people are logged on and the percentage rate of completion, with content modifications for dissemination (P4) on basis of usage statistics, assessment measures and qualitative interviews.

The training will be designed to reduce stigma and develop confidence in communications and de-escalation strategies. For healthcare staff, it will also aim to improve understanding of the basic therapeutics and key safety around prescribing and administering OST, using DHSC/PHE guidelines as core underpinning evidence. It will cover key points in induction, titration and discharge planning of people in receipt of OST. There will be an additional section for the iHOST champions, explaining their role and how to deliver it to maximise effect. It will take no longer than 1 hour to complete for clinical staff, up to 20 minutes for non-clinical staff.

3. ADVOCACY HELPLINE

Release has been providing advocacy and legal support to people who use drugs for over 50 years. The organisation set up a specialised helpline in the early 2000s to support people with their opioid use, to help them access OST if that is what they wanted, and to ensure that the treatment they received met clinical standards. The helpline is operated by a specialist nurse advocate and is supported by volunteers - many of whom have lived experience. At the core of the service is ensuring that those who access support are treated with respect and dignity, that they are listened to, and that their rights are realised.

The hospital helpline, advertised on the 'My Meds' card, would work in a similar way to the advocacy work Release currently does. The helpline would operate between 10am and 6pm (with potential for extension dependent on demand). The helpline number can be texted to organise a call back in operating hours. Details would be taken and Release staff would contact the relevant medical team and hospital pharmacist involved in the patients care, as well as liaising with the community drug services responsible for the patient's prescription. A specific, established contact at each of the participating hospitals will be contacted in the first instance when an issue about OST access arises. Release staff would determine the local policy and whether or not there was a drug liaison service available to refer to. The aim would be to ensure that patients were supported to secure their community OST or be assessed and titrated while an inpatient as quickly as possible, and in line with current clinical guidance [71]. Release will collect data on people accessing the service including demographics, relevant hospital trust, and outcomes. This (anonymised) data will be shared with the team as part of the project evaluation on a monthly basis, or as required.

4. POLICY TEMPLATE

We recognize that supportive structures and policies need to be in place in order for healthcare providers to deliver culturally safe hospital care. In collaboration with our advisory group and hospital provider stakeholders we will develop a 'best practice' substance dependence management policy template. This will be optimised in phase 1, tested in phase 2 and refined iteratively throughout the project for finalisation in phase 4. This template will be informed by our NHS Trust substance dependence policy review, through which we have identified models of best practice, including in relation to use of inclusive, non-stigmatising language. It will be clinically based on the current UK Clinical Guidelines [71]. The Specialist Pharmacy Service support this approach, and we will work with them to publicise and disseminate the policy template.

5. IHOST CHAMPION

Champions, defined as "individual(s) who dedicate themselves to supporting, marketing, and driving through an implementation, overcoming indifference or resistance that the intervention may provoke in an organization"[72], will support the implementation of iHOST. This role will be developed with input from key stakeholders during the optimisation and feasibility phases. A role description with responsibilities and clear lines of accountability will be developed. We expect that in each hospital there will be a number of champions, reflecting different clinical roles and wards (e.g. nursing, pharmacy, A&E, ITU etc), who will support their colleagues with implementing the intervention and sustaining this. iHOST champions will be identified by asking relevant teams for volunteers to take on this role. They will receive additional training via the online course (see above). They will take on the role of encouraging the adoption of the intervention, supporting new and existing colleagues to incorporate the intervention into their practice and be a practical source of local information e.g. signpost to community drug teams and local pharmacies.

Delivery plan

PHASE 1 (MONTHS 1-8): IHOST OPTIMISATION

Systematic optimisation of iHOST will be carried out in collaboration with UCLH, linked drug treatment service providers and PWUO service users. Methods comprise workshops, consultations, evidence review.

Output 1: Optimised TOOLKIT

a. MYMEDS card. (Lead M.H, A.N). METHOD: Workshops (n=2). SITES: Margarete Centre DTS, Better Lives DTS. PARTICIPANTS: ~7 PWUO & 3 providers per workshop (n=~20). AIM: finalise information fields, advocacy message and design. CONSULT: PPI advisory group; Exchange Supplies and Drug Treatment providers (NHS Camden & Islington; CGL, Turning Point, Better Lives) to finalise content & design.
b. Training modules (lead J.S, A.P). METHOD: Workshop (n=1) SITE: UCLH. PARTICIPANTS: UCLH A&E, acute admissions, high burden wards, drug liaison; hospital pharmacy staff (n=~10). AIM: Assess local need, workshop content. CONSULT: Key stakeholders (UCLH education team; NHSEI, HEE, PHE OST leads, PPI group); INTEGRATE: emerging evidence review and cultural safety workshop findings.
c. Advocacy helpline (lead N.E). METHOD: Workshop (n=1) SITE: Release. PARTICIPANTS: Release staff (n=4); PWUO (n=6); Hospital providers (n=4). AIM: Assess local need, workshop content.
d. Policy template (lead JS, RG). CONSULT: Key stakeholders (PHE OST leads; SPS Lead Medication Safety Officer, Guild of Healthcare Pharmacists, PPI group); INTEGRATE: NHS Trust policy synthesis findings.
e. 'Local iHOST champion' (lead AS, Research nurse). SITE: UCLH; CONSULT: key UCLH staff (ward sisters, education team etc); hospital drug liaison teams from key sites where collaborative relationships between hospital and drug treatment teams are well established and/or innovative. AIM: produce role description, inform training component (see b).

Output 2: Evidence and systems review

a. Systematic review (lead DL) of the published peer-review literature describing interventions for improving OST provision in acute hospital settings for people who are dependent on illicit opioids.
b. Policy synthesis: (lead JS) Finalise NHS Hospital policy analysis, write up for peer-review publication and to inform template development.
c. Clinical information systems review: (lead DL). Review patient records systems at UCLH, such as EPIC, to determine the feasibility of identifying patient groups and outcome measures. Refine analysis plan if necessary. Consult leadership within the local integrated care system to understand key strategic opportunities for implementation across the health and social care system.

Output 3: Patient involvement set up (lead MH, AN)

PPI workshop #1: Introduce study. Review all PWUO materials for acceptability. Introduce and invite feedback on cultural safety concept and logic model. Explore training or other research support needs. Agree approach and feedback mechanisms for PPI workshops and cultural safety concept mapping over project.

PHASE 2 (MONTHS 9-14): FEASIBILITY TESTING

We will introduce iHOST components to UCLH and linked drug treatment services and assess the feasibility of their practical application and evaluation measures. Findings will be disseminated to PWUO and providers, who, with the advisory board, will advise of pragmatic adjustments to be made to iHOST components and/or evaluation measures before implementing for evaluation (phase 3).

Output 1: Embed and test iHOST toolkit (Lead MH, AN)

a. Conduct non-participant observations of 'iHOST champion' interactions with UCLH staff to assess the acceptability and impact of methods to sensitise staff to the iHOST concept and toolkit. (n=~8 sessions).
b. Present iHOST concept to staff at local drug treatment services (staff meetings), provide MY Meds cards for distribution to their clients and order/delivery links for restocking.
c. Conduct non-participant observations of My Meds card provision in DTS and use at UCLH (where feasible) to assess acceptability and iHOST implementation fidelity (n=~16 sessions).

d. Conduct in-depth interviews with 6 inpatient PWUO, 6 community based PWUO, 4 hospital staff, 4 drug treatment staff (n=20 total) to explore iHOST acceptability, impact on practice, contextual barriers and facilitators to implementation.

Output 2: Evaluate feasibility of outcome measures at UCLH (lead DL, JS)

a. Compare detailed outcomes at UCLH before and after implementation of iHOST. These include process-related measures such as time from admission to provision of OST, and outcome-related measures such as the risk of DAMA.
b. Conduct a controlled analysis of changes in two outcomes (DAMA and 28-day readmission) between UCLH and other hospitals across England, using HES.
c. Assess inbuilt staff training module evaluation measures for training impact on knowledge/attitude, acceptability and reach.

Output 3: Prepare for phase 3 implementation and evaluation (lead MH, DL, RG)

a. Conduct 2 London workshops (Margarete Centre, Better Lives) with 8 providers & 12 PWUO (n=20): discuss findings, assess and collaboratively refine intervention components. Consult: PPI group meeting.
b. Review clinical information systems at the hospital sites, refine analysis plans if necessary.
c. Conduct 4 focus groups: 1 each at STARS (Staffordshire Humankind) and Forward Leeds (Leeds Humankind) services (14 PWUO & 6 providers, n=20), one at each hospital site (drug treatment liaison team & affiliated staff, n=16) to explore local context (current practice, perceived need), iHOST expectations and perceived quality of collaborative relationships between drug treatment and hospital services.

PHASE 3 (MONTHS 15-28): EVALUATION

We will introduce iHOST to the Staffordshire and Leeds sites, where it will be embedded for 3 months prior to evaluation. The lead clinician and iHOST 'champion' will coordinate set up, staff sensitisation and training promotion. UCLH will continue to implement iHOST.

Our methods are informed by the MRC guidance for evaluating complex interventions [73, 74] and will assess fidelity, quality and acceptability, clarify causal mechanisms, and identify contextual factors that may be associated with success. We will use mixed data collection methods including a quantitative measurement of outcomes based on analysis of routinely captured data, qualitative analysis of staff and patient perceptions of the programme, and reporting of the programme structure including patient volumes and costs of implementation. In-depth fieldwork will be carried out at each site to explore how iHOST 'works' (or does not work) from the perspective of PWUO, hospital staff and drug treatment providers [11].

Output 1: Quantitative evaluation (lead DL, VH, AM)

a. Compare detailed outcomes including those not available in HES such as OST prescription rates, time from admission to OST initiation, at Leeds and Staffordshire hospitals before and after iHOST.
b. Conduct a controlled analysis of changes in two outcomes available across all HES data (DAMA, 28 day emergency readmission) comparing those with HES codes identifying PWUO in Leeds and Staffordshire hospitals with other hospitals across England, using HES.
c. Assess the acceptability, reach and perceived impacts of staff training activities through self-complete survey data embedded into the training platform (n=~150 staff).
d. Assess, from dedicated drug treatment service records, MY Meds card uptake among service users.
e. Undertake a cost-effectiveness / cost-consequences analysis of iHOST compared to not providing it.

Output 2: Qualitative process evaluation (Lead MH)

a. Conduct interviews with 8 PWUO and 6 providers at 4 sites (n=32 PWUO; 24 providers): the 2 intervention hospitals and 2 linked drug treatment services. Interviews to explore: iHOST acceptability, perceived impact on practice, barriers and facilitators to implementation and uptake, contextual and

un/anticipated mechanisms of change, additional needs/concerns (ie, discharge planning; other barriers/facilitators to timely presentation, treatment completion and retention in community OST care)

b. Conduct non-participant observations of iHOST delivery at each site and linked DTS (n=~30) to assess iHOST fidelity, quality, local social and contextual factors shaping iHOST implementation and uptake. Observations will be informed by a tool, developed in phase 1, with categories informed by CFIR constructs (intervention, inner and outer setting, individuals involved and process [75]) to enable quick notation of, for example, types and frequency of patient provider interactions, management and recording of DAMA, to also be expanded on in observational field notes.
c. Integrate analysis from Phases 1-3 to refine cultural safety framework with PPI input.

PHASE 4 (MONTHS 29-36) PROTOCOL DEVELOPMENT AND DISSEMINATION

Output 1: Finalise iHOST toolkit (Lead MH, AN)

a. Conduct co-production workshops at each site (n=3, London, Stafford, Leeds) to disseminate findings, consolidate lessons, co-produce & finalise outputs with 18 PWUO & 12 providers (n=30); then PPI review and meeting.
b. In collaboration with Exchange Supplies and Advisory Board finalise protocols and/or hard copies of card, helpline, policy template and training module for dissemination.
c. Develop implementation toolkit for dissemination of iHOST to other NHS trusts.
d. Develop and deliver online live webinar training and slide-sets to accompany the toolkit targeted at commissioners, drug treatment providers, hospital consultants, A&E, pharmacy and high burden wards.

Output 2: Multi-disciplinary dissemination and policy advocacy (Lead NE, MH, JS)

a. Produce a policy-orientated health service delivery report
b. Open access peer-review publications, community publications/presentations.
c. Targeted presentations & meetings with: Public Health England; National Drug Treatment Providers; Specialist Pharmacy Service; NHS England, Royal College of General Practitioners; ICS commissioners.
d. Resource designed by Linnell publications specifically for PWUO to raise iHOST awareness:

Analysis

QUANTITATIVE EVALUATION

Our quantitative analysis of outcomes has two elements: (1) a detailed analysis of OST provision and patient outcomes before and after implementation of iHOST, using data extracted from local clinical systems at iHOST hospitals (i.e. an uncontrolled analysis) and covering all quantitative outcomes and (2) a controlled analysis of the two primary outcomes (DAMA and 28-day readmissions), comparing PWUO in the iHOST sites with other hospitals across England, using patient-level HES from NHS Digital. These two elements will both be implemented during the feasibility stage at UCLH and the formal evaluation at Leeds and Staffordshire hospitals. Depending on local data availability, there may be some differences in the definition of locally measured outcomes between iHOST sites.

1. Detailed before/after analysis based on local data. This will involve comparison of OST provision and outcomes before and after implementation of iHOST. We will derive patient-level data on each outcome and use regression to test whether there is a difference in the outcomes for patients admitted in the 12 months before the iHOST "go-live" date and those admitted in the 12 months after this date, adjusting for potential patient-level confounders such as the reason for admission. Outcomes will be grouped into: (a) patient outcomes in all those identified as PWUO; b) characteristics of OST prescribing in those receiving OST.

a. Patient outcomes in PWUO: Based on phase 1 feasibility work a range of approaches will be used to identify PWUO in the participating hospitals including: free test records of OST prescriptions in the community, and diagnostic coded for opioid use those with opioid poisoning or injecting-related injuries. Outcomes will include receipt of OST during admission; DAMA; and 28-day emergency readmissions (all binary outcomes). The analysis will then use logistic regression to compare the probability of each outcome for this patient group in the 12 months before vs. the 12 months after the iHOST "go live" date.

Sensitivity analyses will use wash-out periods 3 months either side of the intervention, as there may be changes in practice in the run up to the start date and the intervention may take some time to embed.

b. Amongst people prescribed: People who are prescribed OST in the hospital will be identified using pharmacy records. The time between admission, prescription of OST, receipt of OST and the OST dose will be obtained from clinical records. These outcomes have been selected in discussion with iHOST partners, with delays to OST and low doses cited as problems. The base population will be all patients receiving OST. The modelling strategy will depend on the distribution of the outcomes, for example analysis of the time between admission and receipt of OST may use gamma regression.

UCLH has investigated the feasibility of collecting these data. The outcomes can be extracted from pharmacy and discharge summary records. We have identified several approaches to defining the patient group discussed in (b), including searching free-text using CogStack software, and will refine these and potentially conduct sensitivity analysis with different patient groups.

2. Controlled analysis using HES (difference-in-difference [10]). This analysis will involve measuring the change in primary outcomes at iHOST sites before and after iHOST implementation and comparing this change to other hospitals over the same time period. HES does not show whether patients received OST in hospital, and we will therefore need to identify a group of patients who may benefit from iHOST. Our planned inclusion criteria will be all admissions at acute hospital trusts in the 12 months before or after the iHOST "go-live" date, the patient is aged 18-64 at admission, and the patient has an ICD-10 diagnosis of opioid dependence (F11) in any diagnostic position, either in that admission or an admission at any hospital nationally in the previous 12 months. For each admission we will derive the two primary outcomes: DAMA and 28-day emergency readmission. We have previously used HES to measure these outcomes in comparable populations [32, 76] and are familiar with the structure of HES. We will then fit logistic regression models where the dependent variable is the outcome and the independent variables include an interaction term between the iHOST site status and whether the patient was admitted before or after iHOST implementation. We will also include patient-level confounding variables such as age, comorbidities, and the primary reason for admission, and a random intercept for the hospital site. This analysis addresses the question "did the risk of self-discharge/readmission reduce more at iHOST sites than at other hospitals"? Depending on the number of patients with admissions at the same hospital both before and after iHOST "go-live", or at similar dates at iHOST sites and other hospitals, it may also be possible to conduct a sub-analysis of within-patient differences using conditional regression.

3. Cost-effectiveness (CEA) / cost-consequences analysis (CQA). We will perform a CEA and CQA of the iHOST intervention compared to not using it, using the results from sections 1 and 2 above. Both analyses will use an NHS cost perspective and include the cost of iHOST implementation and the costs of hospital visits. The CEA will be expressed in terms of the additional cost to prevent an episode of DAMA within 28-days of discharge. The CQA will present results in a tabular manner and will additionally include outcomes such as the time to OST prescription. We are proposing to use the simpler approach, rather than undertake a more usual cost-utility analysis, because of the limited opportunity to collect data on health outcomes, and the importance of considering non-health outcomes such as measures of OST prescription. Moreover, given that iHOST is likely to be relatively inexpensive to implement, and the difficulty of linking outcomes such as DAMA to future health events, we will restrict the analysis time horizon to the study period; no decision modelling is planned. Appropriate sensitivity analysis will be undertaken.

QUALITATIVE EVALUATION

Qualitative data generation will be informed by a topic guide informed by our review of the literature and Phase 1 PPI. We will explore with PWUO their experiences and perceptions of health issues, the barriers and facilitators to care seeking, and retention in hospital care. We will orientate toward understanding iHOST acceptability in its local context, but also how this might be improved, and extended (for example, in relation to hospital discharge planning; improvements in community OST treatment and access to primary care). We will undertake non-participant observations, using an observational tool informed by CFIR constructs [75] and through narrative field notes, to understand the local contexts, quality of iHOST implementation, and

contribution of each component toward change (including those unanticipated). With interviews, observations will help build a picture of how the hospital environment, including dynamics of staff-patient interaction and local policies (such as 'conduct contracts') impact the experience and feelings of 'safety' among PWUO, also to understand how/ in what way these are amenable to change.

All interviews and focus groups will be recorded (with the consent of participants) and transcribed verbatim. Interview field-notes and analytical memos will be generated throughout and integrated alongside transcripts in analyses. The PI is an experienced qualitative researcher and will lead analysis. Her approach is informed by constructivist grounded theory principles [77], with analysis beginning alongside and informing ongoing data generation. Initial coding will be inductive, comprising 'open' codes. This will inform the development of a coding framework, and subsequent second level coding and theory development. Preliminary analysis of qualitative datasets will also be conducted in collaboration with PPI working groups, with a focus on co-producing a cultural theory framework grounded in participant data, with meaningful explanatory value for both PWUO and health care providers. This will be iteratively developed, with initial concepts tested through further fieldwork and refined in discussion with multiple stakeholders (see synthesis below).

Our qualitative data will be analysed through triangulation using: (a) multiple forms of qualitative data (interviews, focus groups, observations); (b) multiple forms of participant perspective (service providers, service users); (c) multiple intervention sites; and (e) multiple time points (pre/post intervention). To this end we will employ a triangulation protocol, informed by the six-step process developed by Farmer et al [78]. This involves, for example, using a convergence coding matrix to summarize similarities, differences and points of 'silence' between observational, PWUO interview, and staff focus group data, including at each site and time-point. Through triangulation we will aim to understand the relative effect of each iHOST component on our primary outcomes, as well as the combined or interdependent effects of the iHOST intervention as a whole. This will take place alongside exploration of how local social contextual factors shape iHOST delivery, acceptability and impact. The primary focus of triangulation will be to identify congruence and divergence, including deviant cases for further follow-up or investigation, as well as to maximise the confidence with which judgements are made regarding potential relative intervention effects.

MIXED METHOD SYNTHESIS

Throughout we will triangulate our qualitative data with the quantitative outcomes data to aid interpretation as well as build hypothesis regarding the likely pathways of intervention effect, which in turn will provide grounded data to inform modelling of potential future impacts under different intervention conditions. Quantitative and qualitative data collected at each phase will be analysed separately. Initial findings from each dataset will be then brought together, throughout the project, and triangulated with attention to instances of congruence, dissonance and silence. This will be informed by use of a modified triangulation protocol and convergence coding matrix [79], which – in combination with ongoing team and PPI discussion – will lead to the development of "meta-themes" [79], to provide a more holistic interpretation of intervention effectiveness and the factors critical to success or failure.

Research team meetings will provide an opportunity to critically appraise the evidence as it emerges, deliberate on key findings, resolve and explore any 'inter-method discrepancies' arising from triangulation [79] and shape the direction of the study. Summaries of the mixed method findings pertaining to each evaluation site will be discussed and refined in research team meetings to enable the building and testing of explanatory theories in relation to our outcome measures. We will, for example, be attune to the way in which qualitative interview and observational data enables capture of secular changes at intervention sites to inform before/after analysis interpretation, also to contextual site-specific factors such as discrepancies in staff recording practices of discharge against medical advice, ward absences and inpatient illicit drug use.

Our mixed method synthesis activity scheduled for months 28-33 will involve an iterative process of disseminating and further synthesising these findings, through workshops with the team, PPI and relevant stakeholders to discuss and refine our mixed-method interpretation with attention to considering the

transferability and scalability of iHOST across diverse NHS settings (with or without iHOST adaptations). We will also invite feedback through website and webinar dissemination of preliminary findings, drawing on the approach of Fulop et al. [80] who held a series of mixed media events to engage diverse range of participants to reflect on how the interpretation of mixed-method findings could inform successful system change to improve stroke outcomes, and the potential transferability of their findings to other conditions. Our final analysis and recommendations for policy, practice and service delivery will be based on the combined learning from these synthesis workshops.

REVIEW STRATEGY

We will carry out a systematic review of peer-reviewed research that evaluates interventions aiming to improve opioid substitution therapy in acute hospital settings. The review aims to inform a template policy for opioid substitution therapy and management of opioid dependence in acute hospital settings in the UK. We will search MEDLINE, EMBASE, PsycINFO and CINAHL for articles that include the following concepts in the title and abstract fields:

Concept 1, Acute hospital settings: "hospital*" OR "inpatient" OR "emergency department" OR "accident and emergency" OR "admission" OR "surg*"

Concept 2, Opioid agonist therapy: "opioid agonist therapy" OR "opioid agonist treatment" OR "opiate substitution therapy" OR "methadone" OR "buprenorphine" OR "medication assisted treatment" OR "medications for addiction treatment" OR "medication for opioid use disorder"

The population included in this review are patients at acute hospitals who are dependent on opioids, including those who use illicit opioids such as heroin and those who have prescriptions of opioid agonist therapy (methadone or buprenorphine or other substitution medicines prescribed for opioid dependence). Where some study participants are eligible but others are not (e.g. the study includes both outpatients and inpatients), we will exclude studies where more than 25% of participants are not eligible, see criteria below:

Inclusion criteria:

(1) Participants are patients at an acute hospital, either as an inpatient or in accident & emergency / emergency department.

(2) Study participants have a history of using illicit opioids or are prescribed opioid agonist therapy. Participants may use alcohol or other drugs in addition to opioids.

Exclusion criteria:

(1) Participants are outpatients.

(2) Participants are patients at a specialist mental health hospital.

(3) Participants have no history of using illicit opioids.

(4) Participants are newly born babies (for example being treated for neonatal opioid withdrawal syndrome)

We will limit the review to studies published in the English language, and will not limit by date, country of study, or study type. We will include both quantitative and qualitative studies. We anticipate that the review will include various study designs, interventions, and outcomes. For example, we will include studies that compare patient outcomes associated with different opioid substitution regimes, studies that evaluate non-pharmacological approaches to improving access to opioid substitution such as peer support, and studies of the benefits associated with improved continuity of opiate substitution between community and hospital settings. Studies must compare outcomes with and without the intervention. This comparison may be quantitative or qualitative. The comparator may be defined as "treatment as usual" or alternative OAT strategies. Given the likely diversity of studies included in the review, we will not conduct a standardised risk-of-bias assessment. For each study, we will identify key limitations in the study design so that these can be summarised in analysis. We will describe the quality and results of these studies in narrative review, and we plan to use a "realist review" [81] framework to build a theory-based framework for the potential benefits of opioid substitution in acute hospitals. A "realist review" approach aims to summarise evidence on "what works for whom, in what circumstances, in what respects and how" [81]. The review protocol has been registered on PROSPERO [# CRD42022313237} and is available at this link: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022313237

Population:

Our target population for the iHOST intervention are hospital patients who are dependent on illicit opioids and/or who receive an OST prescription.

Inclusion criteria: PWUO: People who are prescribed OST in a community setting for illicit opioid dependence; 18 years or over; assessed as capable to consent (not in debilitating withdrawal or intoxicated); presenting at A&E, an acute admissions ward or inpatient at one of the hospital sites OR a client at one of the linked drug treatment services. Providers: healthcare staff involved in the prescribing, supply or administration of medicines to patients within A&E, acute admissions and high burden inpatient wards; staff at linked drug treatment services.

Exclusion criteria: under 18; in secure services; lacking capacity for informed consent; no history of opioid dependence or (for providers) OST related service provision.

Participant information materials and consent process: Recruitment flyers and participant information sheets will be designed with PWUO members of our advisory group and taken to the first PPI meeting for checks and finalisation. All participants will be provided with a verbal summary of the research, including data confidentiality and management procedures with the opportunity to ask questions before providing written consent. Information sheets will include additional contacts, such as a research ethics representative and participants will be invited to leave their contact details if they wish to receive study reports, summaries and other outputs.

Reimbursements: All qualitative research participants will be reimbursed for the time: £20 for interview, £40 for focus group and workshop participation. This is in line with current procedure at LSHTM, including for reimbursing PWUO participants in other of the principal investigators (PI)'s research studies.

Setting/context

Phases 1 & 2 (Optimisation, Feasibility): University College London Hospital (UCLH); University College London Hospitals NHS Trust; drug treatment services in the area served by UCLH (NHS Camden and Islington; HumanKind; CGL; Turning Point; Westminster Drugs Project) and GP shared-care services with a high proportion of PWUO clients (such as CHIP, Camden).

Phase 3 (Evaluation): St James's University Hospital, Leeds Teaching Hospital NHS Trust; Royal Stoke University Hospital, University Hospitals of North Midlands NHS Trust; linked drug treatment services (operated by Humankind: Staffordshire Treatment and Recovery Service (STARS), Forward Leeds).

Phase 4 (Dissemination): we will work with all the sites above (London, Staffordshire, Leeds) to disseminate findings and co-produce outputs.

These sites have been purposefully selected to represent different geographical contexts and high proportion of PWUO A&E and impatient admissions. A brief overview of the sites involved:

LONDON: is home to a large street homeless population and is the only UK city with a statistically significant increase in the number of young opioid users (15 - 24 years). UCLH primarily services the urban boroughs Camden, Islington, Haringey and part of Westminster. For 2019/2020 the number of adults on treatment for opioid use in these boroughs was 980, 880, 745 and 515, respectively (total 3120). UCLH report that 208 inpatient admissions between 1 April 2019 and 31 March 2020 included a methadone prescription. The majority were in infectious diseases, emergency or acute admissions wards. Including those treated for complications of opioid use (such as injecting-related skin abscesses), and those where illicit opioid use is recorded in structured data, this number rises to 500 unique patients per year. A small (1.5 WTE) UCLH Alcohol and Drug Liaison Service cover all wards and departments, including partnership working with community services for onward referrals.

STAFFORDSHIRE: is a largely rural area which is relatively affluent but with a few notable pockets of high deprivation. Based on the 2015 Index of Multiple Deprivation, 49 of Staffordshire's 528 lower super output areas fall within the top 20% most deprived nationally. For 2019/2020 the number of adults on treatment for opiate use in Staffordshire was 1685 (NDTMS). The Royal Stoke University Hospital is a general hospital

serving a population of around 700,000 in Staffordshire, as well as providing specialist services to patients from beyond the region. (Staffordshire Evidence Base: Population Demographics and Adult Social Care Needs February 2019) Staffordshire Treatment and Recovery Service (STARS) is the community drug treatment provider for Staffordshire, which is operated by Humankind.

LEEDS: is the fourth most populous urban area in England. For 2019/2020 the number of adults on treatment for opiate use in Leeds was 2705 (NDTMS). St James's University Hospital is Europe's largest teaching hospital, providing local and specialist services for its immediate population of 770,000 and regional specialist care for up to 5.4 million people. In 2019/20 the hospital in-reach (liaison) team reviewed 1044 individuals. The local drug treatment provider is Forward Leeds, operated by Humankind and delivered in partnership with Leeds and Yorkshire Partnership NHS Foundation Trust.

Sampling and Recruitment

All qualitative recruitment and data collection will be subject to COVID-19 contingency measures, that the team are familiar with implementing over the past year. These include facilitating remote interviews with PWUO participants (via phone) and we have procedures in place for ensuring informed consent is through and ethical when conducted via remote means. Our PPI lead has been working with PWUO throughout the pandemic as part of his NHS outreach work as have many of the team members.

• **Clinical review:** We used simulation to estimate that approximately 250 patients per intervention site would be needed for 80% power to detect a 33% reduction in risk of self-discharge; and initial engagement with intervention sites suggests 400-500 PWUO are admitted per site per year. No active recruitment is required: only routinely collected patient data will be analysed.

• **Staff Training evaluation**: From communication with the sites, we estimate at least 300 providers in A&E, acute admissions and high burden wards eligible for training across hospital sites. An evaluation component will be built into the online training platform, comprising validated knowledge and attitude evaluation measures. Training will be promoted throughout the sites, including by the 'iHOST champion' but will not be mandatory. We anticipate 50% take up of training (n=~150), sufficient to assess training reach, acceptability and knowledge/attitudinal impact.

• **Qualitative**: PWUO participants will be purposively sampled for in-depth interview and focus group for variation in My Meds card uptake and use; location (community and hospital); age and gender. Providers for variation in role and location (community vs hospital). Sample size (n=~36 PWU0, ~24 providers for interview, ~14 PWUO, ~22 providers for FG) allows for theoretical sampling and thematic saturation.

Recruitment method: PWUO who access drug treatment services in Leeds, Staffordshire or the boroughs proximal to UCLH (Camden, Islington, Haringey and Westminster) will be offered a My Meds card by their drug treatment service provider during a routine visit. They will not be actively recruited for qualitative data generation. The community sample to be interviewed and/or take part in focus groups will be recruited via study flyers. This 'arm's length' recruitment method removes any sense of obligation or coercion that might be present if invited to participate by providers or researchers. Recruitment notices will be in the waiting room (on the noticeboard, at front desk, etc.) with two options for PWUO to get in contact (directly, via phone or email or indirectly - by letting a service provider know). The latter option will ensure that those without access to a phone or computer are not disadvantaged (service providers will liaise with the research team to establish contact). We will work with services to ensure equal access for people with poor literacy. This might entail key workers mentioning the study to people who cannot read, if deemed appropriate.

A similar process will take place at the hospital sites, with flyers available in A&E, admissions and high burden wards. In addition, given potential logistical issues with flyer visibility and access, we will ensure that all patients deemed eligible (on OST in community) receive a study information flyer at an appropriate time during their admission or inpatient stay (ie, when not in pain/distress, etc.). Patients can either contact the research team directly if interested in taking part or let a provider know, who will then liaise with us. All interested people will have the opportunity to ask questions about the research and will be invited to

answer screening questions, including in relation to gender, ethnicity and housing status. We will purposively sample to ensure variation, with attention to representation from particularly marginalised groups.

6. Dissemination, Outputs and Anticipated Impact

We have a multi-faceted dissemination strategy, designed to translate our research findings into practice and informed by the expertise of key stakeholders, including PWUO. We will coordinate communications teams within LSHTM, Humankind, UCLH and collaborators such as Release, to foster effective findings dissemination. The Advisory Board will inform dissemination strategy, with additional specialised input sought from members of Addiction Professionals, the College of Mental Health Pharmacy, Society for Study of Addiction and Collective Voice. Peers will be actively involved throughout (including as members of the Advisory Board), with outputs co-created and tailored to reach diverse audiences. Together we will target acute NHS trusts including local Medication Safety Officers, Local Authorities and Integrated Care Systems, drug treatment service providers and other key stakeholders for research updates, tailored policy briefings and presentations. Peer-review publication will prioritise multi-disciplinary dissemination, targeting journals such as Addiction; BMJ; Social Science & Medicine. We will work with our Universities' Press Offices to engage the wider public with the research and use our project's Twitter account to develop dialogue and gather feedback about the findings.

We have strong collaborative working relationships with the key drug treatment service providers. JS and RG are lead pharmacists for Turning Point and Humankind, respectively and we have CGL representation on our advisory board. Findings will be shared with local service staff, employed by Humankind and with key partners, such as Leeds and York Partnership NHS Foundation Trust who deliver the community drug treatment service in Leeds. Key learning will be shared pan-Humankind, CGL and Turning Point, across all applicable services nationally via established governance and service user forum structures. We will publicise and disseminate findings though key provider forums, such as Collective voice, NHS Alliance and national drug treatment service pharmacy and medical lead meetings which are attended by team member RG. In 2021 MH presented the iHOST concept in invited presentations for: the Annual CGL National Harm Reduction forum (attended by 119 providers); the RCGP & SMMGP Managing Drug & Alcohol Problems in Primary Care Conference; the Addiction Professionals Webinar and the New York University Center for Opioid Epidemiology and Policy seminar series. She has open invitation to return to present project findings.

Findings will also be disseminated through traditional academic channels: peer-reviewed publications (highly regarded public health, social science and clinical journals), conferences attended by a range of professionals (such as) widely accessed magazines (e.g. DDN) and through our team's existing memberships (e.g. Addiction Professionals, Royal Pharmaceutical Society, British Infection Association) and international links (e.g. College of Mental Health Pharmacy, NYU Opioid Center). A report summarising main findings and recommendations will be publicly available through the LSHTM website and other appropriate forums.

The team are committed to disseminating research findings to community groups and project participants, including through social media (YouTube videos, blogs) and articles for community publications and websites such as DDN, Black Poppy and Injecting Advice. Article links will be sent to DrugWise Daily for inclusion in their news bulletin. We will also present findings through community forums, such as the Camden Drug and Alcohol User Involvement Group and at conferences attended by PWUO and harm reduction activists such as DDN National Service User Involvement Conference and the International Harm Reduction Conference.

Intended outputs:

1. The iHOST toolkit
    - The staff training module will be hosted on the Exchange Supplies training platform. It will be free to access by NHS staff, and contribute to CPD. We will seek to have this endorsed by NICE
    - iHOST champion role description and resource pack for NHS Trusts.
    - My Meds card template, purchase and information links for drug treatment services/commissioners
    - Policy framework template and best practice guidelines for OST provision in secondary care settings.

- Dedicated patient and provider OST helpline, incorporated in Release's advocacy support services.

2. Cultural safety framework developed with PWUO over the research duration.
3. Peer-reviewed publications (systematic review, protocol, policy review paper, > 3 findings papers)
4. Articles in publications aimed at: addiction specialists; healthcare providers and PWUO.
5. Resource designed by Linnell publications, informed by PPI and targeted toward PWUO.
6. International and national conference presentations.
7. Full study report detailing the research, findings and its policy, managerial and practice implications.
8. Project blog/website and Twitter account to disseminate lay information about the study.

We will work with the Specialist Pharmacy Service to ensure our OST toolkit, including our national framework for OST provision in hospitals, is brought to the attention of Medication Safety Officers from every NHS Trust. We will undertake a launch Webinar using the Specialist Pharmacy Service platform. We have hosted previous webinars using this platform to inform the design of this study and will make the toolkit available via their website as well as through the Exchange Supplies site (familiar to Drug Treatment services). This project aligns with Public Health England priorities. Local Authorities selected as Accelerator areas are receiving PHE and Home Office funding for 'whole-system' interventions to reduce drug crime and deaths. Hospital continuity of care is included in the 'menu of interventions' for 'Accelerator' and 'universal' grant funded areas. Given our complementary focus and previous work with PHE, we are confident that we can work with PHE and affiliated organisations to translate our research finding into policy and practice.

Community engagement

The affected community are active in the initiation, design, and process of the study and will work with the research team to translate findings into meaningful and transformative practice. The PI (MH), coming from a 'service user' background, has an established track-record of working with PWUO in the design, implementation, and outcomes of research. Previous co-produced research outputs include social media YouTube videos and the booklets 'Hep C Info' and 'Hep C Care' – developed through workshops with people living with Hepatitis C. Both have strongly resonated with the affected community: the videos are incorporated in peer training and the booklets received British Medical Association 'highly commended' Patient Information Awards. We will work with our advisory committee to develop innovative knowledge translation strategies and have costed for development of patient-orientated resource at the dissemination phase. The project has received written endorsement from the body of Addiction Professionals, the Royal Pharmaceutical Society and Leeds Adults and Health Commissioning Manager, as well as informal verbal endorsements from stakeholders such as Public Health England and Change Grow Live. In collaboration with these organisations we will work to disseminate our research widely to service providers and commissioners including through webinars, news items, conference presentations, clinical updates and policy advocacy.

Anticipated impact

Should iHOST be proven to be effective and cost effective, we anticipate downstream effects to include:

1. Roll-out of simple low-cost interventions on a national scale to improve access to and retention in secondary care among PWUO.
2. Improved care coordination between local drug treatment services and hospitals. This will enable information sharing optimisation, such as embedding OST scripting data into existing and future electronic health record systems.
3. Improvements in hospital discharge planning and co-ordination of follow up community care for PWUO.
4. Increased engagement in community OST treatment among treatment naïve PWUO.

These impacts will directly benefit both patients and providers. Our aim is that iHOST promotes a culture change in which PWUO feel more confident to access the care they need, and better supported to complete their hospital treatment. Enabling timely hospital care has broad patient benefit for this marginalised population. Positive treatment experiences can facilitate health care access for addiction and other chronic health issues. Improving the PWUO patient experience will also benefit providers, many of whom currently struggle with a patient population considered 'challenging'. Our training will provide skills in de-escalation

strategies and culturally safe communication to support staff in providing patient centred care. This will help create a calmer environment and help staff to feel more confident in their role.

7. Project timeline

Activity	Mth *0-3*	*4-6*	*7- 9*	*10-12*	*13-15*	*16-18*	*19-21*	*22-24*	*25-27*	*28-30*	*31-33*	*34-36*
Ethical and R&D approvals												
PPI workshops/review												
Systematic review												
Policy synthesis												
Clinical systems review												
iHOST optimisation workshops												
Test iHOST @UCLH												
Baseline FG @ Leeds & Stafford												
Qualitative interviews												
Clinical & HES data extraction												
Qualitative analysis & triangulation												
Mixed-method synthesis												
Peer review publications												
Dissemination activities												

8. Project management

A senior project manager will be employed at 0.5 fte to work closely with the PI and oversee the day-to day financial and administrative management of the project. They will act as a first point of contact for all team members, and ensure effective communications with academics, implementers and administrative staff within the collaborating institutions. The project manager will be responsible for the management and control of the project budget, and ensuring all procedures are in line with LSHTM and funder regulations, liaising with the School's Research Operations Office and the School's finance office. They will track project progress and report against key milestones, targets, and deliverable dates, to the Strategic Oversight Group, other collaborators, and the funder.

Research team meetings with the research fellows, research nurse, PPI lead, PI and core CIs will be held weekly or fortnightly, as appropriate. These will provide line management support to the RFs but also an opportunity to critically appraise the evidence as it emerges, deliberate on key findings, and shape the direction of the study. Points of convergence and divergence will be explored, along with gaps in evidence and understanding, to inform decisions about subsequent field work and the focus of further observation and inquiry.

The **Strategic Oversight Group** (SOG), comprised of the PI, CIs and Project Manager, will meet every six weeks to update on research progress, review the allocation and feasibility of forthcoming research tasks, discuss problems arising and be kept abreast, by the project manager, of progress in achieving objectives on time, within budget, and keeping the project in scope. A **Study Advisory Group** (SAG) will oversee the conduct, governance and delivery of the project, meeting once every six months with the PI and core CIs to discuss and review progress. The SAG will consist of senior academics, clinicians and drug treatment providers from relevant fields, also three PWUO representatives (Erin O'Mara, Chris Hallam, Mat Southwell) with experience of working with OST guidelines and/or community OST advocacy.

The PI, will also liaise closely with the Sponsor and funder, NIHR, to provide updates on the progress of the project as required and to discuss any study design, conduct, governance and delivery issues as they arise (for example, in relation to substantial amendments and COVID-19). The PI will also liaise closely with the respective R&D Offices involved with this project, including University, NHS, Local Authority and Third Sector R&D Offices who provide research management support and advice.

ETHICS AND REGULATORY APPROVALS

Ethical approval will be sought in parallel from the NHS Research Ethics Committee (NHS REC), Health Research Authority (HRA) and from the LSHTM ethics committee as soon as the project starts. Data collection will not start until ethical approval for the project has been obtained from both LSHTM, HRA and NHS REC review committees. Preparation of protocols for ethics, participant information sheet and consent form, and other supporting documentation for consideration during NHS and LSHTM ethical review will be a priority as soon as the project starts and will be finalised within the first three weeks of the project. We will involve PWUO service users in the development of participant information sheets and consent forms so that the information is as clear and understandable for research participants as possible. MH will attend the meeting at which the NHS REC will consider our application. The NHS REC will give us ethical opinion on our application within 60 calendar days of receiving the application. All project staff involved in primary data collection, data management, and analysis will be required to update their research ethics training requirements to the standard expected by LSHTM (i.e. successful completion of LSHTM research ethics/good research practice trainings or equivalent at other institutions). All LSHTM-based staff have completed GDPR and data protection training. The project team will develop a data management plan, as required by the LSHTM, with support from the LSHTM Library & Archives Service.

Consultation has taken place with service user contacts as well as key health care workers to ascertain that the design of the project does not place any undue burden or risk on potential participants. The PI (MH) has a strong track record of conducting qualitative research with people who use illicit drugs. She and the peer researcher (AN) are cognisant of ethical issues concerning work with vulnerable populations and are attuned to any indications of drug withdrawal and/or intoxication which could impact consent. It is critical that participants do not feel coerced into the research. At all stages of the study it will be emphasised that participation is voluntary and that all care and services provided to participants by the recruiting sites will not be affected in any way should they decide not to participate. Participants are free to withdraw from the interviews and study at any time, and without reason. The team has strong collaborative links with the main drug service providers in the UK and will ensure that all participants have the option of referral to support – including after qualitative interviews if necessary.

All participants will be informed of what will happen to their data and measures taken to ensure confidentiality, prior to providing consent. Qualitative interviews and focus groups will be recorded on an encrypted audio recorder in line with LSHTM standard protocols. Audio files will be destroyed once transcribed. De-identified transcripts will be encrypted and stored on password protected computers located at or provided by the University. These will be accessible only to select research team members (primarily the PI and the qualitative research fellow). Hard copy consent forms with personal details will be stored in a locked filing cabinet in the PIs University Office. The transcription agency will sign a data sharing agreement. For the quantitative component, all patient data will be accessed and analysed only within the

participating NHS Trusts' secure networks. All staff will conduct their research activities in compliance with the requirements of the GDPR and the UK Data Protection Act 2018.

PROJECT TEAM AND EXPERTISE

We are a multi-disciplinary team with expertise in social science, pharmacy practice, implementation science and health economics who have a considerable track record of work in these areas.

MH leads a mixed-method programme of research on health intervention for PWUO in the UK, including through NIHR projects. She has 17 years' experience in qualitative and participatory research with PWUO and holds the 2020 Society for the Study of Addiction Award for Impact on Policy and Practice.
AH, Director of the UCL Institute of Epidemiology & Health Care and NIHR Senior Investigator, has over 20 years research experience on marginalised populations leading to policy change and service improvements.
DL, Specialist Registrar in Public Health, holds an NIHR fellowship at UCL. He has expertise in analysis of electronic healthcare records and has published widely on healthcare quality for PWUO.
VH, Professor of Public Health has over 20 years' experience of research and public health practice related to improving the health of PWUO. He will support quantitative data collection and analysis.
JS, Senior (Clinical) Lecturer in Pharmacy Practice, has expertise in intervention development in community pharmacies including online training development, previous clinical experience in hospital pharmacy and current clinical experience in a community drug treatment team.
SS, Associate Professor in Health Economics, has expertise in the measurement and understanding of the costs of chronic illness – including HIV, TB, chronic non-communicable diseases, and HCV.
RG, Director of Pharmacy for Humankind drug treatment providers, has clinical and research expertise in the management of substance misuse, psychiatry and pharmacy practice in primary and secondary care settings
AS, Find and Treat lead for UCLH, co-ordinates a programme of outreach care for homeless, has published widely on inclusion health for marginalised populations and has extensive experience in operationalising public health interventions amongst vulnerable populations.
AN, is a peer worker with UCLH Find and Treat. He has lived experience of OST, has received research training from MH, has experience in interviewing PWUO about hospital care access and will act as PPI lead.
NE, Executive Director of Release, has extensive legal, advocacy and drug policy experience.
MB, consultant physician in Infectious Diseases and Acute Medicine, UCLH, has led and published on implementation of point of care testing (proposed at UCLH for OST assessment) in acute settings.
PL, Consultant in Infectious Diseases, with a special interest in emerging infections, HIV, blood borne viruses and working to improve medical care delivery for patients who use opioids.
AMM is Emergency Medicine Consultant and Clinical Director for Emergency and Acute Medicine at Tertiary Major Trauma Centre and will be the clinical project lead for the Staffordshire hospital site.

9. Success criteria and barriers to proposed work

The potential risk of pre-existing stigma and prejudice is a barrier to engagement by PWUO and staff. We mitigate this risk firstly, by engaging PWUO through our peer researchers. MH has over 17 years' experience in research with PWUO and AN is an experienced peer outreach worker. Both have strong track records of developing trusting research relationships with people from marginalised communities. Secondly, we will also use a peer model to engage staff: the 'iHOST champion'. We are working closely with a research nurse in Phase 1 to develop this role description with the aim of promoting sustainability. Staff turn-over has here been identified as a risk. The voluntary nature of the training offer is a risk to uptake. The champion model is designed to promote engagement, which will be badged as contributing to continuing professional development and staff will receive a certificate from Exchange Supplies on completion to evidence CPD.

Project activities: We will monitor our progress against a set of activity indicators which will reflect the activities as defined in Section 7 (above) and the planned timelines detailed in Section 8 (e.g. systematic review completed at six months). Our criteria for success will be the completion of each activity in accordance with the project timeline. For dissemination activities we will endeavour to ensure we are impactful by: seeking to place publications in high-impact journals, nurturing our social media presence (e.g.

by producing regular blog posts), ensuring we leverage our collective experience of adult learning and teaching to inform our training, and committing to best practice when engaging service providers and service users in project activities. Our success criteria will reflect our performance against these ambitions.

Project outputs: Our intention is to co-produce - with service providers and service users - an activity/indicator matrix to measure project outputs (i.e. the direct results of the intervention component of the project and the dissemination of the research). This will be an early output of the steering committee. The steering committee will also be responsible for monitoring the progress of the project against the project output indicators. The criteria for success will be good performance against these indicators.

Grant management: LSHTM, alongside partner organisations, is committed to transparent, accountable, and responsible grant management. Additional success criteria relate to adherence to the terms and conditions of the funding award, timely reporting, minimal environmental impact, responsible budget management.

Risks and mitigations

Risk	Risk type	Mitigation
Worsening situation around COVID-19 prevents or complicates qualitative data collection (Phase 3, Output 2)	Risk to completion of the project as planned (i.e. risk to the qualitative component). Health and safety risk	We will collect data remotely. LSHTM has published guidance on remote data collection ('Remote data collection for public health research in a COVID-19 era').
Dissolution of partnership limiting access to PWUO and intervention sites	Risk to completion of the project as planned (i.e. risk to the qualitative component).	We have included multiple partners, including as co-applicants. We have sought express commitment to support the study from partners.
Health databases do not include accurate or complete data for DAMA and readmission within 30 days of discharge (Phase 3, Output 1)	Risk to completion of the project as planned (i.e. risk to the qualitative component).	We have sought confirmation from UCLH that the necessary indicators are collected routinely. Co-applicants have investigated feasibility of collecting these data and though indicators may be collected differently we are confident regarding interpretation.
Difficulty retaining service provider and service user representatives (for steering group and PPI)	Risk to the quality and accountability of the project.	We have sought explicit and earnest commitments from community groups. We will stay in regular contact with people and give special care to how we carry out PPI so that participation is not tokenistic and there is regular and meaningful engagement.

10. Diversity

Our key patient group - PWUO or people prescribed OST – are a highly marginal group in society. We will purposively sample for participant diversity in the qualitative components, with minimum quotas for gender and ethnicity informed by National Drug Treatment Monitoring Service data on PWUO demographic characteristics. We will be cognisant of diversity in our recruitment of PPI representatives. We will ask those already on board with the iHOST project, which includes men and women, to complete an anonymous online survey to gather data on their diversity characteristics of gender, age, sexual orientation, ethnicity, disability and highest educational attainment. The data will be accessible to the PPI lead and PI only. Once we have this data, we will identify the areas of diversity that we need to strengthen and ask our peers to support us in recruiting PPI representatives who will broaden that diversity and increase representation. We have a strong track record of engaging diverse and highly marginal PWUO as research participants and collaborators. Qualitative research and PPI meetings throughout the course of the project will examine how successful the intervention has been and identify whether other actions are required to support PWUO. Our research will strengthen and increase the body of research evidence available to policy makers regarding this population group. Improving health among PWUO will reduce health inequalities.

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